Musculoskeletal diagnoses account the most of the disability pensions along with mental diagnoses. This follow-up study of Finnish and Swedish working age twins investigated various sociodemographic, health and work related factors as predictors of disability pension due to musculoskeletal diagnoses. The findings indicate that negative health behaviours and physically heavy work might be potential targets for interventions to prevent early exit from working life due to musculoskeletal diagnoses.
Risk factors for disability pension due to musculoskeletal diagnoses
SANNA KÄRKKÄINEN

Risk factors for disability pension due to musculoskeletal diagnoses

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ABSTRACT

Musculoskeletal diagnoses (MSD) are the second most common diagnoses leading to a disability pension (DP) after mental health diagnoses. They have not only severe consequences for the individual sufferer but also major financial implications for employers and society as a whole. Relatively few studies on the risk factors for granting a DP due to MSD have been able to access prolonged (several decades) follow-up times that would make it possible to identify potential risk factors early in the adult life course, that is, among people in their 30s and 40s. Moreover, by studying twins, familial factors, including genetic factors and the shared family environment of twin siblings, can be taken into account. The aim of this thesis was to investigate sociodemographic, health and work related factors and stressful life events as risk factors for DP due to MSD, taking into account various covariates and familial factors as possible confounders.

This thesis included data from two population-based twin cohorts: Older Finnish Twin Cohort and Swedish Twin Registry. Information on DP with international diagnosis codes (ICD-10 codes M00–M99) was available from national registers. From the Finnish twin cohort, those aged 18–64 years at the time of the baseline questionnaire (1975), were included (n=24 043, mean age 39 years), and followed until 2004. From the Swedish twin cohort, individuals in the age range 40–64 years at the time of the baseline interview, between the years 1998–2003, were included (n=27 165, mean age 55 years), and followed until 2013. Cox proportional hazards models were used to calculate hazard ratios with 95% confidence intervals.

The number of cases varied from 600 to 1338 participants being granted DP due to MSD during follow-up depending on specific selection criteria in the substudies included in this thesis, such as concentrating on those at work at baseline, or to a specific diagnosis group within the MSD.

Several strong and independent predictive factors were found for DP due to MSD. Sociodemographic factors high socioeconomic status and additional years of education both decreased the risk of DP due to MSD. From the health related factors, self-reported pain, the presence of any chronic disease, being overweight and smoking all increased the risk of future DP due to MSD. With respect to the work related factors, monotonous work and physically heavy work as well as night work increased the risk of DP due to MSD, although familial confounding could not be ruled out in this last association. Of the stressful life events, illness or injury requiring over three weeks of work disability was identified as a risk factor for DP due to MSD. Stressful family related life events increased the risk of future DP due to MSD among discordant twins, which points to a role of familial confounding in this association.

Overall, the results of this thesis indicate that high sociodemographic status decreases the risk of DP due to MSD, whereas negative health behaviours, physically heavy work load and family related stressful life events increase this risk. These predictive factors are mainly independent of familial factors and were identified early during adult life. These findings
imply that preventive actions are available to decrease marginalization from working life because of DP due to MSD, and furthermore, that these actions should be in place early in working life and continue throughout the working years.

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TIIVISTELMÄ


Väitöskyö koostuu neljästä osatyöstä. Perustuen kunkin osatyön tarkempaan valintakriteeriihin, kuten erityiseen diagnoosiryhmään tai seurannan alussa työelämässä oleviin, tapauksien määrä vaihteli osatöittäin 600 ja 1338 välillä.


Tutkimuksen tulokset osoittavat, että negatiivinen terveyskäyttäytyminen, fyysinen työkoimmitus ja kuormittavat elämäntapahtumat ovat riskitekijöitä tuki- ja liikuntaelindiagnoosien perusteella myönnettyille työkyvyttömyyseläkkeille. Nämä
ennustetekijät ovat pääosin riippumattomia muista tekijöistä tai perheitäisyydestä, ja ne voidaan tunnistaa jo varhaisaikuisuudessa. Tulosten valossa tuki- ja liikuntaelindiaagnoosien perusteella myönnettyjä työkyvyttömyyseläkkeitä on mahdollista vähentää ennaltaehkäisevin toimin.

Luokitus: WA 30, WA 900, WE 140
Yleinen Suomalainen asiasanasto: tuki- ja liikuntaelinten taudit; työkyvyttömyyseläkkeet; riskitekijät; terveyskäyttäytyminen; epidemiologia; kaksostutkimus; kohorttitutkimus; seurantatutkimus; Ruotsi; Suomi
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Kuopio, May 2019

*Sanna Kärkkäinen*
List of the original publications

This dissertation is based on the following original publications:


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<th>Description</th>
</tr>
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<tbody>
<tr>
<td>BMI</td>
<td>Body Mass Index [kg/m²]</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>DP</td>
<td>Disability Pension</td>
</tr>
<tr>
<td>DZ</td>
<td>Dizygotic Twin</td>
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<tr>
<td>HR</td>
<td>Hazard Ratio</td>
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<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
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<td>LBD</td>
<td>Low Back Diagnoses</td>
</tr>
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<td>MIDAS</td>
<td>Micro Data for the Analysis of Social insurance</td>
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<td>MSD</td>
<td>Musculoskeletal Diagnoses</td>
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<td>MZ</td>
<td>Monozygotic Twin</td>
</tr>
<tr>
<td>OA</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>OECD</td>
<td>The Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>RA</td>
<td>Rheumatoid Arthritis</td>
</tr>
<tr>
<td>SALT</td>
<td>Screening Across the Life span Twin study</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>STODS</td>
<td>Swedish Twin project Of Disability pension and Sickness absence</td>
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<tr>
<td>WHO</td>
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XVI
INTRODUCTION

Musculoskeletal disorders are a major global problem, as they have been shown to account for 20% of years lived in disability [1]. The common characteristics of all musculoskeletal disorders are long-term pain and physical disability [2]. Thus, musculoskeletal disorders exert a huge impact at many levels i.e. society as a whole, the workplace as well as the individual sufferer.

The main purpose of a disability pension (DP) is to provide financial support for individuals who cannot work due to a chronic illness [3, 4]. In Finland, the number of newly granted DP due to musculoskeletal diagnoses (MSD) has been approximately 6500 per year in the 2000s [5, 6]. The numbers were highest, over 8700 newly granted DPS due to MSD annually, in 2007 and 2008 [7, 8]. Although there has been a decline in newly granted DP due to MSD in recent years, MSD are still the second largest diagnosis group leading to DP after mental diagnoses [5]. Overall, the incidences of DP due to MSD have remained relatively unchanged during 2000s [9, 10]. Instead, during the years from 1975 until 1995, the incidence number of DP due to MSD show relatively large fluctuations, with the lowest level of incidence cases being in year 1980, and the highest in the year 1991 [9, 11].

During the last decades, working life has changed, for example with working careers becoming more unstable and unpredictable, but also with more employee control over his/her own working times [12, 13]. In the future, it is expected that physically heavy work, which is still rather common both in Finland and Sweden, may decline due to digitalisation. Currently, psychically demanding work is rather common: In 2015, one third of employees in Finland and Sweden reported that their work involved carrying or moving heavy loads [13]. This was most common among employees under 35 years old, of whom 40 to 44% considered their work to involve carrying heavy loads [13].

In Finland, 47 000 people, i.e. 1.4% of the working age population, received a DP due to MSD in the year 2016 [5, 14]. In Sweden, a DP due to MSD was being received by 71 500 people in 2016, i.e. 1.2% of the working age population [15, 16]. In both countries, MSD was the main diagnosis in 22% of DP cases. These numbers reflect the situation in the countries of the Organisation for Economic Co-operation and Development (OECD) in general [17]. The financial burden for society related to MSD includes both direct costs, such as social security benefits and health care expenditures including rehabilitation costs [18], and indirect costs, such as productivity loss due to work disability [19]. In all of the Nordic countries, the granting of a DP is based on similar criteria, where at least a year of sickness absence is required to be eligible to apply for DP. A DP can be granted to a person with a fundamentally reduced work capacity that has lasted for more than a year and is caused by medically confirmed disease [4, 5, 18].

To decrease marginalisation from working life due to musculoskeletal disorders and to prolong healthy working years, there is a need for additional knowledge on which factors predict musculoskeletal disorders. Although evaluating risk factors specific to DP for MSD is not directly attributable to risk factors of chronic musculoskeletal disorders, this approach may provide information on factors of importance for musculoskeletal health in general. If risk factors amenable to intervention are found, this would likely promote further the progress in achieving a decline in the numbers of annually granted DP due to MSD.

