INSOMNIA, ILL HEALTH AND WORK DISABILITY
A LONGITUDINAL STUDY AMONG EMPLOYEES

Peija Haaramo

ACADEMIC DISSERTATION

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Unigrafia, Helsinki 2014
5.5 Measures ..................................................................................................................... 45
  5.5.1 Sleep measures ..................................................................................................... 45
  5.5.2 Prescribed medication ......................................................................................... 48
  5.5.3 Disability retirement ........................................................................................... 48
  5.5.4 Covariates ........................................................................................................... 49
5.6 Statistical methods .................................................................................................... 55

6 RESULTS ....................................................................................................................... 57
  6.1 Descriptive results ................................................................................................ 57
    6.1.1 Insomnia symptoms and sleep duration ......................................................... 57
    6.1.2 Medication and disability retirement ............................................................. 59
  6.2 Insomnia symptoms and prescribed medication .................................................... 62
    6.2.1 Insomnia symptoms and psychotropic medication ......................................... 62
    6.2.2 Insomnia symptoms and cardiovascular medication ...................................... 64
  6.3 Insomnia symptoms and disability retirement ....................................................... 67

7 DISCUSSION .................................................................................................................. 71
  7.1 Main findings ........................................................................................................ 71
  7.2 Interpretation of the findings ................................................................................. 72
    7.2.1 Insomnia and ill health .................................................................................. 72
    7.2.2 Insomnia and disability retirement ............................................................... 76
  7.3 Methodological considerations ............................................................................. 79
    7.3.1 Data sources .................................................................................................. 79
    7.3.2 The measurement of sleep .......................................................................... 80
    7.3.3 The measurement of ill health and work disability ....................................... 82
  7.4 An overall view on insomnia, ill health and work disability ................................. 84
  7.5 Conclusions and policy implications ..................................................................... 86

ACKNOWLEDGEMENTS .................................................................................................. 87
REFERENCES ................................................................................................................ 89
LIST OF ORIGINAL PUBLICATIONS


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# ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Chemical classification of medications</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
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<td>CHD</td>
<td>coronary heart disease</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
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<td>CVD</td>
<td>cardiovascular disease</td>
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<tr>
<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, 4th Edition</td>
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<tr>
<td>HDL</td>
<td>high density lipoprotein</td>
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<td>HHS</td>
<td>the Helsinki Health Study</td>
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<td>HR</td>
<td>hazard ratio</td>
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<td>ICD-10</td>
<td>International Classification of Diseases, 10th Revision</td>
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<td>JSQ</td>
<td>Jenkins Sleep Questionnaire</td>
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<td>MET</td>
<td>Metabolic Equivalent</td>
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<td>OR</td>
<td>odds ratio</td>
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<td>SDB</td>
<td>sleep-disordered breathing</td>
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<td>SEP</td>
<td>socioeconomic position</td>
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<td>WHO</td>
<td>World Health Organization</td>
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“Sleep is that golden chain that ties health and our bodies together.”

(Thomas Dekker, 1572–1632, “Patient Grissel”)
ABSTRACT

Insomnia is the most common sleep disturbance and a notable public health problem. Around one third of the working-aged population has at least occasional symptoms, and one tenth has chronic insomnia. Previous studies report associations of insomnia with ill health and work disability. However, there is still a lack of longitudinal research, and especially of studies using register-based outcomes. The aim in this study was to examine the associations of insomnia with subsequent mental ill health, cardiovascular risk factors and disability retirement in a cohort of middle-aged employees by means of longitudinally linked survey and register data.

This study is part of the Helsinki Health Study, which is a longitudinal cohort study set up to examine health, functional abilities and well-being among middle-aged and ageing employees of the City of Helsinki, Finland. The baseline surveys were conducted by means of postal questionnaires during 2000–2002 among 40–60-year-old employees (respondents N=8,960, response rate 67%, 80% women). The survey data on participants consenting to register-linkage was linked with data on prescribed reimbursed medication obtained from the Social Insurance Institution of Finland, and with data on disability retirement obtained from the Finnish Centre for Pensions (consenters N=6,606, 74%). Psychotropic and cardiovascular medication were used as outcome indicators of mental and physical health, and disability retirement as an indication of work disability. The register data in question were from the years 1995–2010.

Data on sleep and several factors potentially associated with it were collected in the baseline survey. Insomnia symptoms during the previous four weeks, in other words difficulties falling asleep, difficulties staying asleep and non-restorative sleep, were measured, alongside average sleep duration. Socio-demographic factors, physical and psychosocial working conditions, previous health and health behaviours were adjusted for in the examination. Logistic regression and Cox proportional hazards models were used for the statistical analyses.

Insomnia symptoms were found to be consistently associated with subsequent ill health and work disability. The associations were especially strong for mental ill health, but also clear for the key cardiovascular risk factors, that is hypertension and dyslipidemia. Associations were also found between insomnia symptoms and subsequent disability retirement on any grounds, as well as due to musculoskeletal diseases or mental disorders. Even more rarely experienced insomnia symptoms increased the risk of subsequent medication and disability retirement, but the risks were strongest among those with frequent symptoms. The associations were, in the main, similar among women and men. A large number of potential confounders were adjusted for in the examination, but the associations remained.
The results of the study indicate that insomnia is a notable risk factor for mental and cardiovascular ill health and work disability. It is a problem not only for those who suffer personally from it, but also for their families and employers, and the economy. The societal costs include increased utilization of healthcare services in terms of medication and early disability retirement. There is thus a need for the better recognition and treatment of insomnia symptoms in primary and occupational healthcare. Preventing the symptoms from turning chronic might help to reduce the extent of chronic disease and severe work disability associated with insomnia.
TIIVISTELMÄ

Unettomuuden yhteys terveyteen ja työkykyyn: seurantatutkimus työntekijöiden keskuudessa


Tutkimuksessa havaittiin unettomuusoireiden olevan johdonmukaisesti yhteydessä myöhempään terveyteen ja työkykyyn. Unettomuusoireilla oli erityisen voimakas yhteys mielenterveysongelmiksi, mutta yhteydet olivat selkeät myös sydäntautien keskeisiin riskitekijöihin eli korkeaan verenpaineeseen ja veren rasvaaineenvaihdunnan häiriöihin lääkekoestojen perusteella. Samoin unettomuusoireilla todettiin selkeitä yhteyksiä myöhemiin työkyvyttömyyseläkkeisiin, sekä kaikkiin.

1 INTRODUCTION

We spend approximately one third of our lives asleep. The fact that nature has invested so much time in sleep suggests that it must be something of great value and serve important functions. Whether sleep in relation to health is mainly a cause, a consequence or a symptom has been a matter of considerable debate (Marmot, 2010). In any case, sleep has been found to affect various areas of health and functioning. Different types of sleep disturbances may seriously jeopardize these functions.

Sleep and its health effects have sparked interest since the dawn of recorded history (Barbera, 2008; Dement, 2011). However, the epidemiological study of sleep and its health consequences dates back just a few decades. A US study conducted in the 1960s with a view to identifying risk factors for key physical complaints was the first to note a U-shaped association between sleep duration and mortality, as short and long sleepers had the highest risks (Hammond, 1964). This finding has since been confirmed in numerous studies (Cappuccio et al., 2010a; Ferrie et al., 2010). One of the first epidemiological studies focusing on sleep disturbances was carried out at the end of the 1970s in the US (Bixler et al., 1979). Epidemiological data on sleep have been collected in Finland at least since the beginning of the 1970s in connection with wide-ranging population-based health surveys (Kronholm et al., 2008). The first Finnish epidemiological studies focusing on sleep date back to the early 1980s (see e.g., Partinen et al., 1984; Urponen et al., 1988), having been preceded by some clinical studies (Kiianmaa and Fuxe, 1977). At first the emphasis of these studies, both in Finland and internationally, was on the effects of sleep duration, but over the time it has broadened to cover other areas, too.

Interest in the epidemiological study of sleep and its causes and consequences has grown steadily during the last fifty years (Ferrie et al., 2011), due at least in part to the fact that sleep disturbances are highly prevalent. The most common disturbance is insomnia. Insomnia symptoms are estimated to affect around one third of the population in affluent societies, and may be more prevalent in Finland than in other parts of Europe (Ohayon and Partinen, 2002). Possible reasons for this include the high prevalence of substance-induced sleep disorders in the Finnish population, as well as the seasonality-related circadian rhythm disorders that are also prevalent in the other Nordic countries. Trends over more than three decades suggest only a slight decrease in sleep duration, but a more substantial increase in occasional insomnia symptoms, especially among the working-aged population (Kronholm et al., 2008; Bin et al., 2012; Calem et al., 2012). Explanations for the deterioration in the quality of sleep have been sought from the structural changes in society and the demands of the modern “24/7 societies” that affect the natural sleep-wake rhythms of individuals (Kronholm, 2011). More specifically, these changes comprise work-time patterns that are becoming more diversified, flexible and irregular (e.g., shift work);
the overall changing nature of work attributable to digital technology in particular; extended working hours and higher levels of stress; growing work and family demands; and life-style changes including increased time spent watching television and using the Internet, lower levels of physical activity and an increase in overweight (Metlaine et al., 2005; Härmä, 2006; Kronholm et al., 2008). Insomnia, in turn, has widespread effects on both the individual and the societal level. It contributes to accidents both in traffic and at work, it imposes work limitations, increases absenteeism and affects the overall quality of life (Léger and Bayon, 2010). All in all, the societal costs are estimated to be considerable.

On the individual level there is increasing awareness of the consequences of insomnia for ill health and work disability (Ferrie et al., 2011). There is also a close interrelationship with mental health (Ohayon, 2002). Mental disorders are prevalent, and in addition to causing substantial individual suffering they have considerable public-health implications, particularly among the working-aged (Pulkki-Råback et al., 2012), and often lead to impaired functioning and work disability. Treatment by means of psychotherapy and medication also adds to the societal costs of these disorders.

In the area of physical health insomnia has been associated with numerous conditions, including metabolic syndrome, diabetes and cardiovascular disease (CVD) (Cappuccio et al., 2010b; Troxel et al., 2010; Sofi et al., 2014). CVD is a notable public health problem, and is the leading cause of death both in Finland and globally: among working-aged Finns it accounts for almost half of all deaths (National Institute for Health and Welfare, 2014). In addition, every year there are around 20,000 other cardiovascular events in the Finnish working-aged population, the majority of them among men. Hypertension and dyslipidemia are common conditions, and are among the key modifiable risk factors of CVD (Graham et al., 2007). As a secondary CVD prevention measure the pharmaceutical treatment of hypertension and dyslipidemia is highly prevalent among the working-aged, thereby further increasing societal costs.

Severely deteriorated health combined with a declining ability to function and unfavourable working conditions may result in work disability, which if severe and long-term or permanent may lead to disability retirement. The two main causes of disability retirement in Finland are musculoskeletal diseases and mental disorders, both accounting for roughly one third of retirement on such grounds (Finnish Centre for Pensions and Keva, 2013). As the population ages, society faces increasing challenges in its attempts to counteract early retirement due to disability and to keep people healthy and fit for work for longer. Although studies examining the association between insomnia and work disability are scarce, the few that have been carried out show evidence of associations with different work disability outcomes (Sivertsen et al., 2009d; Rahkonen et al., 2012).
In addition to the one third of the day that should be dedicated to sleep, another third is typically spent at work or on corresponding activities: this underlines the importance of studying the factors that potentially threaten work ability. The purpose of this study was to investigate the associations of insomnia with subsequent ill health and work disability among middle-aged and ageing employees. It was carried out between 2000 and 2010 among the Helsinki Health Study cohort of 40–60-year-old Finnish municipal employees, including both women and men (Lahelma et al., 2013). The Helsinki Health Study aims to give a comprehensive picture of health, functional abilities and wellbeing among employees of the City of Helsinki, which is the largest employer in Finland encompassing a wide range of non-manual and manual occupations, with varying working conditions.

The harmful effects of insomnia are strong on the working-aged given its high prevalence among the middle-aged and its consequences on health and work ability (Léger and Bayon, 2010). The Helsinki Health Study covers an employee cohort, which makes the examination of disability retirement highly relevant, alongside the study of mental and cardiovascular ill health and their risk factors, all of which are prevalent in this age group. There is a need to deepen understanding of insomnia and its effects, and to find new ways of supporting the ageing working population’s health, wellbeing and work ability. The main aim of this study is thus to enhance understanding of the impact of insomnia on ill health and work disability.
2 THE CONCEPTS OF THE STUDY

The key concepts of this study are sleep, ill health and work disability. Sociological perspectives on health stress its relativity, and focus on the ability to function in determining health and illness. This approach is evident in the writings of the classic medical sociologist Talcott Parsons, who defined illness as “a state of disturbance in the ‘normal’ functioning of the total human individual, including both the state of the organism as a biological system and of his personal and social adjustments” (Parsons, 1951). This multifaceted view on health advocated by Parsons and others still holds: more recently medical sociologist Mike Bury defined health as “both ‘attribute’ and ‘relation’, simultaneously involving biological and social factors. This suggests a dynamic view of health and illness, changing across biographical and historical time” (Bury, 2005). Health thus always exists in the context of the whole life sphere of an individual, and functioning plays an important role in this relationship. It is particularly relevant in the case of disability due to illness. Poor sleep may seriously undermine both health and functioning, thus increasing the risk of later disability.

2.1 Sleep

Sleep can be considered from varying perspectives and thus is of interest in many different fields of science – it has been described as a biological, physiological, neurological, psychological, behavioural, social and cultural phenomenon, for example. Consequently, there are also many different interpretations of the fundamental purpose sleep serves. Three main theories address the physiological purpose of sleep (Porkka-Heiskanen et al., 2013). The first one focuses on energy conservation: energy metabolism is significantly reduced during sleep because both body temperature and caloric demand are lower than during wakefulness. Second, restorative theory posits that sleep provides an opportunity for the body to repair and rejuvenate itself. This theory is supported by findings indicating that many of the major restorative functions in the body, such as tissue repair, muscle growth, protein synthesis and growth hormone release occur mostly, or in some cases only, during sleep. Several studies on both humans as well as animals have shown how sleep loss (i.e. not getting enough sleep) affects the immune function, rendering the body more vulnerable to disease. Third, sleep affects brain plasticity and memory consolidation, meaning that it is associated with changes in the structure and organization of the brain. It is also thought to help in processing and re-organizing memories and information, thus affecting learning and the carrying out of cognitive tasks in particular (Alhola and Polo-Kantola, 2007).

Aside from the effects sleep has on memory and cognition, psychological theories highlight its reciprocal association with mood and emotions, also affecting social relations (Baglioni et al., 2010). Sociological studies show evidence of its effects on
the daily living and performance of individuals in working life (Williams et al., 2010), for example. Sleep also appears to shape social roles, especially regarding gender. An example of the social effects of gender on sleep is the higher likelihood among women than among men to subjugate their own sleep needs to those of their family, such as providing care for young children at night even after returning to employment after having a baby. Some researchers refer to this as “a fourth nighttime shift” (Venn et al., 2008). From the sociological perspective sleep is perceived as constituting an important although hidden dimension of (potential) social and health inequalities. Impaired health and functioning are possible mediators between sleep and its wider social effects on the one hand, and on the other hand socioeconomic factors are likely to play an important role in the sleep differences noted between different socio-demographic subgroups (Arber et al., 2009; Arber, 2012).

Regardless of the still widely disputed purpose of sleep, it is generally agreed that it is fundamental for the life of all human beings. Whatever its ultimate purpose, for the most part it fulfils it admirably. However, it may also be threatened by different disturbances and disorders such as obstructive sleep apnoea, restless legs syndrome or parasomnias (Partinen and Hublin, 2011). This study focuses on the most prevalent of the sleep disorders, insomnia.

2.1.1 Insomnia

The main symptoms of insomnia included in the diagnostic criteria are difficulty initiating or maintaining sleep, or non-restorative sleep, lasting for at least one month and causing distress and reduced performance during wakefulness (World Health Organization, 2004; American Psychiatric Association, 2000). Depending on the duration of the symptoms, insomnia has been classified as transient, acute or chronic (Yang et al., 2013). It could also be described as primary or secondary. In the case of primary insomnia the symptoms cannot be directly linked to other health conditions or problems, whereas secondary insomnia refers to symptoms caused by something else – disease, pain, medication or substance use. Subjectively perceived main reasons for experiencing insomnia symptoms include worry and illness or discomfort, alongside noise, work schedules (e.g., shift work) and caring duties (Calem et al., 2012). The symptoms are clearly associated with different kinds of impairment in daytime functioning (Ustinov et al., 2010).

Insomnia is common, the prevalence of occasional symptoms being around 30 per cent, and of clinical and chronic insomnia around 10 per cent among working-aged adults in affluent societies (Partinen and Hublin, 2011). The symptoms vary in severity as well as in frequency and duration. Research on insomnia has long been dominated by rather clinical and biological views, and there have been fewer epidemiological studies.
The terminology concerning insomnia is not fully established. Several other terms are used in epidemiological studies somewhat interchangeably, such as sleep problems, sleep or insomnia complaints, insomnolence, sleeplessness, disturbed sleep and the inability to sleep. Difficulties initiating or maintaining sleep, and non-restorative sleep are essential symptoms of insomnia, but not specific or unique to it. Similar symptoms could be related to other sleep disturbances as well, insomnia thus partly overlapping them (Trophy, 2011).

2.1.2 Sleep duration

Alongside quality, of which insomnia is one possible indicator, quantity is another key dimension of sleep. There is wide individual variation in the duration of sleep (Ferrara and De Gennaro, 2001), which could be for biological, social or health-related reasons. On the biological level, some people have a physiological need for longer sleep whereas others manage on shorter-than-average amounts. Social circumstances also affect sleep duration in many ways, through work schedules, the effect of having small children in the household on nightly sleep, the sleeping habits of one’s spouse, or the late-night use of television and computers, for example (Kronholm et al., 2008). Different health conditions may have both acute and long-term effects on sleep. Thus, not only does sleep duration vary among individuals, there is also variation over the life course attributable to several causes. Social explanations for individual sleep duration in particular at least partly reflect voluntary choices that, as such, are modifiable, whereas there is less individual power of decision over the biological and health-related causes (Kronholm et al., 2008).

Most people sleep between seven and eight hours a night. Data representative of the adult Finnish population indicates a proportion of around 70 per cent, whereas about 20 per cent sleep for six hours or less, and around 10 per cent for nine hours or more (Lallukka et al., 2012b). In terms of the quantity of sleep it cannot simply be stated that the more the better. One reason for this is the above-mentioned differences in individuals’ need for sleep.

2.1.3 The interrelation of insomnia and sleep duration

Although sleep quality and quantity are closely related attributes, they should by no means be considered coincident or interchangeable indicators. These two characteristics are associated, but their relationship is not linear (Sivertsen et al., 2009d). Insomnia symptoms are more common among ‘short’ and ‘long’ sleepers (Grandner and Kripke, 2004). It has been found in earlier studies that insomnia and sleep duration are individual indicators with divergent effects on health and functioning (Sivertsen et al., 2009d). Nevertheless, because of their close interrelation, care must be taken when these sleep indicators are considered
together – such as adjusting for sleep duration while examining the effects of insomnia: it has been suggested that the close associations may potentially cause the partial neutralization of each other’s effects in the analyses (Hublin et al., 2007). Otherwise it is well justified to take both of these key dimensions into consideration when examining health-related outcomes, for example, in order to obtain a more extensive overall view of the effects of sleep.

2.2 Ill health

Of the various areas of health this study focuses on the key chronic diseases, both somatic and mental.

2.2.1 Mental ill health

A mental disorder is defined as a “clinically significant behavioural or psychological syndrome or pattern that occurs in an individual [which] is associated with present distress (...) or disability (...) or with a significant increased risk of suffering” (American Psychiatric Association, 2000). The most prevalent mental disorders in the Finnish working-aged population are depression, anxiety and alcohol use disorders. The prevalence of each of these disorders according to data representative of the adult Finnish population is between five and seven per cent (Pulkki-Råback et al., 2012). Comorbidity between the disorders is high.

The management of mental disorders involves psychological treatment such as psychotherapy, as well as pharmacological treatment with psychotropic medication. Psychotropic medication comprises a diverse group of chemical substances that mainly affect the central nervous system and thus have an impact on mood and behaviour (Guidelines for ATC Classification and DDD Assignment, 2011). The most commonly used psychotropic medications are psycholeptics and psychoanaleptics, roughly defined as having a calming or an arousing effect, respectively.

2.2.2 Cardiovascular risk factors

Hypertension is a chronic condition manifested as elevated blood pressure in the arteries. It affects more than half of working-aged Finnish men, as well as one third of women of a similar age (Kastarinen et al., 2009). Dyslipidemia indicates abnormal levels of lipids (e.g., cholesterol) in the blood. Cholesterol levels in the Finnish working-aged population are above the publicly recommended figures among about 60 per cent of both women and men (Vartiainen et al., 2012). Although recent decades saw a healthy decrease in both blood pressure and cholesterol levels, it
seems that this positive trend stagnated during the 2000s (Vartiainen et al., 2010; Vartiainen et al., 2012). This has been attributed to population-level changes in diet, especially in saturated-fat intake, as well as increasing alcohol consumption, increasing obesity, and decreasing total physical activity (Vartiainen et al., 2010).

Cardiovascular disease (CVD) is a class of diseases that involve the heart or blood vessels. Among the key modifiable risk factors are hypertension and dyslipidemia (Graham et al., 2007), and other major risk factors include age, gender, prior cardiovascular history, diabetes and smoking. The most common CVDs are coronary heart disease, heart failure and stroke. The prevalence of major CVD is rather modest among those of working age, but its incidence increases with age (Driver et al., 2008). However, hypertension and dyslipidemia are common among the middle-aged, making them a major target in the prevention of later CVD. The examination of cardiovascular risk factors is of particular relevance in Finland, where coronary heart disease morbidity and mortality have been particularly high (Vartiainen et al., 2010).

The early detection and treatment of hypertension and dyslipidemia are essential in the secondary prevention of CVD. The main elements of the treatment comprise changes in health behaviours including smoking, eating habits, alcohol consumption and physical exercise, as well as medication in more severe cases. The most prevalent groups of cardiovascular medication aim to lower the blood pressure and affect the blood lipid levels, or have a thinning effect on the blood (Finnish Medicines Agency Fimea and Social Insurance Institution, 2012).

2.3 Work disability

Alongside the study of ill health per se one could widen the focus to include functioning that is at least partly impaired on account of it. These factors are merged in the concept of work disability, on which research has been comparatively prevalent in the Scandinavian countries. At least three main perspectives on work ability and disability are distinguishable (Gould et al., 2008). First, the medical view is a traditional model of work ability as an individual characteristic, and as such part of the health and functional capacity of the individual. Work disability is thus comprehended as deterioration in health. Second, the balance model, which is used extensively in the social insurance sector, builds on the balance between human resources and work demands, and work disability results from a disturbance in this equilibrium. Third, according to the multidimensional model, work ability is an outcome of the system comprising the individual, the work and the working environment. Work disability entails some sort of interference in this system.

If work disability turns out to be severe and long lasting, or even permanent, it may lead to sickness absence and eventually to disability retirement. The evaluation of
work disability in Finland is based on the individual’s health and ability to function, and the working conditions. Disability retirement is a burdensome economic and public health concern as it causes a high number of premature exits from the workforce: approximately 25,000 persons per year retire on these grounds in Finland (Finnish Centre for Pensions and Keva, 2013). The two most common causes of disability retirement are musculoskeletal diseases and mental disorders, which together account for two-thirds of the cases. Other common causes include CVD and cancer.

### 2.4 The associations of insomnia with ill health and work disability

There are longitudinal interrelationships among insomnia, ill health, and work disability, with insomnia preceding and predicting health-related outcomes, as well as ensuing from and being co-morbid with them (Sivertsen et al., 2009b; Sivertsen et al., 2013). Insomnia may have serious and long-lasting effects on mental and physical health and functioning, and these processes may further lead to work disability. According to findings from previous studies various factors such as health behaviours, socio-demographic factors and working conditions are likely to affect the associations of insomnia with health and work disability (Ohayon, 2002; Phillips and Mannino, 2005; Graham et al., 2007; Colman et al., 2008; Arber et al., 2009; Lallukka et al., 2010; Laaksonen et al., 2012; Lallukka et al., 2012b; Sivertsen et al., 2013). Insomnia, mental disorders, cardiovascular risk factors and disability retirement are all prevalent, and thus are key public health concerns warranting the epidemiological study of their associations. These associations are further elaborated in this study, in which insomnia is examined as a predictor of subsequent ill health and work disability.
3 A REVIEW OF THE LITERATURE

The focus of this study is on the associations of insomnia with mental and physical ill health and work disability. This literature review covers epidemiological studies examining the associations of insomnia with health and work disability outcomes within the study context. Chapter 3.1 reviews studies on associations of insomnia with mental health, focusing more deeply on findings concerning psychotropic medication. Attention turns to associations with hypertension and dyslipidemia in Chapter 3.2, again focusing on studies using medication outcomes. Chapter 3.3 encompasses studies on associations of insomnia with work disability, with an emphasis on disability retirement. The studies analysed in Chapter 3.4 concern the joint associations of insomnia and sleep duration with different health-related outcomes. Finally, Chapter 3.5 briefly summarises previous findings and points out what knowledge is still lacking in this area.

The studies selected for the literature review are described more in detail in Tables 1–3, included in the text. The following selection criteria were set to ensure reasonable comparison with the present study. The main criterion limited the search to epidemiological studies examining the associations of insomnia symptoms with the above-mentioned outcomes, written in English. Given the aim to explore the associations of insomnia symptoms with subsequent health-related outcomes the review focused on longitudinal studies. Both subjective and objective measurements of exposure and outcome were accepted, in other words the gathering of data via postal questionnaires, personal interviews, registers or clinical measurements. The studies to be included were not limited in terms of sample size. Nor were non-response and attrition rates used as limitation criteria: the response rates are included in the tables, if they were reported. The study subjects were adult populations, preferably but not exclusively working-aged, but not elderly. Studies on general populations rather than specific patient cohorts were included. No geographical limitations were imposed, although the focus was on studies carried out in developed countries, in other words areas that best enabled comparison with the Finnish data used in the present study. It was not considered necessary to impose a time limit given that the oldest studies meeting the above criteria dated back less than twenty years.

The tables included in this review summarise the studies and give the key details, whereas the corresponding text summarises and generalises the respective findings. The information in the tables includes the outcomes of the selected studies, the measures of insomnia symptoms used, and the adjusted main results. The terminology used in the different studies is harmonised, especially concerning the measures of insomnia symptoms, and the various measures were scrutinised to verify that the phenomena being compared were substantially similar.
3.1 Insomnia symptoms and mental ill health

Insomnia symptoms are associated with a variety of mental disorders, and are also included in the diagnostic criteria in many cases (Ohayon, 2002; Abad and Guilleminault, 2005; Benca, 2011; American Psychiatric Association, 2000). Associations have been found with mood disorders, anxiety disorders, psychosis, disorders related to substance abuse, eating disorders, and attention-deficit/hyperactivity disorders. Nevertheless, insomnia should not be regarded only as symptomatic of mental disorders because the symptoms may also occur as a primary condition with no mental or somatic disorders present (Harvey, 2001). The order in which they appear – either insomnia symptoms or mental disorders first – is not unambiguous. According to the traditional view, insomnia is mainly a symptom of various mental disorders and thus follows the emergence of these disorders or emerges simultaneously and comorbid with them. Recent research shows evidence of a reverse order of incidence of these symptoms, and the theory that insomnia symptoms often precede and predict depression in particular (Ohayon and Roth, 2003; Tsuno et al., 2005; Baglioni et al., 2011a), but also other mental disorders has attracted support in line with the evidence (Harvey, 2001; Sivertsen et al., 2013).

The tendency is to use self-report outcome measures in examining the associations of insomnia symptoms with mental health. However, psychotropic medication is another worthy indicator of mental disorders, being generally intended for their treatment (Guidelines for ATC Classification and DDD Assignment, 2011). It is also an objective indicator if prescribed by a physician based on a medical examination, and the data is obtained from registers. The associations between insomnia symptoms and the subsequent use of hypnotics, prescribed mainly for the treatment of insomnia, have been more thoroughly mapped and generally found strong (Sivertsen et al., 2009a). Studies on the associations of insomnia with other types of psychotropic medication are scarcer, especially ones that are longitudinal in design.

It has been shown in previous, mainly cross-sectional studies that people who suffer from insomnia use more psychotropic medication than those who do not suffer (Ohayon and Caulet, 1996; Simon and VonKorff, 1997; Léger et al., 2002; Sivertsen et al., 2009a). A few previous longitudinal studies included psychotropic medication among their indicators (Simon and VonKorff, 1997; Hayward et al., 2010; Salo et al., 2012a), and these are described in more detail in Table 1. All of them examined wider mental-healthcare utilization among those with insomnia, thus not focusing solely on psychotropic medication. A small-scale US study from the 1990s on patients in primary care examined the prevalence and treatment of insomnia, functional impairment and healthcare utilization among people with insomnia over a three-month follow-up period (Simon and VonKorff, 1997). Another study on a patient cohort was conducted in the UK among general-practice patients (Hayward et al., 2010), the main interest being the extent to which people with insomnia seek
Table 1. Longitudinal studies on the associations of insomnia symptoms with subsequent psychotropic medication

<table>
<thead>
<tr>
<th>Reference</th>
<th>Setting</th>
<th>Study design</th>
<th>Time period</th>
<th>N, women (W%), response rate (RR%)</th>
<th>Insomnia symptoms measurement</th>
<th>Outcome(s)</th>
<th>Adjusted covariates</th>
<th>Main statistical method</th>
<th>Adjusted results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon and VonKorff, 1997</td>
<td>USA, patients in primary-care clinics, 18–65 years</td>
<td>Follow-up 3 months, survey and interview</td>
<td>NR</td>
<td>327 W 70% RR 61%</td>
<td>Composite International Diagnostic Interview (6 items, 2 categories in the analyses)</td>
<td>Self-reported psychotropic medication combined with health-plan data: any, anti-depressants, benzodiazepines</td>
<td>Age, gender, chronic diseases, depression</td>
<td>Weighted prevalence rates, means with standard deviations and standard errors</td>
<td>Insomnia symptoms were associated with excess healthcare utilization including psychotropic medication.</td>
</tr>
<tr>
<td>Hayward et al., 2010</td>
<td>UK, patients of five general practices, 18–96 years</td>
<td>Follow-up 1 year, postal survey linked with primary-care records</td>
<td>2000–2001</td>
<td>2,192 W 55% RR 56% (of which 82% consented to record review)</td>
<td>Self-reported insomnia symptoms, Jenkins Sleep Questionnaire (4 items, 2 categories in the analyses, also separate symptoms)</td>
<td>Data from primary-care records, prescribed psychotropic medication: anti-depressants, hypnotics, anxiolytics</td>
<td>Age, gender, SEP, pain, depression, anxiety (+ other insomnia symptoms when examining symptoms separately)</td>
<td>Logistic regression analysis</td>
<td>Psychotropic medication was more prevalent among people with insomnia than among those without. When adjusted, medication was statistically significantly more likely among those with insomnia only in the case of hypnotics, OR 3.73 (95% CI 1.76–7.88).</td>
</tr>
<tr>
<td>Reference</td>
<td>Setting</td>
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<td>Time period</td>
<td>N, women (W%), response rate (RR%)</td>
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<tr>
<td>Salo et al., 2012a</td>
<td>Finland, the Finnish Public Sector Study, municipal employees, 19–70 years</td>
<td>Mean follow-up 3.3 years, questionnaire survey (excluded those with baseline depression or sleep apnoea)</td>
<td>Baseline years 2000–2002 and 2004</td>
<td>40,791 W 81% RR 74%</td>
<td>Self-reported insomnia symptoms, Jenkins Sleep Questionnaire (4 items, 3 categories in the analyses, also separate symptoms)</td>
<td>Data from national registers, combined measure of antidepressant medication, psychotherapy and hospitalization</td>
<td>Age, gender, SEP, night/shift work, alcohol consumption, smoking, physical activity, obesity, physical and mental health (psychological distress, anxiety), use of painkillers</td>
<td>Cox proportional hazards model</td>
<td>Insomnia symptoms were associated with an increased risk of incident treatment for depression, including psychotropic medication. Moderate insomnia symptoms HR 1.46 (95% CI 1.29–1.64), severe HR 1.64 (95% CI 1.44–1.86).</td>
</tr>
</tbody>
</table>

CI = confidence interval; HR = hazard ratio; NR = not reported; SEP = socioeconomic position
primary care for their symptoms or mood disorders, and how this might be associated with the presence of anxiety or depression. A recent Finnish study among municipal and hospital employees examined insomnia symptoms as a predictor of subsequent treatment for depression, including antidepressant medication, psychotherapy and hospitalization (Salo et al., 2012a). The data on medication were retrieved in these studies from self-reports (Simon and VonKorff, 1997), primary-care records (Hayward et al., 2010) and a national register (Salo et al., 2012a). Insomnia symptoms were measured by means of self-report questionnaires in all but one smaller study, which used diagnostic interviews (Simon and VonKorff, 1997). Only the Finnish study used a three-category measure of insomnia symptoms, the other ones relying on dichotomous measures in their analyses.

Previous studies report a general association between insomnia symptoms and the increased utilization of mental-healthcare services, including psychotropic medication (Simon and VonKorff, 1997; Hayward et al., 2010; Salo et al., 2012a) (Table 1). Subsequent psychotropic medication was also more prevalent among those with insomnia symptoms. One of the studies identified an association between insomnia symptoms and subsequent incident treatment for depression during a follow-up of three years (Salo et al., 2012a). After extensive adjustments it turned out that the treatment was more likely among those with severe insomnia symptoms than among those without such symptoms. Moreover, it was found in another study that, over a one-year follow-up, insomnia symptoms were associated only with subsequent hypnotics, the reference group being those with no self-reported symptoms (Hayward et al., 2010).

Previous longitudinal studies on the associations of insomnia symptoms with subsequent treatment for mental disorders take into account several factors associated with insomnia and mental health, thus potentially affecting the associations under investigation (Simon and VonKorff, 1997; Hayward et al., 2010; Salo et al., 2012a) (Table 1). These factors include socio-demographic and work-related factors, health behaviours such as alcohol consumption, smoking and physical activity, and previous mental and physical health. The associations were not examined separately among women and men. Mental health at or before baseline is taken into account, not in the form of previous psychotropic medication, but rather through the adjustment or stratification of the analyses by baseline mental disorders.

In sum, previous longitudinal studies report that subsequent treatment for mental disorders, including psychotropic medication, is more likely among those with insomnia symptoms than among those with no symptoms. Overall, these results are in line with findings reported in the above-mentioned studies on the associations between insomnia symptoms and different mental-health indicators. The strength of the associations varied between the studies, as did the types of treatment or medication for which the associations were found.
3.2 Insomnia symptoms, hypertension and dyslipidemia

Previous studies generally report associations between insomnia symptoms and different cardiovascular outcomes (Schwartz et al., 1999). There is growing support for the view that insomnia is a causal factor in the development of cardiovascular disease, independently of classic coronary risk factors (Quan, 2009; Spiegelhalder et al., 2010). Thus it has been suggested that sleep disturbances should be counted among the top 10 potentially modifiable cardiovascular risk factors (Redline and Foody, 2011).

This study focuses on hypertension and dyslipidemia, the key cardiovascular risk factors. There is evidence from previous studies of associations between insomnia as well as other sleep disturbances, and subsequent hypertension in particular (Calhoun and Harding, 2010). It was concluded in quite a recent meta-analysis of previous studies that both insomnia symptoms and sleep duration were associated with hypertension incidence (Meng et al., 2013). Some previous longitudinal studies examining the association of insomnia symptoms with hypertension relied on self-reported data on the outcome (Gangwisch et al., 2010; Rod et al., 2011): prescribed medication for hypertension or dyslipidemia would probably be a more reliable indicator of these conditions, especially if obtained from a register of medications.