Furthermore, health related factors, namely increasing obesity and physical inactivity at population level, are recognised as potentially exerting an influence on prevalence of musculoskeletal disorders [1]. Hence, it seems that musculoskeletal disorders are not only major global concerns themselves, but that they are also linked to other major themes of public health importance [20, 21]. Furthermore, although musculoskeletal disorders are
generally not life-threatening [22, 23], they are considered a major cause of health related suffering [1].

Moreover, being able to decrease the incidences of DP due to MSD, is of particular importance as the population ages, since musculoskeletal disorders are known to become more prevalent with advancing age [5]. Globally, musculoskeletal disorders are expected to increase in countries with ageing populations [1]. Potential routes for successful prevention include both interventions targeted at preventing workers having to work for a long time in tasks promoting a musculoskeletal disorder and interventions aimed at those factors directly known to influence the risk of future DP due to MSD. These would potentially decrease the negative consequences caused by these disorders for individuals and society, including the financial implications at societal, workplace and at individual levels [19]. As MSD is the second most common diagnosis group with regards to DP, actions that reduce the incidences of DP due to MSD would also benefit national efforts to prolong working careers and would reduce health care as well as social security costs.

This PhD thesis investigated those individuals granted DP due to MSD, that is, those who have a medically confirmed musculoskeletal diagnosis that severely impairs their work ability. The follow-up time was three decades at its longest. Moreover, in this thesis, two national twin cohorts with a prospective follow-up design were used to identify factors of importance for future DP due to MSD. In both of these cohorts, comprehensive baseline questionnaire data was combined with register information on DP due to MSD. As the study populations consist of twins, also a familial influence, i.e. the common genetic factors and the shared environment of twin siblings, could be taken into account. As genetic factors have been shown to be responsible for around 35–37% of the variation of receiving a DP due to MSD [24, 25], it is a clear advantage to be able to control for these familial factors.

The general aim of this thesis was to analyse whether selected adulthood factors, including sociodemographic, health and work related factors and stressful life events, are associated with the risk of future DP due to MSD, and furthermore, whether these associations are influenced by confounding due to other covariates or by familial factors. Increased knowledge on factors of importance for DP due to MSD benefits the efforts to identify potential targets for interventions to prevent marginalization from working life due to MSD.
2 REVIEW OF THE LITERATURE

2.1 DISABILITY PENSION DUE TO MUSCULOSKELETAL DIAGNOSES

In all of the Nordic countries, including also Iceland and the Faroe Islands, the grant of a DP is based on similar criteria: A DP can be awarded to a person with fundamentally reduced work capacity that has lasted for more than a year and is caused by a medically confirmed disease [4, 5, 18].

In Finland, 44,000 people received DP benefits based on work incapacity due to MSD; in the year 2016, the majority (21,300) of those were attributable to low back diagnoses (LBD) [26]. In 2015, the majority of those receiving a DP due to MSD were between 55 to 65 years of age, and, considering all those on DP due to MSD, 54% were women, and in those with DP due to LBD, 48% were women [5]. After LBD, the next most common subclasses of MSD were osteoarthritis (OA), which was the main diagnosis for 27% of those with DP due to MSD, and rheumatoid arthritis (RA), that accounted for 7% of all those with DP due to MSD, in the year 2016 [26]. In Sweden, 71,500 persons had been granted a DP due to MSD in the year 2016 [15]. The situation in Finland and Sweden reflects the situation in OECD countries in general [17].

2.1.1 Musculoskeletal disorders

Musculoskeletal disorders are common, with estimates of musculoskeletal disorders, measured as years lived in disability, ranging from 10 to 39% in different countries [1]. Musculoskeletal disorders include a wide range of different conditions, such as low back disorders, disorders of upper extremities and knee and hip OA. Common characteristics to all musculoskeletal disorders include long-term pain and physical disability [2]. Musculoskeletal disorders are a major cause of health and social care expenditure [17, 19], and become more prevalent with advancing age [1].

Musculoskeletal disorders include diagnosis codes M00–M99 of International Classification of Diseases (ICD), 10th revision [27] (Table 1). Although musculoskeletal disorders are not considered life threatening, they have a major influence on working careers, which is reflected in the numbers of sickness absence days and the grant of DP due to MSD [17, 28]. Although chronic musculoskeletal pain is not thought to influence life expectancy [22, 23], there are findings that those individuals granted a DP due to MSD display similar of slightly higher mortality compared to those with no DP [29, 30].

Moreover, along with mental health diagnoses, MSD are a leading diagnosis group responsible for the loss of production, high health care costs, and marginalisation from working life due to DP [17]. The social welfare expenditures due to disability are at a similar level in all Nordic countries; Generally, DP consumes in a range of 3.5 to 4.2% of gross domestic product in these countries [18].

The most common subgroups of MSD in regards of DP are low back disorders, with ICD-diagnoses codes M40–M59 [5, 27]. These include disorders defined by low-back symptoms, that is, as a painful condition in the lower back, which may or may not radiate to limbs [31]. In order to be defined as chronic, pain has to persist for over three months. In addition to LBD, other common subgroups of MSD as a reason for DP include OA and rheumatoid arthritis (RA) [5]. Hence, within MSD, LBD, OA and RA are the most important diagnosis groups for actions to reduce burden of DP due to MSD [2, 5].
Table 1. Diagnosis of musculoskeletal disorders in International Classification of diseases, 10th revision, M00–M99 (modified from International Classification of Diseases 2019) [27].

<table>
<thead>
<tr>
<th>M00–M99</th>
<th>Diseases of the musculoskeletal system and connective tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>M00–M04</td>
<td>Infectious arthropathies, autoinflammatory syndromes</td>
</tr>
<tr>
<td>M05–M14</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>M15–M19</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>M20–M27</td>
<td>Other joint disorders</td>
</tr>
<tr>
<td>M30–M36</td>
<td>Systemic connective tissue disorders</td>
</tr>
<tr>
<td>M40–M54</td>
<td>Low back disorders</td>
</tr>
<tr>
<td>M60–M63</td>
<td>Disorders of muscles</td>
</tr>
<tr>
<td>M65–M67</td>
<td>Disorders of synovium and tendon</td>
</tr>
<tr>
<td>M70–M79</td>
<td>Other soft tissue disorders, including shoulder lesions</td>
</tr>
<tr>
<td>M80–M85</td>
<td>Osteoporosis</td>
</tr>
<tr>
<td>M86–M90</td>
<td>Other osteopathies</td>
</tr>
<tr>
<td>M91–M94</td>
<td>Chondropathies</td>
</tr>
<tr>
<td>M95–M99</td>
<td>Other disorders of the musculoskeletal system and connective tissue</td>
</tr>
</tbody>
</table>

2.1.2 Work life in Europe and in Nordic countries

In the European Union, paralleling the situation in the industrialized countries in general, almost every fifth employee (19%) reported working at night at least once a month in 2015 [13]. Similar numbers have been reported for shift work (21%). This is a substantial proportion of the work force, although it is clear that the majority of employees work in regular daytime schedules. In addition, there are only minor socioeconomic differences among those with night or shift work compared to those with regular day work; being on shift or night work is more common among unskilled manual workers than among upper non-manual workers in Europe [13]. In addition, physically heavy work is also common: 37% of those in employment in Finland, and 36% in Sweden, reported spending at least a quarter of their work time doing jobs involving lifting and carrying of heavy loads [13].

A population based study in Sweden found that although physically heavy work has decreased among men, among women there has been no change since 1970s [32]. Hence, although working life has changed during the past 30 years, a rather large population still is employed in work that can be considered as physically heavy [13, 32].

As DP is a measure of work disability by definition, characteristics of working life influence also incidences of DP. Combined with information on risk factors for DP due to MSD it may help in aim to prevent occurrence of musculoskeletal disorders, or in case of those already affected, to meaningful adjustments to support active work participation despite pre-existing musculoskeletal disorder.

2.2 FRAMEWORK OF THE STUDY

In this PhD thesis, a modified life course approach was used. In general, the life course approach is defined as analyses of the impact of earlier life phases on later life events, i.e. childhood influences on late adulthood events [33]. This thesis uses a broad definition of the life course concept, as earlier adulthood factors, and their impact on later life adulthood event, were studied. Moreover, in this thesis, it was possible to take into account childhood factors indirectly as possible confounding factors, when investigating the association between potential risk factors at early adulthood and the risk of being granted a DP due to MSD in later life.