Some previous studies examine the associations of insomnia symptoms with subsequent medication for hypertension and dyslipidemia. Associations with an increased risk of cardiovascular medication have been found in cross-sectional studies, although the use of medication was self-reported in these cases (Léger et al., 2002; Sivertsen et al., 2009a). The above-mentioned associations are investigated in a few longitudinal studies (Suka et al., 2003; Phillips and Mannino, 2007; Fernandez-Mendoza et al., 2012). All these studies are listed in Table 2. Hypertension incidence was the main interest in most of them, although one also examined the risk of CVD (Phillips and Mannino, 2007), and another metabolic syndrome and its component factors (Troxel et al., 2010): the latter study is the only longitudinal study also to focus on dyslipidemia medication. All the reviewed studies only examined healthy subjects, in other words excluded those with hypertension, CVD or metabolic syndrome at baseline. Medication constitutes part of the outcome in the studies, most of which combine self-reported or hospital-records-based data on medication with blood-pressure measurements, or laboratory blood samples in the case of dyslipidemia. Insomnia symptoms are self-reported in all of them, too, and in most cases are measured only once. One study focuses on their persistence, thus measuring them several times over the follow-up (Suka et al., 2003). Most previous studies used a dichotomous measure in their analyses, with the exception of one that applied a three-category measure on the duration of the symptoms (Fernandez-Mendoza et al., 2012).
**Table 2. Longitudinal studies on the associations of insomnia symptoms with subsequent medication for hypertension and dyslipidemia**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Setting</th>
<th>Study design</th>
<th>Time period</th>
<th>N, women (W%), response rate (RR%)</th>
<th>Insomnia symptoms measurement</th>
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<th>Main statistical method</th>
<th>Adjusted results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suka et al., 2003</td>
<td>Japan, male employees of a telecommunica-</td>
<td>Follow-up 4 years, health examinations and questionnaires (excluded those</td>
<td>1994–1998</td>
<td>6,192 W 0% RR NR</td>
<td>Self-reported insomnia symptoms (3 items, 2 categories in the analyses, separate symptoms)</td>
<td>Measured high blood pressure or hypertension medication</td>
<td>Age, job stress, alcohol consumption, smoking, BMI, diabetes, other insomnia symptoms</td>
<td>Logistic regression analysis</td>
<td>Persistent insomnia symptoms (reporting at all time points vs. never reporting) were associated with subsequent hypertension. Difficulties falling asleep: OR 1.96 (95% CI 1.42–2.70), difficulties staying asleep OR 1.88 (95% CI 1.45–2.45).</td>
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<td></td>
<td>tions company, 40–55 years</td>
<td>(excluded those with hypertension at baseline)</td>
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<tr>
<td>Phillips and</td>
<td>USA, the Atherosclerosis Risk in Communities</td>
<td>Follow-up 6 years, health examinations, interviews, and questionnaires</td>
<td>1990–1998</td>
<td>8,757 W 55% RR NR</td>
<td>Self-reported insomnia symptoms, Maastricht questionnaire (3 items, 2 categories in the analyses, separate symptoms)</td>
<td>Measured high blood pressure or hypertension medication</td>
<td>Age, gender, ethnicity, education, smoking, BMI, diabetes, lung function, depression</td>
<td>Logistic regression analysis</td>
<td>Complaint of either difficulty falling asleep or difficulty staying asleep predicted a slightly increased risk of hypertension, OR 1.2 (95% CI 1.03–1.3).</td>
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<tr>
<td>Mannino, 2007</td>
<td>Study, random population, 45–69 years</td>
<td>(excluded those with hypertension at baseline)</td>
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<tr>
<th>Reference</th>
<th>Setting</th>
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<th>N, women (W%), response rate (RR%)</th>
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<th>Main statistical method</th>
<th>Adjusted results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phillips et al., 2009</td>
<td>USA, the Cardiovascular Health Study, general population, 64–91 years</td>
<td>Follow-up 6 years, health examinations and interviews (excluded those with hypertension at baseline)</td>
<td>1992–1999</td>
<td>1,419 W 59% RR NR</td>
<td>Self-reported insomnia symptoms (3 items, 2 categories in the analyses, separate symptoms)</td>
<td>Measured high blood pressure or hypertension medication</td>
<td>Age, ethnicity, income, alcohol consumption, smoking, BMI, height, CHD, diabetes, lung function, oestrogen use for women (stratified by gender)</td>
<td>Poisson log-link model</td>
<td>Insomnia symptoms were not associated with subsequent hypertension, instead difficulty falling asleep was associated with decreased risk of hypertension among non-African American men, relative risk 0.47 (95% CI 0.25–0.87).</td>
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<tr>
<td>Troxel et al., 2010</td>
<td>USA, the Heart Strategies Concentrating on Risk Evaluation study, community-based sample, 45–74 years</td>
<td>Follow-up 3 years, health examinations and questionnaires (excluded those with metabolic syndrome at baseline)</td>
<td>NR 812 W 67% RR NR</td>
<td>Self-reported insomnia symptoms, Insomnia Symptom Questionnaire (5 items, 2 categories in the analyses, also separate symptoms)</td>
<td>Hypertension: measured high blood pressure or hypertension medication</td>
<td>Dyslipidemia: laboratory blood samples</td>
<td>Age, gender, ethnicity, marital status, alcohol consumption, smoking, sedentary lifestyle, depression, study randomization assignment</td>
<td>Logistic regression analysis</td>
<td>Difficulties falling asleep (DFA) and non-restorative sleep (NRS) were associated with metabolic syndrome, but not with the factors comprising it: hypertension (DFA: OR 1.25 (95% CI 0.64–2.43); NRS: OR 1.39 (95% CI 0.78–2.48)), dyslipidemia (DFA: OR 1.11 (95% CI 0.59–2.09); NRS: OR 1.29 (95% CI 0.76–2.17)). (continues)</td>
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<tr>
<td>Reference</td>
<td>Setting</td>
<td>Study design</td>
<td>Time period</td>
<td>N, women (W%), response rate (RR%)</td>
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<tr>
<td>Fernandez-Mendoza et al., 2012</td>
<td>USA, the Penn State Cohort, random adult population, 20 years and over</td>
<td>Follow-up 7.5 years, telephone interviews, polysomnography (excluded those with hypertension at baseline)</td>
<td>NR</td>
<td>786 W 51% RR 80%</td>
<td>Self-reported insomnia symptoms (4 items, 3 categories in the analyses)</td>
<td>Self-report of receiving treatment for high blood pressure</td>
<td>Age, gender, ethnicity, alcohol consumption, smoking, caffeine use, BMI, baseline blood pressure, diabetes, SDB, depression</td>
<td>Logistic regression analysis</td>
<td>Chronic insomnia symptoms with short sleep duration (&lt;6h) were associated with subsequent hypertension, OR 3.75 (95% CI 1.58–8.95).</td>
</tr>
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</table>

BMI = body mass index; CHD = coronary heart disease; CI = confidence interval; OR = odds ratio; SDB = sleep-disordered breathing
Most previous longitudinal studies report an association between insomnia symptoms and subsequent hypertension, using data on medication (Suka et al., 2003; Phillips and Mannino, 2007; Fernandez-Mendoza et al., 2012) (Table 2). It seems from the accumulated evidence that insomnia symptoms are associated with subsequent hypertension, especially if persistent or occurring in conjunction with short sleep duration. A Japanese study on middle-aged male employees compared those with insomnia symptoms at every time point of the four-year follow-up with those reporting no symptoms at any of these points (Suka et al., 2003). Persistent symptoms were associated with subsequent hypertension, which applied to difficulties in falling asleep and in staying asleep. However, no summary measure of insomnia symptoms was used. It was found in a study of middle-aged members of the US general population that reporting difficulties in either falling asleep or staying asleep was associated with subsequent hypertension during a six-year follow-up (Phillips and Mannino, 2007). However, when these insomnia symptoms were examined in conjunction with non-restorative sleep the associations disappeared. Another more recent US study on the general adult population reported an association between long-lasting insomnia symptoms as well as short sleep duration (<6 hours) and subsequent hypertension during a follow-up of seven-and-a-half years (Fernandez-Mendoza et al., 2012): on the basis of a three-category measure of insomnia symptoms it was found that the risk of subsequent hypertension increased by the duration of insomnia symptoms.

Some previous longitudinal studies reported no associations between insomnia symptoms and subsequent cardiovascular medication (Table 2). The associations that were found concerned middle-aged populations, whereas a US study examining older subjects identified no such associations (Phillips et al., 2009). In this study difficulties falling asleep were in fact associated with a somewhat reduced risk of hypertension in some ethnic subpopulations. Furthermore, the results of the only previous study examining dyslipidemia alongside hypertension in middle-aged and ageing members of the US general population indicated that although insomnia symptoms were associated with subsequent metabolic syndrome, they did not predict any of the separate factors comprising the syndrome, in other words hypertension, dyslipidemia, or a large waist circumference (Troxel et al., 2010).

Previous longitudinal studies on the associations between insomnia symptoms and subsequent cardiovascular medication took into account other major cardiovascular risk factors (Table 2): these included socio-demographic factors such as age and ethnicity; health behaviours including alcohol consumption, smoking and BMI; and both mental and physical health, i.e. depression, diabetes, coronary heart disease, and sleep-disordered breathing as well as lung function. Gender is also a cardiovascular risk factor, although its effects vary in different age groups (Doumas et al., 2013). Only one of the reviewed studies stratified the sample by gender (Phillips et al., 2009): it revealed no significant associations of insomnia symptoms with subsequent hypertension among women, differing somewhat in this respect from
men. None of the studies took previous cardiovascular medication into account in their analyses.

In sum, most of the reviewed longitudinal studies revealed associations between insomnia symptoms and subsequent hypertension, and included medication among the outcome indicators. The only study on dyslipidemia reported no associations. With regard to hypertension these findings are in line with those reported in other studies examining the association between insomnia symptoms and cardiovascular outcomes.

3.3 Insomnia symptoms and work disability

Insomnia symptoms have generally been found to be associated with mental and physical ill health and impaired functioning. If these effects are long lasting they may lead to subsequent work disability. The key elements in the evaluation of work disability are the individual's health, ability to function and working conditions, and previous studies report associations of insomnia symptoms with all these factors (Sivertsen et al., 2009b; Lallukka et al., 2010; Ustinov et al., 2010). Several studies have identified associations between insomnia symptoms and sickness absence, an indicator of work disability (see e.g., Sivertsen et al., 2009c; Salminen et al., 2010; Åkerstedt et al., 2010; Rahkonen et al., 2012). It was found in a Finnish study, for example, that repeatedly measured and thus persistent symptoms were associated with sickness absence over a follow-up of 12 months (Salo et al., 2012b). In another recent study insomnia symptoms and short sleep duration were associated with work functioning and sickness absence, especially among participants suffering from depression or anxiety (van Mill et al., 2013).

Disability retirement is an indicator of even more severe and often permanent work disability. There are no previous cross-sectional studies focusing on the associations of insomnia symptoms with disability retirement. However, a Norwegian study examined insomnia symptoms and several mental and physical health indicators seven years before and seven years after the decision to grant disability retirement (Øverland et al., 2008a): the analysis revealed an inverse U-shaped trend, the prevalence of insomnia symptoms being highest at the time of retirement, compared with before and after. In contrast with the other health indicators, the prevalence of insomnia symptoms increased again later on during the follow-up.

A few previous longitudinal studies have examined the associations of insomnia symptoms with subsequent disability retirement (see Table 3). The bulk of them were conducted in Norway (Eriksen et al., 2001; Sivertsen et al., 2006; Øverland et al., 2008b; Sivertsen et al., 2009d), and one was carried out in Finland (Salo et al., 2010). A Swedish study post-dated the sub-studies included in this PhD thesis (Canivet et al.,
2013). This geographical clustering probably has something to do with the availability of national register data on retirements for research in the Scandinavian countries, which is uncommon in most other countries. The above-mentioned Norwegian studies were based in part on the same dataset as two of the studies using the HUNT-2 data (Sivertsen et al., 2006; Øverland et al., 2008b). The outcome was disability retirement in four of the studies, and in two others the applied outcome was more general work disability combining information on disability retirement and long-term sickness absence with receiving rehabilitation benefits (Eriksen et al., 2001), or deaths (Salo et al., 2010). The data on disability retirement were obtained from national registers for all the studies except one, which relied on self-reports (Eriksen et al., 2001). Insomnia symptoms were self-reported in all the studies, examined as dichotomous measures in most of them, although two used a three-category version (Sivertsen et al., 2006; Salo et al., 2010).

Associations of insomnia symptoms with subsequent disability retirement were found in all the studies included in the table (Sivertsen et al., 2006; Øverland et al., 2008b; Sivertsen et al., 2009d; Canivet et al., 2013), as well as with broader long-term work disability including retirement (Eriksen et al., 2001; Salo et al., 2010) (Table 3). According to the results of a Norwegian study conducted among the adult general population over a follow-up of four years, insomnia symptoms, as opposed to good sleep patterns, were associated with subsequent disability retirement (Sivertsen et al., 2006). The risk was highest among those with insomnia and daytime impairment. Another Norwegian study focusing on the adult general population compared insomnia and depression as predictors of disability retirement over a four-year follow-up (Øverland et al., 2008b). The impact of depression on work disability is widely recognized, but according to this study insomnia symptoms contributed as much or even more to subsequent disability retirement. The results of a recent Finnish study conducted among middle-aged municipal employees indicated that, in addition to all-cause work disability, insomnia symptoms were associated with subsequent cause-specific disability due to mental disorders, diseases of the nervous, musculoskeletal, or circulatory systems, and injuries and poisonings over a follow-up of 3.3 years (Salo et al., 2010). Moderate insomnia symptoms were also associated with subsequent work disability, but the strongest association was with severe symptoms. No association was detected between insomnia symptoms and work disability due to malignant tumours. One of the studies examined the independent associations of not only insomnia symptoms but also sleep duration with subsequent disability retirement in a middle-aged sample of the general population (Sivertsen et al., 2009d): according to the findings, both insomnia symptoms and long sleep duration (>8.5h) were associated with disability retirement, whereas short sleep duration (<5.5h) was not. A recent Swedish study also examined both insomnia symptoms and sleep duration over a follow-up of 12 years (Canivet et al., 2013): at least moderate insomnia symptoms were associated with disability retirement among women and men, and there was an association with long sleep duration (≥9 h) among the women, but not among the men. A further finding was the existence of
<table>
<thead>
<tr>
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<th>Adjusted results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eriksen et al., 2001</td>
<td>Norway, six age cohorts of Ullensaker municipality inhabitants, 20–72 years</td>
<td>Follow-up 4 years, questionnaire survey</td>
<td>1990–1994</td>
<td>1,426 W 50% RR 67%</td>
<td>Self-reported insomnia symptoms (1 item, 2 categories in the analyses)</td>
<td>Self-reported disability retirement, included in the outcome of long-term work disability together with long-term sickness absence and receiving rehabilitation benefits</td>
<td>Age, gender, marital status, physical and psychosocial working conditions, smoking, physical exercise, BMI, self-rated health, emotional symptoms, pain</td>
<td>Logistic regression analysis</td>
<td>Insomnia symptoms were associated with subsequent long-term work disability (including disability retirement), OR 2.16 (95% CI 1.26–3.72).</td>
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<p>| Sivertsen et al., 2006 | Norway, HUNT-2 study, inhabitants of Nord-Trøndelag County, 20–65 years | Follow-up 4 years, physical examination, questionnaire survey, register-based follow-up | 1995–2001         | 37,308 W 53% RR 71% (physical examination), 80% (survey) | Self-reported insomnia symptoms (3 items, 3 categories in the analyses) | Register-based disability retirement | Age, gender, education, SEP, night/shift work, alcohol consumption, smoking, physical activity, somatic diagnoses and symptoms, depression, anxiety | Logistic regression analysis | Insomnia symptoms were associated with subsequent disability retirement, OR 1.19 (95% CI 0.95–1.49). The risk was highest among those with insomnia and daytime impairment, OR 1.75 (95% CI 1.40–2.20). |</p>
<table>
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<tr>
<th>Reference</th>
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<tr>
<td>Øverland et al., 2008b</td>
<td>Norway, HUNT-2 study, inhabitants of Nord-Trøndelag County, 20–66 years</td>
<td>Follow-up 4 years, physical examination, questionnaire survey, register-based follow-up</td>
<td>1995–2001</td>
<td>37,302 W 53% RR 71% (physical examination), 80% (survey)</td>
<td>Self-reported insomnia symptoms (2 items, 2 categories in the analyses)</td>
<td>Register-based disability retirement</td>
<td>Age, gender, education, SEP, alcohol consumption, smoking, physical activity, somatic disorders, pain</td>
<td>Logistic regression analysis, population attributable fractions</td>
<td>Insomnia symptoms were associated with subsequent disability retirement with and without depression, OR 2.76 (95% CI 2.11–3.61) and OR 1.66 (95% CI 1.37–2.01), respectively. The association of depression with disability retirement: OR 1.56 (95% CI 1.24–1.96).</td>
</tr>
<tr>
<td>Sivertsen et al., 2009d</td>
<td>Norway, Hordaland Health Study (HUSK), population-based, 40–45 years</td>
<td>Follow-up 4 years, clinical examinations, questionnaire survey, register-based follow-up</td>
<td>1997–2003</td>
<td>6,599 W NR RR 63%</td>
<td>Self-reported insomnia symptoms, Karolinska Sleep Questionnaire (4 items, 2 categories in the analyses)</td>
<td>Register-based disability retirement</td>
<td>Age, gender, education, income, alcohol consumption, smoking, physical activity, BMI, sleep duration, somatic diagnoses and symptoms, pain, depression, anxiety</td>
<td>Logistic regression analysis</td>
<td>Insomnia symptoms were associated with subsequent disability retirement, OR 1.88 (95% CI 1.00–3.55), as was long sleep duration (&gt;8.5h) OR 2.14 (95% CI 1.07–4.29), while short sleep duration (&lt;5.5h) was not, OR 0.45 (95% CI 0.15–1.33).</td>
</tr>
<tr>
<td>Reference</td>
<td>Setting</td>
<td>Study design</td>
<td>Time period</td>
<td>N, women (W%), response rate (RR%)</td>
<td>Insomnia symptoms measurement</td>
<td>Outcome(s)</td>
<td>Adjusted covariates</td>
<td>Main statistical method</td>
<td>Adjusted results</td>
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<tr>
<td>Salo et al., 2010</td>
<td>Finland, Finnish Public Sector Study, mean age (SD) 44.4 years (9.7)</td>
<td>Mean follow-up 3.3 years, questionnaire survey, register-based follow-up</td>
<td>2000–2005</td>
<td>56,732 W 80% RR 74%</td>
<td>Self-reported insomnia symptoms, Jenkins Sleep Questionnaire (4 items, 3 categories in the analyses)</td>
<td>Register-based disability retirement, outcome: long-term work disability + long-term sickness absence + death</td>
<td>Age, gender, SEP, shift work, alcohol consumption, smoking, physical activity, BMI, somatic health, depression, anxiety, anxiolytics, pain killers</td>
<td>Cox proportional hazards model</td>
<td>Insomnia symptoms associated with disability retirement. All-cause: moderate symptoms HR 1.19 (95% CI 1.10–1.30), severe HR 1.54 (95% CI 1.42–1.67). Severe symptoms and retirement due to mental disorders HR 1.61 (96% CI 1.34–1.94).</td>
</tr>
<tr>
<td>Canivet et al., 2013</td>
<td>Sweden, general population, Malmö Shoulder and Neck Study, 45–64 years</td>
<td>Follow-up 12 years, questionnaire survey, register-based follow-up</td>
<td>1992–2005</td>
<td>4,319 W 48% RR 41%</td>
<td>Self-reported insomnia symptoms (4 items, 2 categories in the analyses, also separate symptoms)</td>
<td>Register-based disability retirement</td>
<td>Age, marital status, SEP, nationality, job strain &amp; support, stress, social participation, alcohol consumption, smoking, obesity, sleep duration, self-rated health (stratified by gender)</td>
<td>Cox proportional hazards model</td>
<td>Insomnia symptoms associated with disability retirement: women HR 1.4 (95% CI 1.1–1.7), men HR 1.4 (95% CI 1.1–1.9). Musculoskeletal diseases, women HR 1.8 (95% CI 1.2–2.8); mental disorders, men HR 2.6 (95% CI 1.2–5.9). Difficulties falling asleep: CVD, women HR 1.7 (95% CI 0.7–4.3); mental disorders, men HR 2.0 (95% CI 0.8–4.8).</td>
</tr>
</tbody>
</table>

BMI = body mass index; CI = confidence interval; HR = hazard ratio; OR = odds ratio; SEP = socioeconomic position
gender-based patterns regarding cause-specific disability retirement with regard to the effects of both sleep duration and separate insomnia symptoms.

The reviewed studies on the associations between insomnia symptoms and subsequent disability retirement took into account several key factors that are linked with both insomnia and work disability. These factors include socio-demographic factors; health behaviours, such as alcohol consumption, smoking and physical activity; and mental and physical health. Although both health- and work-related factors have significant roles in the evaluation of work disability (Gould et al., 2008), somewhat surprisingly the latter were not adjusted for in all the studies. Night or shift work was taken into account in two of them (Sivertsen et al., 2006; Salo et al., 2010), another adjusted for job strain and support (Canivet et al., 2013), and yet another adjusted for a wider array of work characteristics, including working hours, and physical and psychosocial working conditions (Eriksen et al., 2001). All the studies apart from one that applied gender stratification (Canivet et al., 2013) pooled women and men and adjusted for gender.

In sum, all the longitudinal studies under review reported associations of insomnia symptoms with subsequent disability retirement or outcomes of long-term work disability. In the case of disability retirement the associations are generally in line with those identified in previous studies using other indicators of work disability, although stronger for disability retirement than for shorter-term sickness absence.

### 3.4 Insomnia symptoms, sleep duration and health-related outcomes

Examination of sleep quality and quantity together would give a fuller picture of the associations of sleep with different health-related outcomes, and would also allow closer identification of the subgroups facing the biggest health risks. Numerous studies examine the individual effects of insomnia – one indicator of sleep quality – and sleep duration, but only a handful focus on their joint associations with health-related indicators, and none examine work disability outcomes.

The outcome used in most longitudinal studies examining the joint associations of insomnia symptoms and sleep duration is either all-cause or CVD mortality, or CVD morbidity (Hublin et al., 2007; Suzuki et al., 2009; Chandola et al., 2010; Chien et al., 2010; Vgontzas et al., 2010; Hoevenaar-Blom et al., 2011; Fernandez-Mendoza et al., 2012; Sands-Lincoln et al., 2013; Westerlund et al., 2013). One study (Troxel et al., 2012) in which the secondary analyses were based on six previous clinical trials used treatment outcome in depressed patients. Most studies on the joint associations between insomnia symptoms and sleep duration used register-based outcomes, whereas self-report questionnaires have been used for assessing insomnia symptoms. Sleep duration was self-reported in all except three of the studies, which
obtained objective polysomnographic measurements from one to three nights in a sleep laboratory (Vgontzas et al., 2010; Fernandez-Mendoza et al., 2012; Troxel et al., 2012). The study populations of these studies were generally rather large, extending to over 86,000 participants (Sands-Lincoln et al., 2013), and the respective follow-up times were also quite long, most of them between seven and 22 years.

Most earlier studies emphasize the impact of both insomnia symptoms and sleep duration, but depending on the study and the outcome there are some differences in terms of whether sleep quality or quantity appears to dominate the associations. A U-shaped association is common between sleep duration and different health outcomes, the health hazards sometimes clustering at either the short or the long end, depending on the condition studied (Knutson and Turek, 2006). In terms of sleep duration, the majority of the studies report the highest health risks among those who sleep less and have insomnia symptoms (Chandola et al., 2010; Vgontzas et al., 2010; Hoevenaar-Blom et al., 2011; Fernandez-Mendoza et al., 2012; Troxel et al., 2012; Westerlund et al., 2013), although according to some findings the risks are highest among long sleepers with insomnia symptoms (Suzuki et al., 2009; Chien et al., 2010; Sands-Lincoln et al., 2013). One previous study examining all-cause mortality identified an increased risk among short and long sleepers, but only minimal associations with insomnia symptoms (Hublin et al., 2007).

No previous studies have examined the joint associations of insomnia symptoms and sleep duration with work disability outcomes. Following on from the sub-studies included in this PhD thesis we recently examined the joint associations of insomnia symptoms and sleep duration with subsequent sickness absence of various lengths (Lallukka et al., 2013a). We found that insomnia symptoms dominated these associations, given the increased risk of sickness absence among those exhibiting as opposed to not exhibiting the symptoms, regardless of their sleep duration. Nevertheless, a U-shaped association was also detected in the case of sleep duration, the found associations being stronger among short and long sleepers. The risk of longer sickness absences (4–14 days and 15 days or more) was also somewhat higher among long sleepers without insomnia symptoms.

In sum, previous longitudinal studies have shown that examining the effects of insomnia and sleep duration simultaneously gives a valuable and more comprehensive view of the associations of sleep with different health-related outcomes. Whether insomnia symptoms or sleep duration dominates the associations depends on the study and the outcomes examined.
3.5 A summary of the previous research

This literature review covered epidemiological follow-up studies examining the associations of insomnia symptoms first with mental health and psychotropic medication; second, with hypertension and dyslipidemia and the medication used for their treatment; third, with work disability, especially disability retirement; and fourth, in the case of joint associations including insomnia and sleep duration, with different health-related outcomes.

Previous longitudinal studies on the association between insomnia and psychotropic medication indicate that insomnia symptoms are associated with subsequent treatment for depression and increased overall healthcare utilization, including psychotropic medication. Psychotropic medication is usually examined as part of a more general measure of mental healthcare rather than separately. The adjustments made in analysing the associations between insomnia symptoms and the use of such medication tend to be rather restricted, and lack work-related factors in particular. Given the small number of longitudinal studies in this area, it is difficult to summarize and draw conclusions from the results.

According to most previous studies, insomnia symptoms are associated with an increased risk of subsequent hypertension. Only one longitudinal study examined their association with subsequent dyslipidemia, and found no evidence. Thus, given the limited number of previous longitudinal studies, there is still no clear understanding of how insomnia symptoms contribute to these key cardiovascular risk factors. Moreover, as was the case with studies on psychotropic medication, those examining cardiovascular medication, although generally taking health and health behaviours into account, did not control for work-related factors.

Recent studies have reported an association between insomnia symptoms and subsequent disability retirement, but there is still a lack of research in this area. Only two studies include a more detailed, diagnosis-specific examination of the associations between insomnia symptoms and work disability, and only one of them separated disability retirement from other types of long-term work disability. Furthermore, only one study examined the impact of different insomnia symptoms on subsequent disability retirement instead of or in addition to the overall measure. Work-related factors should be taken into account in studies on disability retirement, an adjustment that was not made in all the reviewed studies. In addition, although one of them included sleep duration alongside insomnia symptoms, none examined their potential joint effect on work disability. Nevertheless, it is concluded in previous longitudinal studies examining the joint associations of insomnia symptoms and sleep duration with various outcomes that a combined measure might be a stronger predictor of health-related outcomes than either component of sleep on its own.
In sum, we still lack knowledge on the associations of insomnia symptoms with psychotropic medication that might indicate mental ill health. Another understudied area is their association with hypertension and dyslipidemia, which are among the key modifiable cardiovascular risk factors. Moreover, only a few studies examine insomnia symptoms in relation to severe long-term work disability, indicated by disability retirement. Especially lacking in all these areas are longitudinal studies on the effects of these symptoms. Research on the health-related consequences of sleep would also benefit from the joint examination of insomnia symptoms and sleep duration, an area in which work disability outcomes have not been studied.
4 THE AIMS OF THE STUDY

This study focused on the associations of insomnia symptoms with subsequent ill health and work disability among women and men. It was assumed that these associations were affected by several factors, including socio-demographic and work-related factors, as well as health and health behaviours. The object of the study was to narrow the gaps in the current knowledge in this area, and to produce novel evidence on the associations in question.

The general aim was to examine the associations of insomnia symptoms with subsequent mental disorders, key cardiovascular risk factors and severe work disability. The examination was carried out in an employee cohort consisting of both women and men, and a wide variety of relevant covariates were taken into account. The more specific study aims, addressed in the four sub-studies, were to examine:

1. The associations of insomnia symptoms with subsequent psychotropic medication, including any psychotropic medication, psycholeptics and psychoanaleptics (Sub-study I);

2. The associations of insomnia symptoms with subsequent cardiovascular medication used for the treatment of hypertension and dyslipidemia (Sub-study II);

3. The associations of insomnia symptoms with subsequent disability retirement, including all-cause disability retirement and retirement due to musculoskeletal diseases and mental disorders (Sub-study III);

4. The joint associations of insomnia symptoms and sleep duration with subsequent disability retirement (Sub-study IV).

These sub-studies are henceforth referred to by the above-mentioned Roman numerals.
5 DATA AND METHODS

This study is part of the on-going Helsinki Health Study (HHS) at the University of Helsinki, Finland (Lahelma et al., 2013). The HHS is a longitudinal cohort study set up to examine health, functional abilities and wellbeing among middle-aged and ageing employees of the City of Helsinki. The dataset in question comprises the cross-sectional baseline surveys of the HHS, linked with register data on medication and disability retirement.

Helsinki is the capital of Finland, with an approximate population of 600,000. The City of Helsinki is the single largest employer in Finland, with approximately 40,000 employees (City of Helsinki: Annual Report, 2011). The employees represent a wide range of non-manual and manual occupations, the largest sectors being social affairs and public health, and culture and education.

5.1 Questionnaire survey

The HHS baseline survey data were collected in 2000–2002 among employees of the City of Helsinki reaching the age of 40, 45, 50, 55 or 60 during any of the three study years (Lahelma et al., 2013). The data collection was carried out by means of postal questionnaires in the spring of each study year, following the same method. The survey questionnaire was sent to the work place of each eligible employee. If the recipient was not reached there, the questionnaire was next mailed to the employee’s home address. Non-respondents were sent up to three reminders.

Information on eligible study participants was received from the employer’s personnel register. The inclusion criteria included being employed by the City of Helsinki at baseline, with a monthly salary, and total income of at least 4,000 euro from the City in the previous year. Trainees were excluded. The personnel register data were updated at the end of each survey year, and those who had retired, died, or who had over 300 cumulative days of absence during the survey year and the year before it were excluded. In addition, 16 employees were excluded because they had removed the study identification number from their questionnaires, and no register data was available for another 38 employees.

The study sample, all three survey years pooled, consisted of 13,344 people, of whom 8,960 returned the questionnaire thus resulting in an overall response rate of 67 per cent. The proportion of women in the data is 80 per cent, which corresponds to the gender distribution among employees of the City of Helsinki, as well as among Finnish municipal employees in general (KT: Local government employers, 2013).
5.2 Register data

The HHS survey data have been linked to longitudinal data from several external registers. The follow-up data cover many years before and after the baseline, the exact time depending on the register in question. Register linkages were made for baseline respondents who gave their written informed consent for such linkage (74%). The unique personal identification codes issued to all Finnish residents were used to make the linkages. The register-linked data set included 6,606 employees.

The register data used in this study include:
1) data on reimbursements for prescribed medicine expenses ("the medication data"), obtained from the governmental Social Insurance Institution of Finland (SII/Kela); and
2) data on disability retirement, obtained from the national retirement registry of the Finnish Centre for Pensions (FCP/ETK).

Additional data from the employer’s personnel register were used in coding the occupational class of the participants, and mortality data from the same register, FCP and Statistics Finland were used to identify deaths during the follow-up for censoring purposes in the statistical analyses.

5.2.1 Medication data

The register-based medication data used in this study start at 1.1.1995 and end in 2007. The exact end date varies among the participants because the follow-up time used in the analyses was five years from the individual baseline date onwards in both medication sub-studies (I and II). The data comprise all outpatient physician-prescribed medicine purchases that were subsequently reimbursed by the SII. If the medication in question is reimbursable, the reimbursement is normally made automatically at the time of the purchase. Information on prescribed and reimbursed medication purchases is forwarded from all pharmacies in the country to the SII register. In practice the reimbursed medication data covers the vast majority of all prescription medication purchases, excluding only some of the cheapest medicines, the price of which does not exceed the minimum reimbursement level (Finnish Medicines Agency Fimea and Social Insurance Institution, 2012). Over-the-counter medicines are not included in the register, unless prescribed by a physician.

The data made available for HHS research purposes included among other things information on the medication product bought, coded according to the WHO Anatomical Therapeutic Chemical (ATC) Classification System (Finnish Medicines Agency Fimea, 2010), the amount of purchased medication, the dates of both the prescription and the actual purchase, and the price of the medication as well as the reimbursed sum.
5.2.2 Data on disability retirement

Register data on disability retirement events were available from 1.1.1990 onwards. The data used for this study started from each participant’s individual baseline date (during 2000–2002) and ended at the end of either 2008 (Sub-study III) or 2010 (Sub-study IV). The Finnish Centre for Pensions register includes information on all earnings-based retirements in Finland, whether due to disability or old age (Finnish Centre for Pensions, 2014). The Finnish pension scheme is decentralised. The different earnings-related pension providers manage the insurance policies and pay out the pensions. The Finnish Centre for Pensions serves as the joint statutory co-operative body in the area of earnings-related pensions.

Disability retirement may be granted under Finnish retirement schemes if an employee’s work ability is assessed to have been substantially and continuously reduced due to illness, injury or impairment by at least three-fifths (two-fifths for a partial disability pension) for 12 months or more (Huunan-Seppälä et al., 2003). In practice this requires preceding continuous sickness absence of at least 300 working days. In addition to a diagnosed illness, an employee must have functional limitations, in other words lowered work ability, to be granted disability retirement. Working conditions are also considered in the evaluation of work ability. Disability retirement may be specified as temporary or permanent, partial or full-time, although in the majority of cases it is permanent and full-time. Those aged 63 years or older are not eligible for disability retirement because from that age onwards they qualify for an old-age pension.

The pension register contains detailed data on all retirement events. It includes the principal diagnosis on which the disability retirement is based, coded according to the International Classification of Diseases (ICD-10) (World Health Organization, 2004). Other information includes the type of pension, the date of its granting as well as the effective date when payment started, the possible date and reason for expiry in the case of temporary retirement, and the date of death if it occurred after retirement.

5.3 Non-response and non-consent

Several studies examine the effects of non-response in the HHS data (Lallukka et al., 2002; Martikainen et al., 2007; Laaksonen et al., 2008; Lahelma et al., 2013), based on data from the employer's personnel register covering socio-demographic factors and sickness absence among both respondents and non-respondents. Non-response was somewhat more common among men, younger employees, those in lower socioeconomic positions, and those with more spells of sickness absence. Nevertheless, the differences were rather small, especially among women, and according to the study results the HHS data satisfactorily represent the target
population. It was also concluded that the observed differences in responding were unlikely to seriously affect the associations with health-related outcomes under investigation.

The giving of consent to the external register linkages was associated with the background variables in a similar way as participation in the baseline surveys (Laaksonen et al., 2008; Lahelma et al., 2013). Men were somewhat more likely to give their consent (79%) than women (73%). It was concluded in studies examining this issue that denying register linkage was unlikely to cause substantial bias in the data. No additional attrition occurred during the follow-up because the investigation was based on official register data with full coverage.

5.4 Ethical considerations

The Helsinki Health Study protocol follows the University of Helsinki guidelines and data legislation (Lahelma et al., 2013), having the approval of the ethics committees of the Department of Public Health, University of Helsinki and the health authorities of the City of Helsinki. The City of Helsinki granted permission to collect survey data among the staff, and access to the employer’s retrospective and prospective personnel register data.

5.5 Measures

Data on the sleep measures and covariates were obtained from the HHS baseline surveys, whereas data on medication and disability retirement outcomes were retrieved from the linked registers.

5.5.1 Sleep measures

Insomnia symptoms

The Jenkins Sleep Questionnaire (JSQ) was used to assess insomnia symptoms in the baseline survey (Jenkins et al., 1988). The questionnaire includes the following four questions:

“How often in the past month [four weeks in the Finnish version] did you:
1) Have trouble falling asleep?
2) Wake up several times per night?
3) Have trouble staying asleep (including waking far too early)?
4) Wake up after your usual amount of sleep feeling tired and worn out?”
Table 4. Classification of the frequency measure of insomnia symptoms (Sub-studies I–IV)

<table>
<thead>
<tr>
<th>Sub-study</th>
<th>Frequency of insomnia symptoms</th>
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<tbody>
<tr>
<td></td>
<td>not at all</td>
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<tr>
<td>I</td>
<td>No</td>
</tr>
<tr>
<td>II</td>
<td>No</td>
</tr>
<tr>
<td>III</td>
<td>No</td>
</tr>
<tr>
<td>IV</td>
<td>No or occasional</td>
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</table>

Complementing the first of these items measuring difficulties falling asleep, the second and third items measure difficulties staying sleep – consisting of nocturnal and early-morning awakenings – and the last one non-restorative sleep. Note that the term “insomnia symptoms” was used in all the sub-studies except Sub-study III, which was the first to be carried out and used the synonymous term “sleep problems”.