In this thesis, genetics and shared family environment were used as potential confounding factors. Twins share common genetic factors by descent, in more detail, dizygotic twin
siblings share 50% of their segregating genes, whereas in monozygotic twin siblings, all of their genes are identical. The shared family environment refers to all environmental factors that twin siblings who have lived together as children have in common, for example, parental factors and available health care. In principle, it includes all the factors that twins of the same age and same sex, have in common during life, mainly considered to include shared genetic factors and shared environment during their childhood years. In contrast to the shared environment, the unique environment refers to all of the factors that differ between twin siblings. By being able to control for familial factors, several early childhood factors that cannot otherwise be measured directly, can be controlled for.

There are a few studies suggesting that early childhood factors may influence the risk of DP due to MSD. A Swedish study revealed that low parental education increased the risk of DP due to any cause [34], and hence, it is possible that parental education is a risk factor also for future DP due to MSD. Furthermore, a Finnish study found that those men whose father was a manual worker had an increased risk of DP due to MSD as compared to those men whose father was a non-manual worker [35]. In addition, childhood adversity, measured as information on stressful life events experienced in childhood (none vs any event), including financial difficulties in the family and separation of parents, has been shown to increase the risk of DP due to MSD [36]. When studying twin siblings, these potential influences are taken into account, as they are part of the shared family environment.

Moreover, as education is a rather stable measure of attained education, educational level can be considered as an early adult life factor potentially influencing the risk of DP due to MSD. Furthermore, education not only exerts an influence on working conditions [34], but it also influences other adulthood factors, including adult socioeconomic status and health behaviour [37, 38], and also, has been shown to modify the exit from working life [39]. Educational level can hence be seen as a potential predictive factor for DP due to MSD, but also as a factor potentially influencing work life and health behaviour later in the life course.

A simple definition of work ability involves the balance between perceived work ability and work demands [40]. In this thesis, those individuals whose work life has been shortened due to a discrepancy between work ability and work demand due to medically confirmed MSD were investigated to identify factors important for musculoskeletal health among the working age population. In particular, this was conducted using long follow-up time of up to three decades and with twin cohort allowing consideration of familial confounding, i.e. confounding due to genetic and shared, mainly childhood, environment.

2.3 RISK FACTORS OF DISABILITY PENSION DUE TO MUSCULOSKELETAL DIAGNOSIS

2.3.1 Sociodemographic factors
Several risk factors for DP due to MSD have been identified. With respect to sociodemographic factors, a high socioeconomic status seems to protect from DP due to MSD, whereas a low socioeconomic status and low educational level predict a higher risk for this kind of DP [41-44]. In Finland, it has been shown, that socioeconomic differences in DP due to MSD are large in comparison to DP due to other reason, such as mental or cardiovascular diagnoses [9, 45]. In addition to socioeconomic status and education, also age and sex seem to contribute to DP due to MSD [28, 41, 43].

The influence of age and sex to risk of DP due to MSD has been studied in more detail; older age seems to be a risk factor for DP due to MSD [42, 43, 46-49]. Furthermore, some studies have shown women to be at an increased risk for both DP due to LBD [28, 42] and for DP due to MSD [43, 50], although in some studies, no sex difference has been found [41, 48, 51]. Due to inconsistency in the study findings, the level of evidence for influence of sex to risk of DP due to MSD can still be considered as low [28].
For influence of education, a higher educational level has been shown to decrease risk of DP due to LBD [42, 49]. Accordingly, those in manual labour work [42] or with lower education [52] were reported to have an increased risk of future DP due to LBD. These findings reflect the situation also with DP due to MSD [41].

From sociodemographic factors, also marital status may influence risk of future DP due to MSD. In previous research, an increased risk of DP has been detected among singles compared to those who are married among employed Danish nurses age 44 or older [53]. In a Swedish population based study, among individuals age 25 to 34 years, those divorced compared to married or unmarried showed tendency for increased risk for DP due to LBD, but this finding was not statistically significant [46]. In a report including Swedish twins of 32 to 62 years of age, marital status was shown to have no independent role for DP due to MSD [50].

2.3.2 Health related factors
Several health related risk factors for DP due to MSD have been identified. The strongest risk factor seems to be presence of pain [5, 54, 55]. Although pain symptoms are not the same as having medically confirmed MSD, which is required for being eligible for DP, they potentially reflect the presence of musculoskeletal disorder or can be an early sign of being at risk of developing work impairing musculoskeletal disorder.

Pain has been defined differently in the previous studies. The number of pain sites, measured based on questionnaire with ten given pain sites, has been found to predict future DP due to any reason [55]. Among those who have received medical care for LBD, the frequency of pain (5-point scale from never to experiencing pain day and night) has been found to predict future DP [51]. Other diagnosis based study has revealed that a long sick leave due to LBD is a strong predictor for future DP due to MSD [56]. Self-reported lower back pain has been shown to be a strong predictor for future DP due to LBD [52], and self-reported musculoskeletal pain has been identified as a risk factor for DP due to MSD [41, 57]. Overall, it seems that both diagnosis-based and self-reported measures of musculoskeletal or back pain display strong associations with future DP due to MSD.

In addition to pain, several other health related factors have been studied for their potential association with the risk of DP. For example, consumption of analgesics has been found to be associated with a risk future DP due to MSD [41].

Another health measure that has been found to potentially predict DP due to MSD is poor self-rated health [58], which has been shown to predict also DP due to LBD [49, 59]. Moreover, in a study where self-perceived quality of life was measured separately for physical and mental health, poor physical health was found to increase the risk of DP due to MSD [60].

Being overweight has been shown as a risk factor for both DP due to MSD [61, 62], and DP due to LBD [59]. Moreover, each unit of increase in BMI was found to increase the risk of future DP due to MSD, as was stable overweight or obesity measured with self-reported information on BMI measured at two time points six years apart [61].

With respect to health behaviour, tobacco use has been associated with increased risk of DP due to LBD [51, 59, 63] and DP due to MSD [41, 57, 63]. In one study where current smoking was shown as being a non-predictive factor for DP due to LBD, instead, snuff use was identified as an independent risk factor [52]. Smoking is considered, besides DP due to MSD [41, 57, 63], also as a risk factor for LBD in general [64]. For DP in general, increased risk due to smoking was shown to be especially evident among women [65]. Overall, tobacco use has been shown to play a role both in the development of MSD, and also in consequences of MSD, such as DP. Alcohol consumption, instead, has not been shown to contribute for risk of DP due to LBD [59] or DP due to MSD [41, 57].

As well as investigating individual health related risk factors, also mutual effects of health behaviour have been studied for their influence for risk of future DP due to MSD [66]. In a study conducted among Swedish twins, unhealthy behaviour was assessed as a combination
of smoking status, physical activity behaviour and alcohol use. With this combined assessment, the results indicated that all these three different health behaviours are connected. In more detail, alcohol use was found to influence physical activity levels, which were then associated with smoking behaviour. Nonetheless, only smoking behaviour was identified as a strong risk factor for DP due to MSD. This finding indicates that although it is important to recognise and identify individual risk factors, it is also important to consider the other potential accompanying health behaviours, even in studies where they have not been identified as a directly contributing factor to the outcome of interest.

Comorbidities, MSD and DP due to MSD
MSD refer to multifactorial diseases, with many possible aetiologies and different risk factors [27]. Common factor for musculoskeletal disorders is that they often co-occur, but in addition, comorbidity with other chronic or recurrent diseases, including mental and cardiovascular diseases, is usual [67-69].

In previous studies, it has been shown that LBD is associated with other chronic diseases, including other musculoskeletal diseases, cardiovascular diseases, and cerebrovascular diseases [67-69]. In addition, a study with a self-reported survey that asked if the participants had ever suffered from diabetes, myocardial infarction, angina pectoris or stroke, found diabetes and angina pectoris to be risk factors for future DP due to LBD [59]. Other common comorbidities with LBD include shoulder pain [68], pain in the whole spinal area, and head and leg pain [69]. In addition, myalgia and myositis are commonly linked with LBD [68].

Moreover, women with LBD seem to have more comorbidities compared to men [70]. In addition, the likelihood of comorbidity with LBD has been shown to be associated with the duration of chronic LBD [71]. Among specific health measures, hypertension is shown as a risk factor for DP due to LBD [49]. Although comorbidities are relatively common in LBD, the role of these comorbidities in the incidences of DP due to LBD is unclear. In general, findings reported for DP due to LBD are also considered to be applicable also for MSD in general.

Furthermore, it has been shown that among those diagnosed with multiple sclerosis, the risk of DP is increased if there is comorbidity with MSD [72]. In patients with diabetes, consequent work disability measured as incidences of sick leave or DP, was partly explained by a comorbidity with MSD [73, 74]. Instead, clinically diagnosed insomnia does not seem to have any association with the risk of DP due to MSD [75], although sleep problems have been recognised as a risk factor for DP due to LBD [76] and are hence potentially a risk factor also for DP due to MSD.