Six response alternatives regarding the frequency of insomnia symptoms were included: not at all; 1–3 days; 4–7 days; 8–14 days; 15–21 days; and 22–28 days. Responses to the JSQ were further reclassified in the sub-studies (Table 4). In all of them the symptoms were considered frequent if at least one was reported to have occurred at least 15 times during the previous four weeks, and occasional or rare only in the absence of more frequent symptoms. Those responding "not at all" to all of the above-mentioned four items (with only one response missing at most) were coded as having no insomnia symptoms.

The four JSQ items were statistically significantly correlated among both women and men (all Spearman correlation coefficients p<0.0001) (Table 5). The correlations were similar among women and men, varying between r=0.43–0.67. The strongest correlations were found between the two items measuring difficulties staying asleep, and the weakest between difficulties falling asleep and non-restorative sleep. The standardized Cronbach’s coefficient alpha of the JSQ was 0.84 among women and men, indicating good internal consistency and reliability of the measure.

The JSQ was developed for clinical and epidemiological research purposes and its validity has also been examined (Jenkins et al., 1988). In addition, the JSQ (see e.g., Jerlock et al., 2008; Salo et al., 2012a) and other similar measures have been used in various international studies (Moul et al., 2004) for assessing insomnia symptoms. The assessed symptoms are also fairly well in accordance with the DSM-IV criteria (American Psychiatric Association, 2000), with the exception that the JSQ does not assess daytime impairment attributable to the symptoms. However, it does assess unspecific symptoms, and is not a diagnostic instrument of clinical insomnia disorder.
Table 5. Inter-correlations among the Jenkins Sleep Questionnaire items by gender, men above the diagonal (N=1,341), women below the diagonal (N=4,772).

<table>
<thead>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Trouble falling asleep</td>
<td>1</td>
<td>0.49</td>
<td>0.53</td>
<td>0.47</td>
</tr>
<tr>
<td>2. Waking up several times per night</td>
<td>0.46</td>
<td>1</td>
<td>0.67</td>
<td>0.51</td>
</tr>
<tr>
<td>3. Trouble staying asleep (including waking far too early)</td>
<td>0.50</td>
<td>0.66</td>
<td>1</td>
<td>0.51</td>
</tr>
<tr>
<td>4. Waking up feeling tired and worn out</td>
<td>0.43</td>
<td>0.53</td>
<td>0.52</td>
<td>1</td>
</tr>
</tbody>
</table>

Spearman correlation coefficients (p<0.0001), Cronbach’s coefficient alpha 0.84 for both genders

Sleep duration

The HHS baseline survey contains a question on average sleep duration per day in whole hours during weekdays. The six response alternatives range from five hours or less to ten hours or more. As less than one per cent of the study participants reported sleeping on average ten or more hours (data not shown), this class was merged with the nine-hour sleepers in the analyses, forming a new class "nine hours or more". Similar assessment of sleep duration is common in epidemiological studies (Kurina et al., 2013). There were two per cent of missing responses to the question on sleep duration among both women and men.

The joint measure of insomnia symptoms and sleep duration

The joint variable comprising insomnia symptoms and sleep duration, used in Sub-study IV, was created by dividing each of the five sleep-duration categories by the frequency of insomnia symptoms into 1) no or occasional insomnia symptoms (any of the symptoms 0–14 times during the previous four weeks), and 2) frequent insomnia symptoms (at least 15 times). This new 10-category variable was used in the analyses, with seven-hour sleepers with no or occasional insomnia symptoms serving as the reference group. Seven hours was chosen for the reference category following previous studies examining the joint associations of insomnia symptoms and sleep duration (Chien et al., 2010; Hoevenaar-Blom et al., 2011).
5.5.2 Prescribed medication

Data on medication prescribed by a physician, obtained from the register of the Social Insurance Institution of Finland, were used as an indicator of mental and physical ill health. The outcome used in the medication studies was at least one reimbursed purchase of the medication in question during the follow-up.

Sub-study I examined psychotropic medication during a follow-up of five years. The main outcome was any psychotropic medication, meaning medication coded as psycholeptics (ATC-code N05: mainly hypnotics and sedatives) or psychoanaleptics (N06: mainly antidepressants), excluding medication for dementia (N06D). Separate analyses were conducted for antidepressants (N06A) and the group consisting of anxiolytics, hypnotics and sedatives (N05B and N05C). Those in possession of psychotropic medication at the time of the baseline survey (N=319) were excluded from the analyses in order to make it easier to examine its incidence during the follow-up. These participants were identified from the date and defined daily dose (DDD) of their last pre-baseline medication purchase. All other psychotropic medication (from 1 January 1995 onwards) was dichotomized as 1) no purchases or 2) at least one purchase, one such dichotomous variable for medication before baseline, another representing the follow-up. Pre-baseline psychotropic medication was adjusted for in the analyses.

Sub-study II examined medication affecting the cardiovascular system (ATC-class C), with a five-year follow-up. The focus was on lipid modifying agents (C10) and medication with hypertension as the main indication, including antihypertensives (C02), diuretics (C03), beta-blocking agents (C07), calcium channel blockers (C08), and agents acting on the renin-angiotensin system (C09). As was the case with psychotropic medication, dichotomous measures (no purchases/at least one purchase) were created to represent cardiovascular medication before baseline (starting from 1 January 1995) and during the five-year follow-up. Previous medication for hypertension and dyslipidemia was adjusted for in the analyses.

5.5.3 Disability retirement

Disability retirement was used as an indicator of work disability in Sub-studies III and IV. Relevant data were obtained from the Finnish Centre for Pensions registers. All-cause disability retirement was used as an outcome in both sub-studies, in addition to which the two most prevalent diagnostic groups, musculoskeletal diseases (ICD-10 codes M00–M99, diseases of the musculoskeletal system and connective tissue) and mental disorders (F00–F99, mental and behavioural disorders), were examined separately. The starting date of the pension payment was also used in the analyses.
5.5.4 Covariates

There are several factors that, on the evidence of earlier studies, can be assumed to potentially confound the associations of insomnia symptoms with health and work disability. Factors that need to be controlled for in analyses of these associations include socio-demographic factors, health, health behaviours, and working conditions and work arrangements (Ohayon, 2002; Phillips and Mannino, 2005; Graham et al., 2007; Colman et al., 2008; Arber et al., 2009; Lallukka et al., 2010; Laaksonen et al., 2012; Lallukka et al., 2012b; Sivertsen et al., 2013). The factors used as covariates in this study are described below in terms of their handling and classification. More details on these covariates are to be found in the sub-studies (I–IV). All the following survey-based covariates were measured at baseline. In addition, pre-baseline psychotropic and cardiovascular medication were adjusted for in Sub-studies I and II, respectively. The handling of the medication data is described in Chapter 5.5.2 above.

Socio-demographic factors

Age was adjusted for in all the analyses. Gender was adjusted for in Sub-studies III and IV focusing on disability retirement, whereas the analyses were stratified by gender in Sub-studies I and II, which concern medication. The reasons for this are discussed in more detail in the next section (Chapter 5.6) dealing with the statistical methods applied. Marital status was questioned in the baseline survey, with five response alternatives that were further categorized as single; married or cohabiting; and previously married (divorced, separated or widowed). Occupational class was used as an indicator of socioeconomic position. Occupational data were obtained from the employer’s personnel register and completed from the questionnaires for those who did not consent to the use of personnel register data. Occupations were classified into four hierarchical categories according to the socio-economic group classification of Statistics Finland: 1) professionals and managers (employees usually with a university degree, e.g., teachers and physicians); 2) semi-professionals (intermediate-level white-collar employees, e.g., nurses, technicians and foremen); 3) routine non-manual employees (non-professional clerical employees and other lower white-collar employees, e.g., child minders); and 4) manual workers (e.g., working in transport and other technical occupations, or in cleaning and canteens) (Statistics Finland, 1989; Lahelma et al., 2005).

Work-related factors

Both psychosocial and physical working conditions at baseline were taken into account when the associations between insomnia symptoms and both subsequent health (Sub-studies I–II) and work disability (Sub-studies III–IV) were examined. Karasek’s Job Content Questionnaire was used to measure psychosocial job strain
(Karasek et al., 1981). Karasek’s model suggests that job strain at the workplace results from the interaction of two types of work characteristics, namely the psychological demands and stressors in the particular work situation, and the amount of control available to the employee facing these demands. The questionnaire version used in the HHS baseline survey included ten items on job demands and nine on job control, the five response alternatives ranging from “fully agree” to “fully disagree”. The medians in the distribution of the job-demands and job-control scales were used as cut-off points to yield four categories of job strain: low strain (low job demands, high control of the work process), passive work (low demands, low control), active work (high demands, high control) and high strain (high demands, low control).

The mental and physical strenuousness of the work were both assessed on single-item questions with four response alternatives ranging from very light to very strenuous. The distribution of the responses was uneven at both ends of the scale: less than five per cent of the participants considered their work physically very strenuous, and less than two per cent considered it mentally very light. Thus the measures were reclassified into three categories following the merging of these small classes with their neighbours.

Physical working conditions were assessed on an 18-item inventory covering environmental and physical exposure at work and developed at the Finnish Institute of Occupational Health (Piirainen et al., 2003). The consequent three-factor solution was based on a factor analysis of these 18 dichotomous items (Laaksonen et al., 2010). The first factor comprised physical workload, such as uncomfortable postures and repetitive movements; the second included environmental exposure such as to hazardous chemicals and noise; and the third comprised sedentary work at a desktop computer. These factors were used as covariates in a four-category form, the quartiles used as cut-off points.

The work arrangements controlled for in all the sub-studies were shift work and working overtime. The current working schedule was elicited in a question with six response alternatives, reclassified into the following four categories: regular daytime work, shift work with no night shifts, shift work with night shifts (including regular night work), and other working arrangements. Weekly working hours were measured on a five-point scale ranging from “1–10 hours” to “more than 50 hours”. The cut-off point for overtime was working more than 40 hours a week.

*Health behaviours and weight*

Smoking, heavy drinking, physical inactivity and eating habits were included in the investigations to indicate key behavioural risk factors. Smoking was dichotomized into current smoking (cigarettes, cigars or a pipe) and non-smoking. The classification of heavy drinking was based on Finnish Current Care Guidelines (Working group
appointed by the Finnish Society of Addiction Medicine, 2010). Alcohol consumption was measured as the sum of self-reported weekly portions of beer, wine and spirits. Each of these portions contains approximately 12 grams of absolute alcohol, the cut-off point for heavy drinking being 140 grams of absolute alcohol per week for women and 280 grams for men. The baseline survey included questions about the amount and intensity of leisure-time physical activity, and the Metabolic Equivalent (MET) scores were based on this information (Kujala et al., 1998). Those in the lowest MET quintile (calculated separately for women and men) were classified as physically inactive. Fruit and vegetable consumption was used as a proxy for healthy eating habits, and measured by means of a food-frequency questionnaire in the baseline survey. The questions concerned the consumption of fruit, berries and fresh vegetables over the previous four weeks, with seven response alternatives ranging from not at all to more than twice a day. Body mass index (BMI) was calculated from self-reported weight and height measured at baseline \(\text{BMI} = \frac{\text{weight (kg)}}{\text{height (m)}^2}\). It was used in the sub-studies as a continuous or a dichotomous variable, the latter divided at BMI<30 or ≥30, BMI=30 being the generally used cut-off point for obesity (Flegal et al., 2013). Sleep duration was used as a covariate in Sub-study III (see Chapter 5.5.1 for the measurement).

**Health**

Chronic diseases were assessed by means of dichotomous self-reports of physicians' diagnoses over the lifetime. The diseases taken into account in the sub-studies included asthma, diabetes, cardiovascular disease (comprising angina pectoris, myocardial infarction, cerebrovascular disorders and intermittent claudication, all assessed separately), musculoskeletal diseases (similarly comprising gout, osteoporosis, osteoarthritis and rheumatoid arthritis), and mental disorders (similarly comprising depression, anxiety and other mental disorders).

**The distribution of the covariates**

Table 6 gives the crude distributions by gender of the background factors measured at baseline. The distribution of the participants was quite even in all age groups except the 60-year-olds, who were fewest in number. Over two-thirds of the participants were married or cohabiting. The largest group in terms of socioeconomic position comprised routine non-manual employees (41%) among the women, and professionals and managers among the men (44%).

Most of the study participants (>70%) worked in regular daytime jobs (Table 6). Of the women, 13 per cent regularly worked overtime, as did 21 per cent of the men. With regard to the physical strenuousness of work half the participants fell into the intermediate category (both genders). A bigger proportion of women than men
considered their work physically strenuous, whereas it was the other way round in the case of work considered physically light. Almost two-thirds of the participants fell into the intermediate category regarding the mental strenuousness of work. Given that the measure for psychosocial strain was based on the medians of the job-demands and job-control scales, the participants were quite evenly distributed among the final four classes.

Nine per cent of the women and seven per cent of the men reported heavy drinking (Table 6). Almost a quarter of the participants were current smokers, and one fifth of them were physically inactive, among both women and men. Women had healthier eating habits overall, 63 per cent of them reported eating fruit daily (vs. 37% of the men) and 70 per cent eating vegetables daily (vs. 49% of the men). Fifteen per cent of the male and female participants were obese.

The most prevalent of the self-reported diseases among the study participants were musculoskeletal diseases (19% of women, 15% of men) and mental disorders (19% of women, 13% of men) (Table 6), followed by asthma and CVD; the least prevalent was diabetes.

**Missing values**

There were generally rather few (0.5–3%) missing values in the covariates used in the analyses: there were more only in the measurements of psychosocial job strain (7.5%) and chronic diseases (around 10% in each). Some variables lacked missing values due to their nature – being either register-based or key identification background variables, such as age and gender. Given that all the outcomes were register-based, there was no missing data there either. There were missing values for less than one per cent of the participants in the reclassified measure of insomnia symptoms, and they were excluded from the study.

A conservative approach was used in the case of missing values in the covariates. Four alternative strategies were applied in the analyses, depending on the case: 1) in some cases the missing values were not replaced with other values/imputed, but left as missing data; 2) some variables were reclassified, the missing values being in their own class (i.e. the above-mentioned measurements of job strain and diseases); 3) in some cases the missing values were merged with the “no”/“other” class; or 4) in the case of continuous variables they could also be substituted with the gender mean. These strategies were adopted to avoid the exclusion of too many participants from the analyses on account of missing values. Careful consideration and preliminary analyses preceded the procedures described above. It was considered particularly important to check that the chosen strategy did not significantly affect the examined associations.
Table 6. Distribution of covariates at baseline by gender (%) (N=6,606)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Women (N=5,185)</th>
<th>Men (N=1,421)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td>45</td>
<td>22</td>
<td>20</td>
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<tr>
<td>50</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>55</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>60</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>single</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>married or cohabiting</td>
<td>68</td>
<td>78</td>
</tr>
<tr>
<td>previously married</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td><strong>Socioeconomic position</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>professionals and managers</td>
<td>28</td>
<td>44</td>
</tr>
<tr>
<td>semi-professionals</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>routine non-manual employees</td>
<td>41</td>
<td>10</td>
</tr>
<tr>
<td>manual workers</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td><strong>Shift work</strong></td>
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<td></td>
</tr>
<tr>
<td>regular day-time work</td>
<td>78</td>
<td>70</td>
</tr>
<tr>
<td>shift work with no night shifts</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>shift work with night shifts</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>other working arrangements</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Working overtime</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(&gt; 40 hours/week)</td>
<td>13</td>
<td>21</td>
</tr>
<tr>
<td><strong>Physical strenuousness of work</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>light</td>
<td>19</td>
<td>35</td>
</tr>
<tr>
<td>intermediate</td>
<td>43</td>
<td>50</td>
</tr>
<tr>
<td>strenuous</td>
<td>38</td>
<td>15</td>
</tr>
<tr>
<td><strong>Mental strenuousness of work</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>light</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>intermediate</td>
<td>62</td>
<td>59</td>
</tr>
<tr>
<td>strenuous</td>
<td>14</td>
<td>15</td>
</tr>
</tbody>
</table>

(continues)
### Table 6 (continued)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Women (N=5,185)</th>
<th>Men (N=1,421)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosocial job strain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>low strain</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>passive work</td>
<td>26</td>
<td>30</td>
</tr>
<tr>
<td>active work</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>high strain</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td><strong>Heavy drinking</strong></td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td><strong>Current smoking</strong></td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td><strong>Physical inactivity</strong></td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td><strong>Eating fruit daily</strong></td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td><strong>Eating vegetables daily</strong></td>
<td>70</td>
<td>49</td>
</tr>
<tr>
<td><strong>Obesity (body mass index ≥30)</strong></td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td><strong>Chronic diseases during lifetime</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>diabetes</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>asthma</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>musculoskeletal diseases</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>mental disorders</td>
<td>19</td>
<td>13</td>
</tr>
</tbody>
</table>

1 Heavy drinking: absolute alcohol, women > 140 g/week, men > 280 g/week
2 The lowest quintile of the score for physical activity
3 CVD: angina pectoris, myocardial infarction, cerebrovascular disorders, intermittent claudication
4 Musculoskeletal diseases: gout, osteoporosis, osteoarthritis, rheumatoid arthritis
5 Mental disorders: depression, anxiety, other mental disorders
5.6 Statistical methods

Descriptive analyses were conducted using cross-tabulations with the chi-square test for heterogeneity and the Cochran-Armitage test for trend. Additionally in Sub-study III, Kaplan-Meier survival curves were computed to show the time to the first outcome event, comparing groups with different frequencies of insomnia symptoms.

The associations of baseline insomnia symptoms with subsequent psychotropic (Sub-study I) and cardiovascular (Sub-study II) medication were examined by means of logistic regression analysis. The results were presented as odds ratios (OR) with 95-per-cent confidence interval (CI). The Cox proportional hazards model was used in the studies examining disability retirement (Sub-studies III and IV) to calculate the hazard ratios (HR) with a 95-per-cent CI for the first disability retirement event during the follow-up. Participants who retired on the grounds of age, died, or turned 63 during the follow-up were censored.

Generally, no statistically significant gender interactions were found in the associations between insomnia symptoms and the examined outcomes. By way of an exception, an interaction was detected between gender and the joint variable of insomnia symptoms and sleep duration in the analysis of disability retirement (Sub-study IV). Nevertheless, given that the examined associations were largely similar in both genders (and because of the smaller number of men in the cohort) the analyses of disability retirement were carried out on gender-pooled data, gender being adjusted for as a covariate. Because the preliminary analyses suggested some gender differences in the studied associations, albeit not significant gender interactions, the analyses conducted in Sub-studies I and II on medication were stratified by gender.

Bivariate associations of the covariates with insomnia symptoms and the different outcomes were tested in the preliminary analyses. Covariates with the strongest associations were chosen for the analyses proper. They were generally entered in hierarchical order (Sub-studies I–III), more variables being added in each model, the last one being the full model. In the case of Sub-study IV, three alternative models were built on the first age- and gender-adjusted model. The grouping of the variables in the different models is described in detail in the respective sub-studies.

Various sensitivity analyses were carried out in each of the four sub-studies, in addition to analyses of the gender interactions and the associations separately among women and men. Different classifications for both the explanatory factors and the outcomes were tested. Each covariate’s individual effect on the studied associations was also examined to facilitate understanding of their contribution in the models. The different insomnia symptoms were examined separately in the analyses carried out in Sub-study III, and the same was done in the form of sensitivity analyses in Sub-studies I and II. The sensitivity analyses carried out in the medication studies
(Sub-studies I and II) excluded those taking the medication in question before baseline. Different follow-up and lag times were tested in the studies on disability retirement (Sub-studies III and IV). Finally, the sensitivity analyses also allowed a more detailed examination of the outcomes, regarding antipsychotic medication in Sub-study I and different somatic conditions in Sub-study III, for example, even if the results were not statistically significant due to the small number of respondents in these sub-categories.

SAS software, versions 9.2 and 9.3 (SAS Institute Inc., Cary, NC, USA) was used for the analyses. The R program, version 2.11.0 (R Foundation for Statistical Computing, Vienna, Austria) was used for computing the Kaplan-Meier survival curves in Sub-study III.
6 RESULTS

6.1 Descriptive results

6.1.1 Insomnia symptoms and sleep duration

Table 7 shows the detailed distribution of the original responses to the Jenkins Sleep Questionnaire in the baseline survey. The percentage of missing responses was between two and five, depending on the item, and no larger gender differences were noted. The most prevalent insomnia symptoms were nocturnal awakenings and non-restorative sleep, which over two thirds of both women and men reported having at least occasionally. The least prevalent symptom was difficulty falling asleep, which half of the participants reported not having experienced even once during the previous four weeks. Among the participants reporting insomnia symptoms the most responses fell in the frequency categories 1–3 days or 4–7 days. According to the sum measure, 20 per cent of the participants reported frequent symptoms (15–28 days), 33 per cent reported occasional (4–14 days) symptoms, 34 per cent rare (1–3 days) symptoms, and 13 per cent reported no symptoms (see Sub-study II, Table 1).

Table 7. Distribution of responses in the Jenkins Sleep Questionnaire by gender: the Helsinki Health Study baseline surveys in 2000–2002 (N=6,606)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>How often during the previous four weeks (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
</tr>
<tr>
<td><strong>Women (N=5,185)</strong></td>
<td></td>
</tr>
<tr>
<td>Trouble falling asleep</td>
<td>50</td>
</tr>
<tr>
<td>Waking up several times per night</td>
<td>27</td>
</tr>
<tr>
<td>Trouble staying asleep (including waking far too early)</td>
<td>42</td>
</tr>
<tr>
<td>Waking up feeling tired and worn out</td>
<td>29</td>
</tr>
<tr>
<td><strong>Men (N=1,421)</strong></td>
<td></td>
</tr>
<tr>
<td>Trouble falling asleep</td>
<td>52</td>
</tr>
<tr>
<td>Waking up several times per night</td>
<td>31</td>
</tr>
<tr>
<td>Trouble staying asleep (including waking far too early)</td>
<td>44</td>
</tr>
<tr>
<td>Waking up feeling tired and worn out</td>
<td>36</td>
</tr>
</tbody>
</table>
Insomnia symptoms were slightly more common among women than men, frequent symptoms being reported by 21 per cent of women versus 17 per cent of men, for example (see Sub-study II, Table 1). Frequent symptoms were also more common among older participants, those with adverse health behaviours, diabetes or mental disorders, and those with high psychosocial job strain. Experiencing several insomnia symptoms was common. Of the participants reporting at least occasional symptoms (four times or more during the previous four weeks), one third (34%) reported at least two different symptoms (data not shown). Almost one tenth (9%) of them reported experiencing all four of the measured symptoms at least occasionally.

The prevalence of frequent insomnia symptoms was highest among those sleeping five hours or less (57%), followed by those sleeping six hours (29%) or nine hours or more (21%) (Figure 1). Frequent symptoms were least prevalent among those sleeping for eight hours (14%). The gender differences at the extreme ends of the scale, in other words among those sleeping for five hours or less or nine hours or more, were negligible, and the mean and median sleep duration was around seven hours among both men and women (data not shown).

![Insomnia symptoms by sleep duration among women and men (N=6,464)](image)

**Figure 1.** Insomnia symptoms by sleep duration among women and men (N=6,464)
6.1.2 Medication and disability retirement

Figure 2 shows the prevalence of psychotropic medication pre-baseline and during follow-up. In the case of antidepressants the prevalence was 11 per cent 5–7 years before baseline and 15 per cent during the five-year follow-up, the respective figures for anxiolytics, hypnotics and sedatives being 15 and 12 per cent. The total prevalence of any psychotropic medication remained stable from pre-baseline to follow-up (see Sub-study I). The prevalence was higher among women than men, and also increased with the increasing frequency of insomnia symptoms. The two medication subgroups combined covered most of the sum outcome "any psychotropic medication". The proportion of subjects taking any psychotropic medication and taking *either* antidepressants *or* anxiolytics, hypnotics or sedatives – or both kinds – was 91 per cent pre-baseline and 96 per cent during follow-up (data not shown). The median number of psychotropic purchase events among women and men during the follow-up was four.

![Figure 2. The prevalence of antidepressant medication and anxiolytics, hypnotics and sedatives among women and men (N=6,227)](image)

- **5-7 years prior to baseline**
  - Antidepressant medication: 11%  
  - Anxiolytics, hypnotics and sedatives: 15%

- **5-year follow-up**
  - Antidepressant medication: 15%  
  - Anxiolytics, hypnotics and sedatives: 12%
Figure 3 shows the prevalence of hypertension and dyslipidemia medication pre-baseline and during follow-up. Hypertension medication was more common than dyslipidemia medication, the respective prevalence being 23 and six per cent pre-baseline and 32 and 15 per cent during follow-up. Cardiovascular medication was slightly more common among men than women: 31 per cent of women and 34 per cent of men were in possession of hypertension medication during the follow-up, the respective figures for dyslipidemia medication being 14 and 20 per cent (data not shown). The prevalence of cardiovascular medication increased as the frequency of insomnia symptoms increased (see Sub-study II, Table 2). The median number of purchase events during follow-up for hypertension medication was 16 among women and 18 among men, the respective figures for dyslipidemia medication being nine and 10 (data not shown).

Figure 3. The prevalence of hypertension and dyslipidemia medication among women and men (N=6,477)
Up until the end of 2010, 561 (9%) of the study participants retired due to disability, the proportions of retired employees being similar for women and men (Figure 4). The prevalence of disability retirement was highest among those with frequent insomnia symptoms (see Sub-study II, Figure 2). Among women, 45 per cent of the retirements were attributable to musculoskeletal diseases and 25 per cent to mental disorders, the respective figures among men being 29 and 30 per cent (see Sub-study III). The next most common causes of disability retirement were tumours/neoplasms, diseases of the nervous system and diseases of the circulatory system.

Figure 4. The prevalence of disability retirement due to the main diagnoses between 2000–2010, among women and men (N=6,042)
6.2 Insomnia symptoms and prescribed medication

The first two sub-studies focused on the associations of insomnia symptoms with subsequent psychotropic (Sub-study I) and cardiovascular (Sub-study II) medication. Outcome data on medication was retrieved from a national register. Both studies used a follow-up time of five years, adjusting for previous medication five to seven years before baseline.

6.2.1 Insomnia symptoms and psychotropic medication

Sub-study I examined the association of insomnia symptoms with subsequent mental health, as indicated by psychotropic medication. The examination was carried out separately for any psychotropic medication, antidepressants, and for the medication group combining anxiolytics, hypnotics and sedatives. The analyses were conducted stratified by gender.

Women with insomnia symptoms were more likely to have some subsequent psychotropic medication, compared with those who reported no symptoms at baseline (see Sub-study I, Table 2). The association with psychotropic medication followed a gradient: the risk was highest among those with frequent insomnia symptoms (OR 4.96, 95% CI 3.74–6.57, adjusted for age), followed by those with occasional (OR 2.70, 95% CI 2.06–3.55) or rare (OR 1.54, 95% CI 1.16–2.04) symptoms. Adjusting for pre-baseline psychotropic medication and previous mental disorders attenuated the association most. However, the association remained – if somewhat weakened – after additional adjustment for several socioeconomic and work-related factors, heavy drinking and obesity. The association between insomnia symptoms and subsequent psychotropic medication was generally similar among men, albeit slightly stronger than among women. Here, too, a graded association was noted: it was strongest among those with frequent insomnia symptoms (OR 6.61, 95% CI 3.63–12.01, adjusted for age), followed by occasional (OR 3.72, 95% CI 2.10–6.60) and rare (OR 2.05, 95% CI 1.13–3.71) symptoms. The adjustments had similar effects among men and women.

The associations of insomnia symptoms with antidepressants on the one hand and anxiolytics, hypnotics and sedatives on the other were largely similar to those observed with any psychotropic medication (Figures 5 and 6). No larger gender differences were noted, although the association with subsequent antidepressant medication was a little stronger among men than among women. The frequency of symptoms also played a role in these associations, which were strongest among both women and men with frequent symptoms, the strength gradually decreasing as the frequency decreased (antidepressants, adjusted for age, among women with frequent symptoms: OR 5.31, 95% CI 3.77–7.47; men: OR 5.72, 95% CI 2.87–11.38;
Figure 5. Insomnia symptoms and subsequent *antidepressant medication* during a five-year follow-up: odds ratios (OR) with 95% confidence interval (CI) (women N=4,868, men N=1,359)

Figure 6. Insomnia symptoms and subsequent *anxiolytic, hypnotic and sedative medication* during a five-year follow-up: odds ratios (OR) with 95% confidence interval (CI) (women N=4,868, men N=1,359)
anxiolytics, hypnotics and sedatives, adjusted for age, among women with frequent symptoms: OR 5.06, 95% CI 3.41–7.50; men: OR 5.06, 95% CI 2.37–10.79). Again, adjustment for psychotropic medication pre-baseline, socioeconomic and work-related factors, lifetime mental disorders, obesity and heavy drinking attenuated the associations, which nevertheless remained.

Given that this was a sensitivity analysis, all participants with any psychotropic medication before baseline (N=1,398) were excluded (data not shown). This had a negligible effect on the observed association of insomnia symptoms with subsequent psychotropic medication among women, and although attenuating the association among men, it nonetheless remained for any psychotropic medication and antidepressants. Another sensitivity analysis examined different insomnia symptoms separately and revealed similar associations with subsequent psychotropic medication (data not shown).

6.2.2 Insomnia symptoms and cardiovascular medication

Whereas Sub-study I focused on the association between insomnia symptoms and subsequent mental health, Sub-study II extended the examination to the area of physical health. The outcomes in this study were medication for hypertension and dyslipidemia, which are among the key modifiable risk factors of cardiovascular disease. The analyses were conducted both on pooled data and stratified by gender, and were adjusted for a large number of potential confounders.

According to the results, insomnia symptoms were also associated with subsequent hypertension medication with a consistent gradient – the more frequent the symptoms, the more likely was the medication. The strongest risk for subsequent hypertension medication was among participants with frequent insomnia symptoms (OR 2.01, 95% CI 1.65–2.45, adjusted for age and gender), followed by those with occasional (OR 1.68, 95% CI 1.39–2.02) or rarely experienced symptoms (OR 1.33, 95% CI 1.11–1.61) (see Sub-study II, Table 3). Following gender stratification it was noted that the association was similar among women to that observed in the gender-pooled data, whereas it was slightly stronger among men (Figure 7). Adjusting for hypertension medication pre-baseline had a somewhat attenuating effect, whether in the pooled data or among women or men. However, the association remained following additional adjustment for various health behaviours, BMI, diabetes, mental disorders, socioeconomic status and work-related factors.
Figure 7. Insomnia symptoms and subsequent hypertension medication during a five-year follow-up: odds ratios (OR) with 95% confidence interval (CI) (women N=5,084, men N=1,393)

Figure 8. Insomnia symptoms and subsequent dyslipidemia medication during a five-year follow-up: odds ratios (OR) with 95% confidence interval (CI) (women N=5,084, men N=1,393)
The associations of insomnia symptoms with subsequent dyslipidemia and hypertension medication were largely similar (see Sub-study II, Table 3). The only bigger difference was the lack of association with rarely experienced insomnia symptoms in the case of dyslipidemia medication. Again, those with frequent symptoms were most likely to have subsequent dyslipidemia medication (OR 1.61, 95% CI 1.25–2.07, adjusted for age and gender), and the risk also increased among those with occasional symptoms (OR 1.45, 95% CI 1.14–1.85). Contrary to the case with hypertension medication, the association between insomnia symptoms and dyslipidemia medication was slightly stronger among women than among men (Figure 8). The adjustments, including pre-baseline dyslipidemia medication, had only a modest effect on the associations between insomnia symptoms and subsequent dyslipidemia medication.

Sensitivity analyses stratified by the existence of pre-baseline medication revealed somewhat stronger associations between insomnia symptoms and subsequent hypertension or dyslipidemia medication among those with no previous cardiovascular medication (data not shown). Another set of sensitivity analyses was carried out in the subpopulation of participants with no self-reported history of CVD (angina pectoris, myocardial infarction, cerebrovascular disorders, and intermittent claudication). The results obtained in the main analyses remained, as they did following adjustment for the history of CVD as an additional covariate. No major differences between the different insomnia symptoms emerged.
6.3 Insomnia symptoms and disability retirement

The aim in Sub-studies III and IV was to give an extensive view of the association between insomnia symptoms and subsequent disability retirement over a register-based follow-up of up to ten years. All-cause disability retirement was examined, as well as retirement on the two most common grounds, musculoskeletal diseases and mental disorders. The examination was further extended to include the joint effects of insomnia symptoms and sleep duration. A dichotomous measure of symptom frequency was applied in this case, whereas a three-category version of the scale was used when sleep duration was not included in the analysis.

An association was found between insomnia symptoms and subsequent disability retirement during a mean follow-up of eight years. Frequent symptoms were associated with an increased risk of all-cause disability retirement (HR 3.22, 95% CI 2.26–4.60, adjusted for age and gender), as well as for retirement due to musculoskeletal diseases (HR 3.27, 95% CI 1.91–5.61) (Figures 9 and 10). However, in the case of retirement due to mental disorders even those with occasional insomnia symptoms had a strongly increased risk (frequent: HR 9.06, 95% CI 3.27–25.10, occasional: HR 3.44, 95% CI 1.25–9.43) (Figure 11). The observed associations were somewhat attenuated, but nevertheless remained, after extensive adjustments for socio-demographic and work-related factors, chronic diseases, obesity, health behaviours and sleep duration. Most of the attenuation was attributable to adjustment for physical working conditions and chronic diseases.

The associations between different insomnia symptoms and subsequent disability retirement were also examined separately (see Sub-study III, Tables 2–4). Of these symptoms, frequent difficulties falling asleep showed the strongest association with disability retirement, regardless of whether it was all-cause (HR 4.70, 95% CI 3.48–6.34, adjusted for age and gender) or attributable to musculoskeletal diseases (HR 4.48, 95% CI 2.82–7.12) or mental disorders (HR 10.66, 95% CI 6.23–18.24). In the case of retirement due to musculoskeletal diseases, non-restorative sleep also showed a strong association (HR 4.27, 95% CI 2.82–6.46). However, the other symptoms were also associated with an increased risk of subsequent disability retirement. The adjustments affected the associations between the four different insomnia symptoms and disability retirement in a similar way as with the combined measure. Here, too, adjusting for physical working conditions and chronic diseases attenuated the associations most, but they nonetheless remained.
Figure 9. Insomnia symptoms and subsequent *all-cause disability retirement*, from baseline in 2000–2002 through 2008: hazard ratios (HR) with 95% confidence interval (CI) (N=5,986)

Figure 10. Insomnia symptoms and subsequent *disability retirement due to musculoskeletal diseases*, from baseline in 2000–2002 through 2008: hazard ratios (HR) with 95% confidence interval (CI) (N=5,986)
Figure 11. Insomnia symptoms and subsequent disability retirement due to mental disorders, from baseline in 2000–2002 through 2008: hazard ratios (HR) with 95% confidence interval (CI) (N=5,986)

Figure 12. Joint association of insomnia symptoms and sleep duration with subsequent all-cause disability retirement, from baseline in 2000–2002 through 2010: hazard ratios (HR) with 95% confidence interval (CI) (N=6,042)
The examination of the association between insomnia symptoms and disability retirement was further extended to include sleep duration, with a mean follow-up of ten years. The reference group in this case comprised seven-hour sleepers who reported no or occasional insomnia symptoms. The association of the joint variable comprising insomnia symptoms and sleep duration with disability retirement was stronger and statistically significant only among those with frequent insomnia symptoms (Figure 12, see also Sub-study IV, Table 3). With regard to all-cause disability retirement, among the participants with frequent symptoms most likely to retire were those who slept \( \leq 5 \) hours (HR 3.92, 95% CI 2.57–5.97, adjusted for age and gender), followed by those who slept \( \geq 9 \) hours (HR 3.73, 95% CI 1.97–7.06). The association was similar for disability retirement due to musculoskeletal diseases, and the risk of retirement was strongest among those with frequent insomnia symptoms and sleeping \( \leq 5 \) hours (HR 3.63, 95% CI 1.87–7.06) or \( \geq 9 \) hours (HR 4.47, 95% CI 1.80–11.07). As in the case of the independent associations between insomnia symptoms and disability retirement, the strongest association of the joint sleep variable was with retirement due to mental disorders. Again, the participants most likely to retire were those who had frequent insomnia symptoms and slept \( \leq 5 \) hours (HR 6.58, 95% CI 3.17–13.69) or \( \geq 9 \) hours (HR 8.56, 95% CI 3.36–21.80). The analyses were further adjusted for socio-demographic and work-related factors, and chronic diseases self-reported at baseline. All these had attenuating effects on the studied associations, adjustment for previous mental disorders being the most influential. Nonetheless, all the associations of frequent insomnia symptoms with subsequent disability retirement survived the adjustments.