Another aspect of comorbidity is that MSD, measured as sickness absence due to MSD, is shown to be a strong risk factor not only for DP due to MSD, but also for DP due to other diagnosis groups [77]. These other diagnosis groups include DP due to mental, cancer or circulatory diagnosis, even though the strongest association is with DP due to MSD. In addition, in a study of sickness absence due to back pain and its association with future DP due to MSD, it was found that when taking into account potential comorbidities, measured as prior sickness absence, attendance to outpatient care and by use of medication, they only partly explained the association between back pain and DP due to MSD [56]. This suggests that possible comorbidity is more likely to have an independent effect on future DP rather than acting as a confounder in an association between early MSD and future DP due to MSD.

2.3.3 Work related factors
Physical work load
Physical work load has been identified as a risk factor both for MSD [78] and DP due to MSD [34, 50, 79, 80, 81, 82] and also for DP due to LBD [59].

The overall evidence for a link between physical work load and the risk of DP due to MSD seems unequivocal. Occupation has been identified as a risk factor for DP due to MSD [50, 79], and both socioeconomic status, which can be seen partly to reflect work characteristics,
and physical work load point towards an increased risk of DP due to MSD [44, 79, 82, 83]. Moreover, for DP due to any reason, an unfavourable physical work environment (light, noise, climate, dust and vibrations) and unfavourable ergonomic situation (heavy lifting, twisted positions, kneeling and needing to hold the hand above the shoulder level) have been found to increase the risk of future DP due to any diagnosis [79]. Since MSD is a common reason for DP, it can be assumed that these factors contribute also to DP due to MSD. Specific to DP due to MSD, years of exposure to physically heavy work has been shown to have strong association with future DP due to MSD [82].

Nonetheless, there are studies that suggest that this association between physical work load and the risk of DP due to MSD is not straightforward. In a study of physical work load and DP due to LBD, the found association attenuated when taking into account lifestyle factors and familial confounding, suggesting that physical work load is not an entirely independent risk factor for the future DP due to LBD [84]. As LBD are largest subgroup within DP due to MSD, this finding may apply also for DP due to MSD. Hence, although physical work load and DP due to MSD are strongly associated, the potential confounding due to lifestyle or familial factors is to be considered when studying physical work load and its association with DP due to MSD.

In a study of DP due to MSD that excluded LBD (ICD-10 –codes M45–54), it was found that work including mainly lifting and carrying, measured at two time points six years apart, increased the risk of future DP due to MSD, as did increased physical loading within those two different time points [81]. Instead, for stable physically heavy work and decreased physical loading, the associations with DP due to MSD were seen to be affected by confounding due to sociodemographic or health related factors [81]. These findings may partly explain the conflicting results regarding physical work load and risk of DP due to MSD.

**Shift work and night work**

Rather few studies have focussed on shift or night work and the risk of DP due to MSD. In a study of Danish nurses, night work was associated with an increased risk of DP in general [53]. Studies on musculoskeletal pain and its association with night work in turn seem to point towards either minor or no association [85, 86].

Night work is more frequent in low socioeconomic classes [13, 87]. Further, a low socioeconomic status often co-occurs with a lower educational level [34]. When these factors, which are recognized as increasing the risk of DP due to MSD [43], are combined with unusual working hours, such as night work, they all may predispose to an accumulation of negative health effects in the individual. It also seems that working in shifts or night work (or both, a shift work commonly includes also night work) poses different kinds of challenges and opportunities for families and social life compared to conventional day work [88, 89].

Shift workers have been compared to regular day workers in terms of health behaviour, in means to find out if the health behaviour is contributing for the health influences of working shift. In these studies, only a few differences have been found. Regarding physical activity, shift workers in manual occupations, including construction workers, cleaners, garbage collectors, manufacturing workers, and workers in the health service sector, seem to have a more sedentary working life compared to day workers doing similar work [90, 91]. They were also shown to walk more in their free time [92], but no other differences in physical activity levels have been found [90, 92]. In terms of other health behaviours, shift and night workers were seen to be more often smokers and to have an increased calorie intake despite a similar diet quality compared to day workers in a population-based study [93]. In a study among women, those with night work experience were found to differ from those only doing day work in terms of sociodemographic and health related factors [94], i.e. those with night work experience had a lower socioeconomic status and were more often current smokers or obese than those with no night work experience.
Night work potentially can contribute to temporary or permanent work ability, namely, DP, due to the fact that night work inevitably interrupts the normal circadian rhythm, which may predispose to negative health effects. Accordingly, fatigue caused by disrupted sleep has been associated with suboptimal health [95]. In addition, it has been shown that the worker’s age when conducting night work may influence its health effects, with young workers being less prone to negative health influences [96]. Also, age may alter the adaptation to night work, both in terms of coping with unusual working hours as well as hindering adaptation to varying working schedules [97, 98].

Altogether, these previous findings indicate that shift or night work may contribute to work capacity and consequently to DP through several pathways, for example, due to their influence on health behaviour. Other potential pathway may be mediated through the direct sleep disturbing effects of night work because night work is conducted when the diurnal rhythm promotes sleepiness [99]. Moreover, it has been suggested that skeletal muscle function and circadian rhythm may be linked, and hence night and shift work may have a direct impact on musculoskeletal function at the cellular level [100].

Overall, with respect to shift and night work and its association with DP due to MSD, sociodemographic and health related factors are most likely correlated and can modify the association between night and shift work and risk of future DP due to MSD.

2.3.4 Stressful life events
Stressful life events refer to a wide range of life events, such as change of residence, interpersonal conflicts at work, or the death of a close one [101]. At present, although there is evidence that life events may affect future health [102-104], there is only limited knowledge on the associations between stressful life events and DP due to MSD or LBD.

Earlier studies on stressful life events and DP include information on work related life events, such as unemployment. Employment status may be of importance for DP due to MSD, as being unemployed has been found to be a risk factor for DP in general [17], and for DP due to RA [105]. Instead, for future DP due to LBD, unemployment was not seen as an independent risk factor [84]. In addition, it has been shown that a period of unemployment is associated with suboptimal self-rated health and health behaviour [106], which both have been shown to contribute for future DP due to MSD [41, 49, 51, 57-59, 63].

Furthermore, although there are only a few earlier studies investigating the association between stressful life events and the risk of DP, some previous results suggest that life events may have some influence. In a study among municipal workers, interpersonal conflicts at work increased the risk of any DP among women, especially among those with simultaneous marital conflicts [102]. In addition, in a study where the risk of sickness absence among men [103]. As DP due to MSD is one of the main diagnosis groups for DP and sickness absence is a strong predictor of DP [17], these previous findings indicate that both family and work related life events may have association with future DP due to MSD. Furthermore, it is possible that they have different, or even additive, influences on the risk of future DP due to MSD.

Also, it seems that both sociodemographic and health related risk factors are associated with life events as well as with the risk of DP due to MSD [107, 108]. For example, having gone through divorce or experienced the death of a spouse increases smoking prevalence and decreases physical activity levels [107]. In addition, both separate, and accumulation of stressful life events have been shown to affect physical activity [108]. These findings demonstrate that it is reasonable to assume that life events influence health behaviour, which in turn, may modify the risk of future DP due to MSD [51, 52, 57, 66].

In addition, in a study including both sexes, those individuals with no children still living at home were found to have an increased risk of DP due to MSD [50]. If one considers DP due to any cause, having no underage children at home were identified as risk factors for DP.
among women [109]. These findings indicate that aspects of family life may be of importance when studying the risk factors of DP due to MSD.

2.3.5 Stress of daily activities and being a provider for the family
Perceived overall stress of life may also influence risk of DP due to MSD. In a previous study, where stress was measured as stress of daily activities, stress was shown to be an independent risk factor for DP due to MSD [81]. In the study, stress was measured at two time points six years apart. For DP due to any reason, stress, measured as having any psychosocial loading in participant’s life situation, was not shown to associate with risk of future benefits at 3 or 10 years of follow-up [48]. The study included those who had participated to rehabilitation based on musculoskeletal disorders. In a population based study where stress was measured as burnout with survey questionnaire, it was shown that burnout predicts future DP due to any diagnosis [166]. Also, being a provider of the family may be regarded as additional source of stress in life. There is limited knowledge if it may influence risk of future DP due to MSD [46, 50, 53].