Sensitivity analyses incorporating both the independent effects of insomnia symptoms as well as the joint associations of the symptoms and sleep duration were run to test the different follow-up and lag times (data not shown). Excluding all disability retirement events occurring 0–6 months, 0–12 months or 0–18 months post-baseline did not significantly alter the main results, especially because most of the events occurred later on during the follow-up (see Sub-study III, Figure 2). The longer the follow-up times, the weaker were the studied associations, which nevertheless remained. Given the general lack of significant gender interactions, the examinations were carried out on gender-pooled data. However, sensitivity analyses stratified by gender indicated that among participants with insomnia symptoms men were somewhat more likely to retire than women.
7 DISCUSSION

The aim in this study was to examine the associations of insomnia with ill health and work disability. Survey data on sleep was linked with longitudinal register data on medication and disability retirement among middle-aged Finnish women and men employed by the City of Helsinki at baseline.

7.1 Main findings

The results revealed consistent associations between insomnia and subsequent health-related outcomes among both women and men. The main findings are summarised below.

First, insomnia was associated with subsequent mental ill health, as indicated by the presence of prescribed psychotropic medication. The associations were largely similar regarding the main medication subgroups examined, and remained after previous psychotropic medication and mental disorders, alongside a number of other factors, had been taken into account.

Second, insomnia was associated with subsequent key cardiovascular risk factors, in other words hypertension and dyslipidemia, as indicated by the presence of prescribed medication. The associations were similar with both types of medication, and remained after adjustments for previous cardiovascular medication, diabetes and health behaviours, for example.

Third, insomnia was associated with subsequent disability retirement. The associations were clear for all-cause disability retirement and retirement due to musculoskeletal diseases, but especially strong with retirement due to mental disorders. When the examination was extended to include the joint effects of insomnia and sleep duration, the contribution of insomnia was dominant. The associations remained following adjustments for socio-demographic and work-related factors and health, for example.

Fourth, the above-mentioned associations generally followed a gradient, which was strongest in the association between frequent insomnia symptoms and subsequent health-related outcomes. However, for most of the outcomes the risks also increased among those with occasional or even quite rarely experienced symptoms compared with those who reported no such symptoms.
7.2 Interpretation of the findings

7.2.1 Insomnia and ill health

Insomnia, indicated by difficulties falling asleep, difficulties staying asleep and non-restorative sleep, was examined in connection with two key subdomains of ill health. The investigation covered mental ill health and cardiovascular risk factors, and medication was used as their indicator.

Insomnia and mental health

The results revealed an association between insomnia and subsequent psychotropic medication. The medication was prescribed by a physician, based on a medical examination, and could thus be considered an indicator of mental ill health. Associations between insomnia and mental health are reported in many previous studies based on a variety of outcome indicators such as psychological inventories, diagnostic interviews or sickness absences due to mental disorders (Salo et al., 2010; Baglioni et al., 2011a). A few previous longitudinal studies included psychotropic medication among their indicators of healthcare (Simon and VonKorff, 1997; Hayward et al., 2010; Salo et al., 2012a). The results of the present study are in line with these previous findings in terms of identifying associations between insomnia and subsequent mental ill health. The associations between insomnia and subsequent mental-health indicators consistently followed a gradient in the present study: even the most prevalent, quite rarely experienced insomnia symptoms increased the risk of medication, and the risks were strongest among those with frequent symptoms. This is in line with the findings of another Finnish study in which a three-category measure of insomnia was used (Salo et al., 2012a). The other earlier longitudinal studies did not examine occasional insomnia symptoms, but relied on dichotomous measures of the existence of frequent symptoms. Although the results of the present study indicate a higher prevalence of both insomnia and psychotropic medication among women than men, the associations with medication did not differ noticeably between them. The effects of insomnia were slightly stronger among men with regard to any psychotropic medication and antidepressants. A recent Finnish study reported similar overall results regarding gender: the researchers looked for possible gender interactions in the association between insomnia and subsequent treatment for depression, and found none (Salo et al., 2012a). Previous studies have not reported results stratified by gender.

Given the results of previous studies on the overall associations between insomnia and mental health, the associations revealed in the present study were largely to be expected (Sivertsen et al., 2009b; Benca, 2011). The findings support the recent view of insomnia as a predictor of mental disorders (Baglioni et al., 2011a; Sivertsen et al.,
Particularly strong associations with subsequent depression, which is the most prevalent mental disorder, have been reported (Pulkki-Råback et al., 2012), and even a causal association has been proposed (Turek, 2005). Results regarding the exact role of insomnia on the aetiological pathway to depression are still inconclusive. Preceding insomnia symptoms could be interpreted as inducing depression on the one hand, or as the first markers of a beginning depression on the other (Baglioni et al., 2011a). The overall associations between insomnia and mental disorders are bidirectional. In addition to primary insomnia that exists co-morbidly with mental disorders, secondary insomnia may be a symptom of these disorders. The fact that insomnia symptoms are included in the symptomology of many mental disorders may also lead to an overlap or circular argumentation in the search for causes and consequences (American Psychiatric Association, 2000). There has been discussion about exactly what mechanisms operate between insomnia and mental disorders. Chronic sleep loss, often associated with insomnia, may lead to diminishing pleasure in life (Gujar et al., 2011), which is one of the characteristics of depression (van der Helm and Walker, 2009). People with insomnia also tend to become anxious about not sleeping, and anxiety, in turn, is associated with an increased risk of depression (Lamers et al., 2011). There are also hypotheses explaining the possible neurobiological pathways between insomnia and mental disorders, including neurotransmitter (e.g., serotonin, norepinephrine and dopamine) imbalance, changes in brain activity, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and genetic polymorphisms (Peterson and Benca, 2011).

Similar associations between insomnia and different types of psychotropic medication were identified in this study. This finding implies a comparable influence of insomnia on subsequent mental health in general. Given that the main indication of hypnotics is in the treatment of insomnia, a strong association between the two could be assumed. This may somewhat exaggerate the strength of the overall associations of insomnia with psychotropic medication, however. Nevertheless, it would be virtually impossible to separate and exclude from the outcome all the medication used to treat insomnia, of which there is a great variety. In addition to hypnotics, examples include sedative antidepressants, antipsychotics such as quetiapine, and neuroleptics with sedative effects (Morin and Wooten, 1996; Omvik et al., 2010). Furthermore, the noted association was even stronger with antidepressants than with the medication group including hypnotics. Some of the previous studies examined different medications separately. In contrast to the present findings, the results of a study carried out among British general practice patients revealed, after full adjustments, an association between insomnia and increased risk only in the case of hypnotics (Hayward et al., 2010). According to an earlier US study, which did not examine the associations of insomnia with different types of psychotropic medication, the prevalence of both antidepressants and benzodiazepines during the follow-up was similarly higher among those with insomnia symptoms compared with participants without these symptoms (Simon and VonKorff, 1997). A recent Finnish study focused on the treatment of depression, thus
including only antidepressant medication in the outcome (Salo et al., 2012a). The results are not presented separately for medication, but the study revealed associations between insomnia and subsequent treatment for depression.

Many participants of the present study had previously taken psychotropic medication, which was strongly associated with medication during follow-up, as were previous mental disorders: these two measures were largely overlapping. Nevertheless, even when both of these factors were taken into account, insomnia was still associated with subsequent psychotropic medication: this finding supports the independence of the association. No adjustments were made for previous psychotropic medication in the earlier studies. However, mental health at or before baseline was taken into account by different means, either excluding those with previous depression and adjusting for baseline psychological distress and anxiety (Salo et al., 2012a), or stratifying the examination by baseline anxiety or depression (Simon and VonKorff, 1997; Hayward et al., 2010). One of these studies reported a higher prevalence of psychotropic medication among those with both insomnia and depression (Simon and VonKorff, 1997). The other study also examined the associations, the results revealing a stronger association between insomnia and both hypnotics and anxiolytics among those without baseline depression or anxiety than among those with these conditions, whereas the differences were negligible with regard to antidepressants (Hayward et al., 2010). The third study did not separately report the effects of adjusting for psychological distress and anxiety (Salo et al., 2012a). Research on psychotropic medication patterns has shown that previous mental disorders and previous medication are strongly associated with subsequent psychotropic medication (Colman et al., 2008), because mental disorders tend to be persistent (Ohayon et al., 1998).

**Insomnia and key cardiovascular risk factors**

According to the results of this study, insomnia is associated with subsequent hypertension and dyslipidemia, which are key risk factors for cardiovascular disease, as indicated by medication for these conditions. In this the findings comply with those concerning mental ill health. In the case of hypertension, the finding is in line with those reported in most previous longitudinal studies focusing on medication (Suka et al., 2003; Phillips and Mannino, 2007; Fernandez-Mendoza et al., 2012). Phillips et al. (2009), however, did not find associations between insomnia and hypertension, but their cohort differed substantially from the present one in that it consisted of older adults and was enriched with African Americans. Furthermore and in contrast to the present study, the only previous study examining insomnia in connection with subsequent dyslipidemia failed to show any association between insomnia and either dyslipidemia or hypertension (Troxel et al., 2010). Again, the explanation for this difference could lie at least partly in the two cohorts, which differed substantially in ethnic composition. Both insomnia and hypertension are
clearly more prevalent in black populations, which could also somehow affect their associations (Egan et al., 2010; Pigeon et al., 2011).

Similar associations between insomnia and both hypertension and dyslipidemia were found in the present study. Again, the pattern generally followed a gradient by the frequency of insomnia symptoms. Even those rarely experiencing such symptoms faced an increased risk of hypertension, whereas the risk of dyslipidemia was higher among those with at least occasional symptoms. These findings are in line with those reported in a previous study on hypertension that used a three-category measure of insomnia: the risk of hypertension increased by the duration of insomnia symptoms (Fernandez-Mendoza et al., 2012). Most previous studies used a dichotomous measure of insomnia. The associations found in the present study were fairly similar among women and men. Potential gender differences were noted in that insomnia was somewhat more strongly associated with subsequent hypertension among men than women, whereas the effect was the other way round for dyslipidemia: the associations were stronger among women. The main findings of this study are in line with those reported in previous studies in identifying no notable gender differences in the associations between insomnia and hypertension or dyslipidemia (Phillips 2009, Troxel 2010). The results in most previous studies were not stratified by gender. Gender is a risk factor for both hypertension and dyslipidemia, although its effects vary in different age groups, especially regarding hypertension (Ilanne-Parikka et al., 2004; Doumas et al., 2013). In any case, it should be taken into account. Nevertheless, as the present and previous studies show, gender may not play an especially important role in the associations of insomnia with hypertension and dyslipidemia.

There are several possible pathways linking insomnia, and the loss of sleep often associated with it, with subsequent cardiovascular health. Among them are biological mechanisms, such as changes in the autonomic nervous system or in the immune and neuroendocrine systems, including the HPA axis (McEwen, 2006; Mezick et al., 2011; Aho et al., 2013). On the behavioural level, associations have been found between insomnia and many adverse health behaviours, unhealthier food choices and overall diet (Janson et al., 2001; Grandner et al., 2014).

Other key factors associated with the risk of cardiovascular outcomes were taken into account in the present study. In addition to age and gender, these included diabetes, several different health behaviours and work-related factors. Given that hypertension and dyslipidemia are chronic conditions, previous medication for them is a strong predictor of subsequent medication, thus it was also taken into account. The main associations remained following the adjustments. Similar covariates have been used in previous studies, and no remarkable effects have been reported.
7.2.2 Insomnia and disability retirement

Insomnia was found in this study to be associated with an increased risk of subsequent disability retirement, whether due to any cause, musculoskeletal diseases or mental disorders. These results are in line with those reported in other studies in this area (Eriksen et al., 2001; Sivertsen et al., 2006; Øverland et al., 2008b; Sivertsen et al., 2009d; Salo et al., 2010; Canivet et al., 2013). The evaluation of work disability is based on the individual's health, ability to function and working conditions, and previous studies on insomnia report an association with all these factors (Ohayon, 2002; Lallukka et al., 2010). Thus it is likely that insomnia is associated with disability retirement thorough several different pathways.

The associations between insomnia and subsequent disability retirement identified in this study followed a consistent gradient, the risk of retirement increasing by the frequency of symptoms. This finding is in line with those of previous studies (Eriksen et al., 2001; Salo et al., 2010). According to a Norwegian study, which did not examine the frequency of symptoms, those with insomnia faced an increased risk of disability retirement compared with good sleepers, and the risk was highest among those with insomnia-related impaired daytime functioning (Sivertsen et al., 2006). The other studies included in the review used dichotomous measures of insomnia (Øverland et al., 2008b; Sivertsen et al., 2009d; Canivet et al., 2013). One of the aims of the present study was to explore the possible diverging effects of the different insomnia symptoms, which were therefore examined separately to complement the summary measure. Although some minor differences were noted, the overall associations followed similar patterns. The strongest associations of subsequent disability retirement were with frequent difficulties falling asleep and non-restorative sleep. Difficulties falling asleep also stood out in a recent study conducted in Sweden (Canivet et al., 2013). Some gender- and cause-specific effects were noted, specifically an association with retirement due to cardiovascular disorders among women, and due to mental disorders among men, but not vice versa. The differences between the above-mentioned and the present study may be partly attributable to the fact that the former was conducted in a selected, healthy population, excluding all those with previous ill health, whereas this study applied no such exclusion criteria. None of the other longitudinal studies on disability retirement presented separate results for different insomnia symptoms, although most of them used some measure that assessed several symptoms (Sivertsen et al., 2006; Øverland et al., 2008b; Sivertsen et al., 2009d; Salo et al., 2010). The present findings are in line with those of previous longitudinal studies based on different outcomes of work disability, such as sickness absence, in that they did not reveal large differences between separate insomnia symptoms, either (Vahtera et al., 2006). The present investigation involved gender-pooled data. Additional sensitivity analyses implied that the associations were generally similar for both genders, albeit slightly stronger among men. The main results are in line with those reported in most other studies in this area, which do not note differences between women and men, either. Most of them
relied on similarly pooled data and adjusted for gender. The only exception is the above-mentioned study from Sweden, in which the analyses were stratified by gender, and gender differences in the studied associations were found (Canivet et al., 2013).

Particularly strong associations between insomnia and subsequent retirement due to mental disorders were found in the present study. This is not surprising given the ample evidence of associations between insomnia and mental health, insomnia predicting depression in particular (Baglioni et al., 2011a). Depression was the most prevalent diagnosis among those retiring due to mental disorders. Nevertheless, it is worth noting that insomnia was also associated with retirement related to musculoskeletal diseases, a relationship that is perhaps not so obvious. There is some previous cross-sectional evidence on the association between insomnia and musculoskeletal disease (Sivertsen et al., 2009b). Pain may possibly play one of the key roles in this relationship, as previous studies have shown it to be associated with both insomnia and musculoskeletal diseases (Brooks, 2006; Sivertsen et al., 2013). The association of pain with insomnia tends to be seen as bidirectional, with pain interfering with sleep and, vice versa, insomnia worsening the pain experience (Tang et al., 2012). According to a recent study based partly on the present data, insomnia and pain are jointly associated with an increased risk of subsequent work disability, as indicated by sickness absence and disability retirement (Lallukka et al., 2013b). However, given that the temporal order of insomnia and pain is still under debate (Tang et al., 2012), and that pain might act as a mediator in the association between insomnia and work disability, the decision was made not to adjust for pain in this study.

The present findings are in line with those of previous research. As reported in a recent Finnish study, frequent insomnia symptoms were associated with work disability in most of the diagnostic categories examined (Salo et al., 2010), the strongest associations being with disability related to mental disorders. The above-mentioned recent Swedish study reported an association between insomnia symptoms and retirement due to musculoskeletal diseases especially among women, and due to mental disorders among men (Canivet et al., 2013). The associations between insomnia and disability retirement due to different diagnoses were not modelled in a recent Norwegian study, but the incidence of retirement due to mental disorders was largest among those with depression alone or combined with insomnia, compared with those with only insomnia (Øverland et al., 2008b). A corresponding finding was reported in another Norwegian study, in which the incidence of disability retirement due to mental disorders was largest among those with insomnia and daytime work impairment, compared to those with insomnia but no impairment, or with no insomnia (Sivertsen et al., 2006).

The investigation was extended to include sleep quantity in addition to quality in order to give a deeper view of the associations between sleep and disability.
retirement. This involved assessing the joint effects of insomnia and sleep duration, which turned out to be jointly associated with subsequent disability retirement. Insomnia was dominant in this association, as the risk of disability retirement increased among all groups with frequent insomnia symptoms, regardless of their sleep duration. Nevertheless, among the subjects with frequent insomnia symptoms those with short or long sleep duration faced the biggest risk, following the classic U-shaped pattern found in most studies on sleep duration. No larger differences were noted between short and long duration. No previous studies have examined the joint associations of insomnia and sleep duration with work disability outcomes. With regard to insomnia these results are in line with those of other studies in this area (Eriksen et al., 2001; Sivertsen et al., 2006; Øverland et al., 2008b; Sivertsen et al., 2009d; Salo et al., 2010; Canivet et al., 2013). Two of these also examined the independent association of sleep duration with subsequent disability retirement: Sivertsen et al. (2009d) found in the context of Norway that long but not short sleep duration was associated with disability retirement, and Canivet et al. (2013) reported a similar finding in their Swedish study that long sleep duration and disability retirement were associated among women, but not among men.

The research group involved in the present research recently examined the joint associations of insomnia and sleep duration with subsequent sickness absence of various lengths (Lallukka et al., 2013a). The findings were in line with the results on disability retirement reported here. Most previous longitudinal studies focusing on the joint associations between insomnia and sleep duration concern either all-cause or CVD mortality, or CVD morbidity (see e.g., Fernandez-Mendoza et al., 2012; Westerlund et al., 2013). The findings are somewhat inconsistent in that insomnia dominates the associations in some of the studies, whereas sleep duration has a stronger effect in others. However, people with insomnia are also more likely to report shorter sleep duration (Sivertsen et al., 2009d), which could affect the joint associations. It is also proposed that short sleep duration may be a biological marker of the severity of insomnia, and thus at least partly explains the increased health risks among those suffering from both insomnia and short sleep (Vgontzas et al., 2013).

The key socio-demographic and work-related risk factors of disability retirement were taken into account in the present examination of the associations between sleep and disability retirement, alongside indicators of health and health behaviours. The factors that affected these associations most were baseline physical working conditions and health. Of the health factors previous mental disorders played an important role, although previous musculoskeletal diseases also had an effect, especially on the associations between insomnia and disability retirement due to musculoskeletal diseases. Previous studies on the associations of insomnia or sleep duration with subsequent work disability largely relied on similar adjustments. In the case of two Norwegian studies, adjusting for mental and physical health as well as pain attenuated the studied associations the most (Sivertsen et al., 2006; Sivertsen et al., 2009d). Work-related factors were taken into account in only some of the
previous studies examining the associations between sleep and work disability, and no remarkable effects were noted following adjustment for these factors (Eriksen et al., 2001; Sivertsen et al., 2006; Salo et al., 2010; Canivet et al., 2013). The fact that working conditions and health appear to affect the associations between insomnia and disability retirement is understandable, as both are key evaluative elements in the granting of disability retirement. It is also possible that physical working conditions have an adverse effect on sleep and bring on the ill health associated with it, possibly leading to disability retirement. It was found in a recent study based on the present data that physical and psychosocial working conditions were associated with subsequent disability retirement (Lahelma et al., 2012).

7.3 Methodological considerations

7.3.1 Data sources

The data for Helsinki Heath Study baseline survey were collected from postal questionnaires distributed to 40–60-year-old employees of the City of Helsinki. The survey data was longitudinally linked with register data on prescribed reimbursed medication and disability retirement. Follow-up times ranging from five years in the medication studies up to eight and ten years in the studies on disability retirement facilitated analysis of the longitudinal associations of insomnia with health and work disability. Generalization of the results to the wider Finnish working-age population is not warranted because the cohort in question only included predominantly female middle-aged municipal employees living in the metropolitan area. However, the City of Helsinki is the single largest employer in Finland with almost 40,000 employees in a diversity of manual and non-manual occupations (City of Helsinki: Annual Report, 2011). The proportion of women in the data reflects the gender distribution in the Finnish municipal sector (KT: Local government employers, 2013).

This large and contemporary cohort of middle-aged municipal employees provided a good basis for the study of the associations of insomnia with subsequent health and work disability. Insomnia symptoms are prevalent in this age group, especially in the working population. The same applies to the studied health outcomes – mental disorders, hypertension and dyslipidemia, as well as musculoskeletal disease, which is the most common cause of disability retirement. Moreover, the incidence of disability retirement increases sharply in the age group in question (Pensola et al., 2010). The wide range of occupations within the City of Helsinki allowed examination of the effects of insomnia more generally among municipal employees, not restricted to certain types of occupation.

The survey response rate was 67 per cent, which is in line with many recent (Finnish) questionnaire surveys (Tolonen et al., 2006). Of the survey respondents, 74 per cent
gave written informed consent for register linkage. According to analyses of non-
response and consent giving carried out within the Helsinki Health Study data,
although there are some socio-demographic differences, the data nevertheless
satisfactorily represent the target population (Laaksonen et al., 2008; Lahelma et al.,
2013).

All the study participants were employed at baseline and thus presumably healthier
than the general population of the same age group. A healthy worker effect is
probable in that healthier individuals are more likely to be employed than their less
healthy peers (Pearce et al., 2007). This could also apply to insomnia, those with the
most severe symptoms possibly already being outside the workforce.

On account of the low proportion of men in the cohort most of the analyses were
carried out with gender-pooled data. Nevertheless, given that gender is a major risk
factor in the aetiology of the examined health outcomes, further studies involving
more male participants are warranted to confirm whether or not there are
differences between women and men regarding the associations found in this study.

The disadvantage of using register-based outcomes is that the researcher does not
usually have a say in the variables included and cannot otherwise influence the
gathering of the data. Nevertheless, the data in health registers are basically
collected for administrative purposes to be used as the basis of monetary
reimbursement, and are therefore highly accurate (Gissler and Haukka, 2004; Rikala
et al., 2010). National registers are also extensive, giving complete coverage of those
giving permission for data linkage.

7.3.2 The measurement of sleep

Insomnia

The assessment of insomnia was based on self-reported symptoms that were
measured only once, at baseline. It has been noted that those with insomnia tend to
misperceive their sleep (Harvey and Tang, 2012). Nevertheless, self-reported
measures are generally considered suitable for the study of insomnia symptoms,
especially in large-scale epidemiological studies in which more objective
measurements would not be feasible (Moul et al., 2004). Most previous studies
examining the longitudinal associations between insomnia, medication and disability
retirement also relied on a single measurement of insomnia symptoms. A recent
study conducted with the HHS cohort found insomnia symptoms to be very persistent
over a follow-up period of between five and seven years (Lallukka et al., 2012a).

The symptoms included in the Jenkins Sleep Questionnaire (JSQ) are not exclusively
specific to insomnia. Although the assessed symptoms are certainly characteristic of
the condition, they could also be related to other sleep disturbances such as obstructive sleep apnoea and restless legs syndrome (Trophy, 2011), and other illnesses such as chronic obstructive pulmonary disease (Collop, 2010). Another unfortunate limitation of the JSQ is that it does not assess possible daytime impairment. The diagnostic criterion for primary insomnia requires that “the sleep disturbance or daytime fatigue causes clinically significant distress or impairment in social, occupational, or other important areas of functioning” (American Psychiatric Association, 2000). Previous studies have shown stronger associations between insomnia and health-related outcomes when daytime impairment is a factor (Sivertsen et al., 2006). However, the JSQ was developed for clinical and epidemiological research purposes (Jenkins et al., 1988). Similar measures have been used in various international studies of insomnia (Moul et al., 2004). Although the JSQ lacks assessment for daytime impairment, it covers the other key symptoms included in the diagnostic criteria for primary insomnia (American Psychiatric Association, 2000). The Cronbach's alpha of the JSQ was 0.84 in the present data, indicating internal consistency and reliability. It is also in line with previous studies using the same measure. The Cronbach's alpha in Jenkins' original measure-validation study conducted among male employees was 0.79 (Jenkins et al., 1988).

It was necessary to make extensive adjustments when examining the effects of insomnia on subsequent ill health and work disability, such as for socio-demographic factors, physical and psychosocial working conditions, previous health and health behaviours. Nevertheless, there are other factors that would have been valuable additions but were not included in the measurements. One such factor is coffee consumption. Coffee contains caffeine, which promotes wakefulness and thus disrupts sleep (Porkka-Heiskanen et al., 2013). Given that Finland has the world’s highest per-capita coffee consumption, taking coffee into account in the examination of insomnia would be well warranted (International Coffee Council, 2012).

Sleep duration

Sleep duration, examined jointly with insomnia in Sub-study IV, was also assessed only at baseline and on a single-item self-report question about sleep during weekdays, with whole hours as response alternatives. The focus on weekdays could somewhat underestimate average sleep duration in that weekends and holidays are ignored. Compared with objective measurements such as actigraphs and polysomnography, self-reported sleep duration may be liable to certain bias (Lauderdale et al., 2008). Self-reported sleep duration is generally overestimated compared with objective measures on the one hand, and on the other hand, individuals with insomnia tend to underestimate their sleep duration more than those sleeping well (Means et al., 2003). However, as with insomnia, self-reports are more common in epidemiological studies, as it is often not feasible to use objective measurements on a large number of participants. Crude measures such as this also
tend to be accurate enough for interpreting the results on a more general level, and for comparison among groups with short, average and long sleep duration. Although a single measure of sleep duration was used in this case, it was found in a previous study on the same cohort that sleep duration remained relatively unchanged for a large proportion of the participants over a follow-up period of between five and seven years (Lyytikäinen et al., 2010).

7.3.3 The measurement of ill health and work disability

Medication

Objective, register-based data on medication was used in this study as an indicator of certain conditions, in other words mental disorders, or hypertension or dyslipidemia. However, the intention was not to make any direct diagnostic deductions or claims based on this information, especially because the data do not include information on the diagnoses on which the physicians based their prescriptions. There are also various intended indications for all the medications used in this study as outcomes (Gardarsdottir et al., 2007; Sihvo et al., 2008). Nevertheless, although the exact indication of each prescribed medication is not known, it is fairly safe to assume that the majority of prescribed psychotropic medication is intended for the treatment of mental disorders and, respectively, the examined cardiovascular medications for cardiovascular conditions. Especially in the latter case the most prevalent indications of the medications selected for the study point clearly to cardiovascular conditions, more precisely to the treatment of hypertension and dyslipidemia. Moreover, the fact that all the included medication had been prescribed by a physician indicates that the severity of the condition – whether psychiatric or cardiovascular – experienced by the individuals in question had been considered clinically significant.

Neither the amount of purchased medication nor the number of purchase events were used as outcomes, although these data were available. Sensitivity analyses using the data were carried out, but as they did not extend the examination in any relevant way, they were excluded from the actual analyses. Over-the-counter medications and non-reimbursed prescribed medication purchases were not included in the data either, but this is not likely to have had any substantial effects given the marginal prevalence of the latter, in particular, in Finland. It is also worth noting that the use of psychotropic medication was not measured, merely the reimbursed purchases of prescribed medication. Previous studies show considerable non-adherence to and noncompliance with psychotropic medication in particular (Julius et al., 2009; Vartiainen et al., 2009), although adherence is likely to be somewhat better among those who have actually purchased the medication. However, not having data on usage is not a significant loss regarding the main interest of this study, ill health: the fact that a physician found it necessary to issue a prescription indicates the existence of some kind of disorder that required treatment.
Neither does medication equal the actual and total psychiatric and cardiovascular morbidity among the study participants. Regarding both mental and cardiovascular health, a fair share of these conditions remains undiagnosed and thus unmedicated. Previous studies indicate that most of those with mental disorders (Hämäläinen et al., 2004; Hämäläinen et al., 2009) do not seek treatment for their condition, and a similar tendency appears to be present among those with hypertension and dyslipidemia (Kastarinen et al., 2009; Vartiainen et al., 2009). In that sense, using medication as the indicator leads to selection because the data only cover those who have sought help in connection with their symptoms.

Adjusting for pre-existing ill health – indicated by medication – in the examination of subsequent health outcomes may potentially lead to partial overlap of the independent and dependent variables. However, the associations in question largely remained after these adjustments. Similar adjustments have been made in previous studies. In the case of health-related outcomes, adjusting for health at and before baseline brings out the independent effects of insomnia more clearly.

Finally, the medication-outcome measures were all defined as at least one reimbursed purchase of the medication in question during the follow-up period. Only one reimbursed prescription is not a very strong indicator of ill health, compared with more continuous medication. Nevertheless, in reality most study participants with psychotropic or cardiovascular medication made several purchases during the follow-up. Moreover, even one purchase of medication prescribed by a physician is quite likely to reflect some kind of health problem. The number of purchases of psychotropic medication did not notably vary by the frequency of insomnia symptoms.

_Disability retirement_

Register-based information on disability retirement is an objective and valid indicator of severe long-term – usually permanent – work disability. The data are extensive and accurate, having been gathered for administrative purposes. The data on disability retirement also include detailed diagnostic information on which the granting of the retirement is based. Yet, although the retirement data include information on the diagnoses, they do not give an overall picture of the circumstances leading up to the retirement decision: the evaluation takes into account not only the health status of the individual seeking retirement, but also his or her working conditions and ability to function in the job. Thus, disability retirement is always a relative outcome: of two individuals with similar health conditions but different tasks one might be retired due to disability, the other still working. In order to take the key factors of the evaluation into account in the examination, adjustments were made for overall working conditions and work-time arrangements, as well as for issues related to psychosocial wellbeing at work, alongside health.
In Finland, granted disability retirement may be permanent or temporary, full- or part-time, all of which are included in the retirement outcome. Nevertheless, for the most part the retirement is permanent and full-time. Additionally, only the primary diagnosis leading to retirement is considered. There may also be secondary diagnoses that are registered – or secondary diagnoses that are not registered (Komulainen, 2012). Co-morbidities are common, and there may be some conventions or social-desirability issues regarding the primacy of certain diagnoses over others – such as a preference for registering musculoskeletal diseases as the primary cause instead of alcoholism. However, according to the instructions the evaluator should register the main medical cause of retirement as the primary one.

Some of the study participants may already have been in the process of applying for disability retirement when completing the baseline survey, which could be a potential cause of protopathic bias, in other words of the outcome affecting the exposure. In order to avoid this, sensitivity analyses were carried out testing different lag times. All disability retirement events occurring 0–6 months, 0–12 months, or 0–18 months post-baseline were excluded one at a time. The different lag times did not alter the main results, particularly because a large proportion of the retirement events occurred later on during the follow-up. Different follow-up times were also tested, and although the associations became weaker the longer the follow-up time, they nevertheless remained.

7.4 An overall view on insomnia, ill health and work disability

According to the results of this study, insomnia is associated with subsequent ill health and work disability among middle-aged employees. It is common among the working-aged, and because of its adverse effects on functioning it is among the main causes of work incapacity. One fifth of the study participants reported experiencing insomnia symptoms frequently, and an additional one-third occasionally. Insomnia is a burden not only for those who suffer personally from it, but also for their families, employers and the public economy (Metlaine et al., 2005; Léger and Bayon, 2010). Previous social-epidemiological research on the associations of sleep with ill health and work disability has concentrated on the effects of sleep duration and sleep apnoea, relying largely on cross-sectional data, and the use of register-based outcomes is rare. The strengths of the present study include its longitudinal design and the use of register-based data on ill health and work disability.

Insomnia was found to be consistently associated with subsequent health-related outcomes. The impact of insomnia symptoms was essentially similar on psychotropic and cardiovascular medication and disability retirement, especially concerning the gradient noted in all the studied associations. The more frequent the symptoms, the higher were the health risks. There may well be some shared mechanisms in the
associations between insomnia and the different outcomes under investigation, although they have also their own distinctive pathways.

The findings from this study add to the evidence on the associations of insomnia with subsequent ill health and work disability: the effect of sleep on work disability in particular has been poorly understood. The results provide novel evidence of the associations of insomnia symptoms with disability retirement. This investigation covered different causes of disability retirement, the individual effects of different insomnia symptoms, and the joint associations of insomnia and sleep duration with disability retirement. Examining sleep quality together with sleep quantity gives a broader view of the overall effects of sleep on health-related outcomes, and facilitates more detailed identification of the sleep subtypes that carry the highest health risks. Further novel findings of the study include the association between insomnia and dyslipidemia, on which previous research is almost non-existent. Thus there is a clear need for further studies focusing on insomnia and cardiovascular risk factors.

The results revealed a consistent gradient in the studied associations by the frequency of insomnia symptoms. The strongest health risks were among those with frequent symptoms, but they were also marked among those with more occasional symptoms, thus putting a larger population at risk. Further research would benefit from using more detailed measures of insomnia instead of dichotomous ones, which seem still to dominate in this field. The findings of this study did not indicate any significant gender differences in the main associations of insomnia with subsequent ill health and work disability. However, given the indications of some differences in the strength of the associations, there is a need for further studies examining the role of gender in more depth. There may some gender differences in the aetiology of insomnia that could, in turn, affect its associations with health.

In addition to the fact that insomnia is common among the working-aged, the outcomes of this study also reflect key public health problems. The prevalence of mental disorders among the working-aged is high (Pulkki-Råback et al., 2012). Hypertension and dyslipidemia, the key cardiovascular risk factors, are common in the studied age group, too (Graham et al., 2007). The ageing of the population constitutes a substantial social challenge, and early retirement due to disability adds considerably to the societal costs (Léger and Bayon, 2010). Thus, insomnia associated with these adverse health outcomes should be better recognized in the future.
7.5 Conclusions and policy implications

The results of this study reveal consistent and graded associations between insomnia and subsequent health-related outcomes. These findings imply that insomnia should be counted among other key risk factors of ill health and work disability.

The public health significance of this study lies in the opportunity to make use of the gathered evidence in the prevention of insomnia, and the ill health and work disability associated with it. The findings could be exploited in primary and occupational healthcare with a view to reducing the incidence of insomnia-related mental and somatic ill health, the redundant use of medication and early retirement. Such measures could support the health and wellbeing of those with insomnia symptoms and their families, and help in reducing the cost to employers and society of the increased utilization of healthcare services associated with insomnia. All this calls for the early detection of insomnia and investment in its early prevention – at least preventing occasional symptoms from turning chronic – and treatment. Treatment, in turn, could contribute to the prevention of subsequent mental disorders (Baglioni et al., 2011b), and if effective could also be expected to reduce the risk of a number of other related conditions (Matteson-Rusby et al., 2010). In addition to promoting better sleep hygiene – in other words good sleep habits, and controlling the behavioural and environmental factors that may interfere with sleep – the most commonly used and researched treatments are cognitive behavioural therapy for insomnia (CBT-I), and different sleep medications (Working group appointed by the Finnish Medical Society Duodecim and the Finnish Sleep Research Society, 2008; Buysse, 2013).

The contribution of this study is in adding to the evidence base of the associations of sleep with ill health and work disability. Insomnia is among the risk factors for mental and cardiovascular ill health, as well as for disability retirement. Recognizing its impact might help in preventing the loss of work ability and early exit from work due to disability, and in supporting the ageing working population’s health and quality of life.
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