2.4 ROLE OF GENETICS AND SHARED FAMILY ENVIRONMENT IN DISABILITY PENSION DUE TO MUSCULOSKELETAL DIAGNOSES
Musculoskeletal disorders are known to have moderate to large genetic influences. With respect to the subgroups of MSD, genetics have been shown to play a relatively important role in both self-reported and medically diagnosed low back disorders [71, 110-112]. Heritability estimates for low back pain (30–68%) [110, 111], self-reported sciatica (20%) [112] and neck pain (35–58%) [110] are an average, moderate. For clinically assessed low back disorders, the role of genetics is higher (67%) [113]. The highest genetic estimates have been demonstrated for quantitatively assessed lumbar spinal stenosis (81%) [113]. For other subgroups of MSD, moderate to high heritability estimates are reported for RA (45–65%) [114-116]. For OA leading to arthroplasty, heritability estimates have been found to be dependent on age, and be different for hip (68%) [117] and knee OA (18%) [118]. In summary, MSD include diagnoses for which it is shown that genetic and environmental influences have varying roles.

In studies on DP due to MSD, studies from the Nordic countries have shown that genetic factors contribute from 35 to 37% of the variation of DP due to MSD [24, 25].

In addition to MSD, and DP due to MSD, genetic factors may also influence other factors, which impinge on MSD, such as smoking [119] and BMI [120, 121]. With respect to stressful life events, genetics have been shown to have a role (27%) [122]. In a study including specific occupations, namely being a teacher, salesperson or manager, the heritability estimates were found to range between 30–46% [123]. Hence, sociodemographic factors also may be partly influenced by genetic factors.

In conclusion, it seems that genetic factors are involved and may play a role both in MSD and its risk factors, and also may influence the consequences of MSD, such as DP. In the twin studies which have investigated the genetic contribution [24, 25, 124], unique environmental effects, e.g. exposures or choices not shared either biologically or socially with twin sibling, explained the majority of the variation in DP due to MSD. Instead, the shared environment of twin siblings was not considered to play any significant role [24, 25, 124]. This indicates that the unique environmental effects may explain 63–65% of the variation in risk, and up to 35% of variation may be due to genetic factors. As majority of variation is explained by unique environmental factors, this points to the existence of modifiable risk factors. These factors could potentially be the targets for interventions to prevent future DP due to MSD.
3 AIM OF THE STUDY

In the Nordic countries, DP due to MSD can be granted to a person with long lasting reduced work capacity due to musculoskeletal disorder, that is, when there has been at least a year of sick leave due to objectively diagnosed musculoskeletal disorder, and impairment in work capacity is considered to be permanent.

To study the long-term effects of sociodemographic, health and work related factors, and life events, on risk of future DP due to MSD, longitudinal population-based studies with long follow-up time and extensive baseline information of such risk factors are needed. Further, a study including twin design allows to further analyze, whether familial confounding (i.e., genetic and shared, mainly childhood, environment) influence the association between factors of interest and DP due to MSD.

The overall aim of this PhD thesis was to explore earlier adulthood factors, such as education, health and work related factors, for their potential influence on risk of future DP due to MSD, taking into account various potential confounders, including familial factors. In this thesis, two national twin cohorts with registry information on DP events with diagnosis codes, with prospective follow-up of up to three decades were used.

The specific aims were:
1. To examine if sociodemographic factors have an influence on the risk of future DP due to MSD.
2. To analyse if health related factors are associated with risk of future DP due to MSD.
3. To assess if work related factors have an influence on the risk of future DP due to MSD.
4. To investigate if stressful life events, including family and work related life events, exert an influence on the risk of future DP due to MSD.
4 MATERIAL AND METHODS

This study investigated risk factors for DP due to MSD among Finnish and Swedish twin cohorts. First, the study populations used in this study are introduced. Then, the outcome, DP due to MSD, is explained in more detail followed by a description of selected factors of interest and covariates. Last, the description of main statistical analyses is presented. A more detailed description about the data and methods can be found in the method sections of studies I–IV.

4.1 STUDY POPULATION

The study populations for this thesis consisted of twins from Finnish (studies I, II and IV) and Swedish twin cohorts (study III).

4.1.1 Finnish Twin Cohort

The Finnish Twin Cohort was established in 1974 and consists of all Finnish same-sex twin pairs born before 1958, with both co-twins alive in 1975 [125]. Twins were identified from the Population Register Centre of Finland. A comprehensive questionnaire including sociodemographic, health and work related factors was sent to all twins in 1975 (response rate 89%). A follow-up questionnaire was sent in 1981 to all twins in this birth cohort irrespective of whether they had participated in the first survey (response rate 84%). In addition to questions included in the 1975 questionnaire, this second questionnaire included questions on stressful life events. At the beginning of prospective follow-up in 1975, the total number of MZ and DZ twin pairs was 13,888 [125].

In the Finnish twin cohort, zygosity was determined based on questions of similarity of physical appearance at school age, as assessed in the 1975 questionnaire; this has been found to be highly accurate in recognising MZ and DZ twins [24, 126].

4.1.2 Swedish Twin Cohort

The sample in this thesis includes Swedish twins that are part of the “Swedish Twin project Of Disability pension and Sickness absence” (STODS) started in 2008 [127]. From STODS, 29 799 complete twin pairs born between 1925 and 1958, including also opposite-sex twin pairs, were included in this thesis.

“Screening Across the Life-span Twin” (SALT) -study was conducted by the Swedish Twin Registry as a computer-assisted telephone-interview study between years 1998 and 2003 [128]. Data from the SALT-study (n= 39 262, response rate 66%) was included in STODS along with Swedish national register data on pensions and mortality [127].

Within the Swedish Twin Registry, DNA based analysis, questionnaire information, and interview responses have been used for zygosity determination [129, 130].

4.1.3 Study populations in studies I–IV

In studies I and II, participants from the Finnish twin cohort, between 18–64 years, who were alive, had not immigrated or been granted DP or an old age pension before January 1st 1975, were included. The final study sample consisted of 24 043 twin individuals, from whom both twins had responded the questionnaire sent in year 1975 [24]. For study II, only those responded that they were at work at 1975 were included (n=16 028). Basic demographic information for study I and II were obtained from the questionnaire administered to all twins in 1975 (Table 2).
In study III, individuals from the Swedish twin cohort, between 40 to 64 years of age at baseline, and who had participated in SALT-interview, were included. Those on an old-age pension, aged 65 or older, or on DP before or at the time of the SALT-interview were excluded. The final study sample included 27 165 twin individuals. The baseline in this study was the SALT-interview conducted between the years 1998 and 2003 [128].

In study IV, those individuals from Finnish twin cohort, who were alive, had not immigrated or been granted DP or an old age pension at follow-up from Jan 1st 1982, were included (n=18 530). Education and socioeconomic status were established from the 1975 questionnaire. Other information was derived from the 1981 questionnaire.

**Table 2. A summary of studies I–IV with information on study population, follow-up time and factors of interest.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Cohort</th>
<th>Outcome</th>
<th>Follow-up time</th>
<th>Factors of interest</th>
<th>Age of cohort</th>
<th>Number of participants</th>
<th>Number of complete same-sex twin pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Finnish twin cohort</td>
<td>DP due to LBD</td>
<td>1975–2004</td>
<td>Sociodemographic and health related factors</td>
<td>18–64</td>
<td>n=24 043 (50% women)</td>
<td>3519 MZ, 7667 DZ pairs</td>
</tr>
<tr>
<td>II</td>
<td>Finnish twin cohort</td>
<td>DP due to MSD</td>
<td>1975–2004, those at work at 1975</td>
<td>Work related factors</td>
<td>18–64</td>
<td>n=16 028 (44% women)</td>
<td>1870 MZ, 3959 DZ pairs</td>
</tr>
<tr>
<td>III</td>
<td>Swedish Twin cohort</td>
<td>DP due to MSD</td>
<td>From baseline interview 1998–2003 until 2013</td>
<td>Night work</td>
<td>40–64</td>
<td>n=27 165 (51% women)</td>
<td>2640 MZ, 3506 DZ pairs</td>
</tr>
<tr>
<td>IV</td>
<td>Finnish twin cohort</td>
<td>DP due to MSD</td>
<td>1982–2004</td>
<td>Stressful life events</td>
<td>23–64</td>
<td>n=18 530 (51% women)</td>
<td>2498 MZ, 5127 DZ pairs</td>
</tr>
</tbody>
</table>
4.2 DISABILITY PENSION IN FINLAND AND SWEDEN

4.2.1 Musculoskeletal diagnoses
In this PhD thesis, those granted DP with MSD were defined as those with International Classification of Diseases (ICD), 10th revision, rubrics M00–M99 [131] as a reason for being granted a DP. As the data collection started in the year 1975, changes in ICD-revisions have taken place. Hence, all the diagnostic codes were encoded to their equivalent ICD-10 codes. DP diagnoses were categorized into low back diagnoses (LBD) and other musculoskeletal diagnoses (MSD). In the group LBD, the diagnoses ICD-10 rubrics M40–M54 were included, with corresponding rubrics of ICD-8 (717, 720–722, 725, 726, 728) and ICD-9 (720–724). For studies on DP due to MSD, all diagnosis rubrics M00–M99, with corresponding rubrics of ICD-8 and ICD-9, were used. Among those granted DP due to MSD, LBD is the largest diagnosis group [5].

4.2.2 Disability pension
In the Nordic countries, a DP can be awarded to a person with fundamentally reduced work capacity that has lasted for more than a year and is due to a medically confirmed disease [4, 5, 18]. In Finland and Sweden, as in the Nordic countries in general, three main pension schemes for DP exists. These include income-related compensation for those in employment, a guarantee benefit for those with little or no income from employment, and the national pension scheme that covers all permanent citizens living in the country [4, 5, 18]. In both Finland and Sweden, DP has been in place for a relatively long time. The current definition of being eligible for DP can be considered as having been established in year 1957 in Finland due to the National Pension Act, and in Sweden in year 1955 due to the National Sickness Insurance Act [3, 132]. In both Sweden and Finland, permanent work impairment is defined as being expected to last for at least a year.

In Finland, the eligibility for DP is defined as having an illness, which reduces both work capacity and the possibility of earning a fair living [5]. Work ability is defined as being able to manage in a work that is reasonable, taking into account the applicant’s education, age and previous activities. In order to obtain a full pension, a work capacity reduction of at least 60% is required. For partial pension, reduction of work capacity estimated to be between 40 to 60% is required. Partial DP has been available in Finland since 1972. In addition, from year 1986, individual early retirement pension was available as one form of DP, but this pension form was gradually abolished by year 2005. For this individual early retirement, the requirement to have objectively shown work disability was less stringent than for full DP [3]. In the DP cases included in this PhD thesis, all diagnoses based pensions are included.

In Sweden, medical reason, which reduces work capacity by 25% or more, and is estimated to last at least a year, is required to be eligible for DP [132]. When determining work ability, all available work in the labour market is considered. In Sweden, where a temporary DP has been available as long as a permanent DP, its role has been minor for DP due to MSD [4].

There have been changes in the social, sickness insurance and pension legislation both in Sweden and Finland during the last decades. However, we do not know if these changes have influenced the outcome DP due to MSD during the follow-up period in this PhD thesis, i.e. from 1975 to 2004 in Finland [3] and from 1998 to 2013 in Sweden [132]. In Sweden, after 2003, activity and sickness compensations replaced the previous early retirement pension and temporary disability pensions [4]. For those under 30 years old, activity compensation is available, and for those over 30 years of age, sickness compensation is available. For those with MSD, the role of activity compensation, as well as partial sickness compensation, is minor, but for full sickness compensations, the proportion of MSD has been 16–44% of newly granted sickness compensations since 2003. As the activity and sickness compensation corresponds to DP, available in Sweden until 2003, the term DP is used. In addition, as
temporary DP has been relatively rare among those with DP due to MSD, both temporary and full DP have been included to maximize the sample size.

In total, although there are some differences in eligibility for DP in Finland and Sweden, it is considered that those granted DP due to MSD in either of these countries are comparable with respect of their work incapacity due to MSD.

4.3 MEASUREMENT OF EXPOSURES

In all studies (I–IV), age, sex and education were taken into account. Both Finnish and Swedish twin cohorts had similar estimates for sociodemographic and health related variables. For work related factors, the Finnish and Swedish twin cohorts complemented each other. In the Finnish twin cohort, information on physical work environment, including physical work load, was present. In the Swedish twin cohort, self-reported information on work history, including information on years of night work, was available.

The Finnish twin cohort was used when analysing the associations between sociodemographic, health and work related factors, and stressful life events and their association with future DP due to MSD. To analyse the association between night work and DP due to MSD, a study among Swedish twins was conducted. In addition to these factors of interest, also several other variables were taken into account. Factors used only as covariates in this summary of thesis are introduced separately after the factors of interest (Table 3).

4.3.1 Sociodemographic factors

Education was measured in nine categories of highest attained education, and were transformed to years of education and used as a continuous variable. The categories were: a) less than elementary school b) elementary school c) elementary school and at least one year of vocational education d) middle school or adult education college/vocational school e) middle school or adult education college/vocational school and at least one of vocational education f) matriculation examination g) matriculation examination and at least one of vocational education (also studies in college) e) college or university degree f) other education.

Socioeconomic status was based on self-reported main lifetime occupation, classified using the 1970 census classification of occupational and social class [133]. Socioeconomic status has six main categories: upper and lower non-manual workers, skilled and unskilled manual workers, farmers, others (including students, conscripts, and otherwise not classified). Those not employed at baseline were asked to report their previous occupation.

Marital status was used as a dichotomized variable, single (unmarried living alone, widowed, or divorced) vs. married (those living with another adult, including cohabitating, married, or remarried).

4.3.2 Health related factors

Musculoskeletal pain was self-reported, and assessed with a question about whether the individual had experienced pain in neck, shoulder, or low back area that had affected their work capacity (0–3 locations) during recent years. Response alternatives were “yes” or “no” for each pain location.

To determine the presence of any self-reported physician-diagnosed other chronic diseases, participants were asked to reply “yes” or “no” if this was the case for several specific chronic diseases. These chronic diseases included in the questionnaire were bronchitis, pulmonary emphysema, asthma, allergic rhinitis, allergic dermatitis, urticaria, hypertension, angina pectoris/myocardial infarct, stroke, gastric ulcer, cholelithiasis, diabetes and gout. The dichotomised categorisation of having no disease or having at least one was used.
The frequency of use of analgesics was asked as five frequency categories, with the number of days of use during last year. This variable was dichotomized into “yes” for those responding to using analgesics on 10 or more than 10 days in the previous year and “no” for those responding that they had taken analgesics for less than 10 days in the previous year.

Body mass index [BMI (kg/m²)] was computed from self-reported weight and height and classified as low/normal (<22.5), normal weight (22.5–24.99), overweight (25–29.99) and obese (>30). The reliability of self-reported BMI has been found to be high [134]. When used as a covariate, BMI was included as a continuous variable.

Smoking status was measured by a detailed smoking history [135] and grouped into four categories: never smoked, occasional smoker, ex-smoker, or current smoker.

4.3.3 Work related factors
Physical work load was enquired by asking if the respondent’s work included mainly sitting, standing, lifting and carrying or was considered physically heavy work.

Work type was queried by asking if their work was considered monotonous or variable, and was assessed by the options of “very monotonous”, “quite monotonous”, “quite variable”, and “very variable”, and dichotomized into monotonous and variable work.

Indoor- or outdoor work or a combination of both was assessed with options of “yes” or “no”.

Shift work was assessed with a question about whether work was considered to be mainly day, evening, night, or shift work. Those who reported mainly shift work were compared to those with mainly day work.

Night work experience was assessed with a question: “For how many years have you had working hours that meant that you worked night at least now and then” [136]. Night work experience was categorised as those with no night work experience, those with 1–10 years of night work experience, and those with over 10 years of night work experience. [Swedish twin cohort].

4.3.4 Stressful life events
Stressful work related life events was a combination of five questions: loss of job, change to a different kind of work, interpersonal conflict at work, increase in responsibilities at work, and increase in amount of work (Appendix A). Those with no events were compared to those with work events within five years, categorized as “no events”, “1 to 2 events”, “3 or more events”.

Periods of unemployment included lifetime number of times being without a job and were categorized as “none”, “1–4 times”, “more than 5 times”.

Changes of workplace included lifetime number of workplace changes, and were categorized as “none”, “1–4 times”, or “more than 5 times”.

Illness or injury causing over 3 weeks work disability was categorised as “no” for those who never had experienced such an event, and “yes” for those with an event within 5 years.

Stressful family related life events were a combination of 14 questions: death of spouse, death of friend, change in health of family member, sexual difficulties, financial problems, gain of new family member, divorce or separation, interrupted pregnancy in family, change in residence, family member leaving home, serious conflict in close relationship, change in number of arguments with spouse, taking a loan (more than half of yearly income), living away from spouse due to work (Appendix A). Those not experiencing these events were compared to those with family related life events within five years, categorized as “no events”, “1–3 events”, “4 or more events”.

A positive change in life was categorised as “no” for those never experiencing an event, and “yes” for those who responded to have a positive change in life-event within the past 5 years.
4.3.5 Stress of daily activities and being provider for the family
Stress of daily activities was assessed using Reeder Stress Inventory [137] and included four items: feelings of tension and nervousness, perceived stress, demands associated with daily activities, and daily mental and physical exhaustion [138]. Each of the four items was rated on a four-point scale. The total score for stress was 4–16, where a high score indicated low stress. The stress score was reversed to simplify the interpretations of statistical analyses. For descriptive purposes, the stress associated with daily activities was categorized into three classes: much (4–8 points), some (9–15 points), and little stress (16 points).
Provider for the family was measured as respond options “yes” or “no”.

4.3.6 Covariates
In addition to the selected factors of interest, several factors were taken into account as covariates. Covariates included in the studies based on the Finnish and Swedish twin cohort are presented in Table 3. Covariates used in study III based on Swedish twin data are introduced in below:
Educational level was categorized as “those with compulsory education” and “those with additional years of education”.
Marital status was a dichotomized variable with those “married/cohabiting” and those “unmarried”, including non-married, divorced and widowed.
Having children was a dichotomized variable into “those with no children” and “those with at least one child”.
BMI (kg/m^2) was calculated from self-reported measures of height and weight and analysed as a continuous variable.
Tobacco consumption, including the use of cigarettes and snuff, was categorized as those who had “never tried or tried once”, those who were “current occasional or regular users”, and “former users”.
Chronic widespread pain was assessed with a question on suffering general pain over the last three months. If the answer was yes, additional three questions were asked regarding generalized pain during over the last three months: pain in both the upper and lower body, pain in both left and right sides, and any back pain over the last 12 months. Those who answered “yes” to all these four questions were defined as having chronic widespread pain [139].
Self-rated health was assessed with the question “How would you rate your general health status?” and categorized into “good” (for those responding excellent or good), “moderate”, and “poor” (for those reporting fairly poor or poor) [140].
The number and severity of diseases was assessed by taking into account the expected impact of the most severe illness reported by the participant. The number and severity of diseases was categorized as “those with no disease”, and those with any diseases as “those with not at all life-threatening”, “somewhat life-threatening”, and those with “life threatening disease” [140].
Table 3. Summary information on study variables and covariates in studies I–IV. Column "Factors of interest" includes variables that were studied for their potential association with DP due to MSD, and "Covariates" variables included in full models of studies I–IV.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline information (year)</th>
<th>Factors of interest (study number)</th>
<th>Covariates (study number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographic factors</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years of education</td>
<td>1975</td>
<td>I, II, IV</td>
<td>I, II, IV</td>
</tr>
<tr>
<td></td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>1975</td>
<td>I, II</td>
<td>I, II, IV</td>
</tr>
<tr>
<td>Marital status</td>
<td>1975</td>
<td>I, II</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Health related factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>1975; 1981</td>
<td>I</td>
<td>I; IV</td>
</tr>
<tr>
<td>Widespread pain</td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Presence of any chronic disease</td>
<td>1975; 1981</td>
<td>I</td>
<td>I; IV</td>
</tr>
<tr>
<td>Frequency of use of analgesics</td>
<td>1975; 1981</td>
<td>I</td>
<td>I; IV</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1975; 1981</td>
<td>I</td>
<td>I, II; IV</td>
</tr>
<tr>
<td></td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1975; 1981</td>
<td>I</td>
<td>I; IV</td>
</tr>
<tr>
<td>Tobacco and snuff use</td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>The number and severity of diseases</td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Work related factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical work load</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Work type (monotonous vs variable)</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Indoor- or outdoor work</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Shift work</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Night work</td>
<td>1998–2003</td>
<td>III</td>
<td></td>
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<tr>
<td>Stressful life events</td>
<td></td>
<td></td>
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<tr>
<td>Stressful work events</td>
<td>1981</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Periods of unemployment</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Changes of workplace</td>
<td>1975</td>
<td>II</td>
<td>II</td>
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<tr>
<td>Illness or injury causing over 3 weeks</td>
<td>1981</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>work disability</td>
<td>1981</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Stressful family events</td>
<td>1981</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Positive change in life</td>
<td>1981</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td>Other factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stress of daily activities</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
<tr>
<td>Having children</td>
<td>1998–2003</td>
<td>III</td>
<td></td>
</tr>
<tr>
<td>Provider for the family</td>
<td>1975</td>
<td>II</td>
<td>II</td>
</tr>
</tbody>
</table>

4.4 FOLLOW-UP DATA

Information on the date of DP with diagnoses (ICD-10 revisions) during the follow-up time was obtained in Finland from the Social Insurance Agency and the Finnish Centre for Pension. Information on the date of migration or death was obtained from regular updates from the Population Register of Finland. For the record linkage, the unique personal identification codes of all Finnish citizens were used.

In Sweden, data were obtained and linked to all twins from the National Social Insurance Agency database “Micro-Data for Analysis of the Social Insurance system” (MiDAS database). All participants were followed-up from the baseline to the date of DP, the date when the person began to receive an old age pension, the date of death, date of emigration or to the end of the follow-up. Information on DP with diagnoses codes was obtained from Swedish Social Insurance Agency. Data on mortality was obtained from the National Board of Health and Welfare, and the data on old-age retirement and emigration were from the Statistics Sweden.

In the Finnish twin cohort, the follow-up time was from 2nd January 1975 (study I and II) and from 1st Jan 1982 (study IV) until 31st Dec 2004. In the Swedish twin cohort (study III), the follow-up time was from baseline interview conducted between 1998–2003 until 31st Dec 2013.

4.5 STATISTICAL METHODS

Cox proportional hazards models

All studies were conducted as follows:

a) standard cohort analysis (analysis including whole study cohort),

b) a model controlling for various covariates, and

c) a co-twin-control design (matched case -control analysis including discordant twin pairs). For evaluation purposes, the risk estimates received from model controlling for various covariates, are compared to standard cohort analysis -model for the potential influence of selected covariates. Independently from this evaluation, model co-twin-control design, is compared to risk estimates received from standard cohort analysis, for the potential influence of familial factors.

The analysis were conducted using Cox proportional hazards models and conditional Cox proportional hazards models to assess hazard ratios (HR) with 95% confidence intervals (CI). Cox hazards models were calculated with the follow-up time in days. The proportional hazards assumption of categorical variables was tested by graphical observation of log-log curves for the categories of risk factors [141]. The Kaplan-Mayer curves were parallel and did not violate the proportional hazards assumption.

In the standard cohort analysis, HR and CIs were calculated for the exposure variable and outcome variable DP due to MSD or DP due to LBD. Study participants contributed with a person time as days until the date of disability pension, old age pension, emigration, death or end of follow-up. All Cox proportional hazard analyses were adjusted for age at baseline (continuous variable), and clustered on pair identity to take into account the fact that twin pairs, rather than independent individuals, were sampled [142].

The standard cohort analysis was first conducted to detect a possible association between sex and future DP due to MSD. As no significant association was found between sex and DP due to MSD, the analyses were then stratified by sex, to provide own baseline hazard for men and women, to control for the possible underlying effect of sex that may be presents also in absence of any clear indications for sex differences [143]. This procedure was done in all of the substudies of this thesis.

Next, modelling which controlled for various pre-selected covariates that differed for each substudy I–IV, based on careful consideration for most applicable, was conducted using
backward selection method, where the least significant variable, i.e. the factor with the highest p-value, was removed one at a time to find a final model where all factors in the model contributed significantly at p ≤ 0.05-level. In study I, the final model included all significant factors at p ≤ 0.05 level identified in the standard cohort model where analyses for each variable was run separately. In study II and III, also marital status was included in the final model.

The third step of the analysis involved a discordant twin pair analysis with conditional Cox proportional hazards models to analyse if familial factors (genetics and shared environment) played any role in the association between exposure variable and DP due to MSD. This co-twin control study analyses those twin pairs discordant for DP due to MSD, i.e. those twin sibling pairs, where only one twin of the pair had been granted DP due to MSD, whereas the other had not been granted DP for any reason (in study I, twin pairs discordant for DP due to LBD). Conditional Cox proportional hazard models were conducted by analysing the follow-up time to DP in relation to the follow-up time of the co-twin. The modelling was performed with stratification by twin pair meaning that each twin pair were their own baseline hazard.

With this co-twin control analysis, it is possible to evaluate if associations found between baseline risk factors and DP due to MSD are explained by unique environmental factors, or if the association is at least partly explained by factors shared by twin siblings, by comparing the results of this discordant twin pair analysis to the standard cohort analysis [144]. If associations are similar in both models, the association can be considered to be independent of familial factors. However, if an association found in the model including all twins is significantly attenuated when conducting a discordant twin analysis, familial factors are considered to play a role in the association.

Further, discordant twin pair analysis can be conducted separately for DZ and MZ twins if enough cases are available. If the analyses are conducted separately for DZ and MZ pairs, the difference in risk estimates between DZ and MZ pairs would point to the presence of genetic influence [144, 145]. This is due to the fact that the shared family environment is similar for DZ and MZ pairs, but DZ twins are dissimilar in their genetic match, sharing 50% of their segregating genes, while MZ twins are identical in their genetics. For the comparisons of DZ and MZ pairs, only the pairs that are discordant both for the outcome event and for variable that is being studied are included. However, when interpreting the differences between discordant MZ and DZ twin pairs, then the possibility of a limited number of cases needs to be taken into consideration when interpreting the results.

The statistical analyses for this thesis were carried out with Stata statistical software versions 8.2, 9.2, 12.1 and 13.1 (Stata Corporation, College Station, TX, USA), and R software with packages survival, Epi, epicalc, and MASS distributed through Comprehensive R Archive Network (cran.r-project.org).
5 RESULTS

5.1 CHARACTERISTICS OF THE STUDY POPULATION

DP due to LBD was granted to 600 (2.5%) participants during the follow-up (Table 4). On average, they were 39 (standard deviation, SD, 10) years of age at baseline (Appendix B). Those with no DP during the follow-up (n=19149) were on average 32 (SD 12) years of age. There were a total of 504 twin pairs discordant for DP due to LBD (Table 5). Those granted DP due to LBD were more likely to be married, report pain in any musculoskeletal site, and to be a former or current smoker at baseline in comparison to those not granted a DP during the follow-up (Table 6).

Those twins granted a DP due to MSD during the follow-up, and who were in the labour force in 1975 (n=1297), were on average 39 (SD 9) years of age, being older than those in the same cohort with no DP during the follow-up (n=12 667), who were on average 32 (SD 11) years of age. Additionally, those granted DP due to MSD had shorter education and were more likely to be married than those not granted a DP during the follow-up (Appendix B). The number of twin pairs was 1870 MZ and 3959 DZ pairs, including 186 MZ and 524 DZ pairs discordant for DP due to MSD.

In the Swedish twin cohort, the participants were between 40 and 64 years of age at the time of the baseline SALT-interview. Those twins granted DP due to MSD (n=1338) were on average 55 (SD 5) years of age at baseline. Those with no DP due to MSD during the follow-up (n=25 827) were on average 53 (SD 6) years of age. Those granted DP due to MSD during follow-up were more likely to have only had the compulsory level of education (Appendix B). The distributions between same-sex DZ and MZ twins were 2640 MZ and 3506 DZ pairs, including 201 discordant MZ and 283 discordant DZ twin pairs for DP due to MSD.

Those Finnish twins granted DP due to MSD in the follow-up from the beginning of year 1982, and who had responded to the questionnaire in 1981 (n=1273), were on average 44 (SD 9) years old, with a mean follow-up time of 10 years (SD 6), and had on average, 7 (SD 1) years of education Compared to those not granted any DP during follow-up, they were older, with a shorter follow-up time and with shorter education (Appendix B).

In study I, those granted DP due to LBD were selected as a case. For studies II–IV, those granted DP due to MSD were selected as a case.

Table 4. Studies I–IV presented with information on study population, outcome factor of interest, and number of participants and cases.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cohort (n)</th>
<th>Outcome (n)</th>
<th>Factors of interest</th>
<th>Number of participants and cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Finnish cohort</td>
<td>twin DP due to LBD</td>
<td>Sociodemographic and health related factors</td>
<td>24 043 participants, 600 cases</td>
</tr>
<tr>
<td>II</td>
<td>Finnish cohort</td>
<td>twin DP due to MSD</td>
<td>Work related factors</td>
<td>16 028 participants, 1297 cases</td>
</tr>
<tr>
<td>III</td>
<td>Swedish cohort</td>
<td>Twin DP due to MSD</td>
<td>Night work</td>
<td>27 165 participants, 1388 cases</td>
</tr>
<tr>
<td>IV</td>
<td>Finnish cohort</td>
<td>twin DP due to MSD</td>
<td>Stressful life events</td>
<td>18 530 participants, 1273 cases</td>
</tr>
</tbody>
</table>
5.2 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: SOCIODEMOGRAPHIC FACTORS

Among Finnish twins, each one year longer education was associated with a decreased risk of DP due to LBD (Table 5) or DP due to MSD. For those granted DP due to MSD during the follow-up and reported being at work in 1975, the HR for each one-year increase in education was 0.79 (95% CI 0.77–0.82) (unpublished data). Familial confounding did not influence these associations.

With respect to socioeconomic status, a higher socioeconomic status decreased the risk of DP due to LBD, whereas a lower socioeconomic status seemed to increase the risk (Table 5). When familial confounding was taken into account, the risk estimates for the association between being an unskilled manual worker and DP due to LBD became attenuated to non-significance in the discordant twin pair analysis. These findings were similar for DP due to MSD, among those who reported to be at work in baseline year 1975. Higher socioeconomic status was observed to be a protective factor (HR 0.28, 95% CI 0.19–0.41, upper non-manual worker), whereas both skilled and unskilled manual workers were shown to be in increased the risk in comparison to being lower non-manual worker. The HRs were 1.92, 95% CI 1.66–2.22 for skilled and HR=2.49, 95% CI 2.08–2.97 for unskilled worker (unpublished data). These findings were independent of familial influence.

Marital status was not found to be an independent risk factor for DP due to LBD (HR 1.09, 95% CI 0.89–1.32), and the risk estimates remained at similar level when familial confounding was taken into account (Table 5). For DP due to MSD, the risk estimates pointed towards an increased risk (HR 1.13. 95% CI 1.00–1.30), but taking into account familial confounding diluted the risk estimates for DP due to MSD to non-significance (HR 1.16, 95% CI 0.94–1.43) (unpublished data).

5.3 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: HEALTH RELATED FACTORS

With respect to the health related factors, the strongest predictors of DP due to LBD during the follow-up were self-reported pain in any given area: For neck pain, risk estimates were HR 2.36, 95% CI 1.97–2.83, for shoulder pain, HR 2.39, 95% CI 1.98–2.88, and for back pain, HR 2.36, 95% CI 1.99–2.81 (Table 6). Other health related predictors of future DP due to LBD were the presence of other self-reported chronic conditions diagnosed by a physician (HR 1.44, 95% CI 1.22–1.70), use of analgesics (HR 1.67, 95% CI 1.38–2.02), being overweight (HR 1.43, 95% CI 1.16–1.77) and being a former (HR 1.39, 95% CI 1.09–2.22) or current smoker (HR 1.82, 95% CI 1.49–2.22). The risk estimates for use of analgesics attenuated when confounding due to sociodemographic and other health related factors was taken into account. Musculoskeletal pain at any location, the presence of chronic conditions diagnosed by physician, overweight, and being a current smoker increased the risk of DP due to LBD independently of any confounding.

Moreover, among those granted DP due to MSD during the follow-up, and at work at baseline, from health related factors, each one-unit increase in BMI was shown to increase risk of DP due to MSD (HR 1.09, 95% 1.07–1.11) (unpublished data). When taking into account familial influence, the results became non-significant (HR=1.01, 95% CI 0.98–1.05). Risk estimates were similar when restricted to those individuals with DP due to LBD.
5.4 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: WORK RELATED FACTORS

5.4.1 Physical work environment
With respect to the work-related factors, physical workload was seen as a risk factor for DP due to MSD. All measured factors, including work that included mainly standing (HR 1.19, 95% CI 0.99–1.43), lifting and carrying (HR 1.83, 95% CI 1.58–2.12), or physically heavy work (HR 2.08, 95% CI 1.70–2.54), were found to be risk factors (Table 7). From these, work involving mainly lifting and carrying was seen as independent risk factors, i.e. they were unaffected when various covariates or familial confounding were taken into account. Physically heavy work was statistically significant when taking into account familial confounding HR=1.37, 95% CI 1.00–1.88) but attenuated to non-significance when adjusted with sociodemographic and other work-related covariates (HR 1.27, 95% CI 0.94–1.72).

In addition to physical work load, work that was considered monotonous compared to being varied, was observed to be an independent risk factor of DP due to MSD (HR 1.62, 95% CI 1.42–1.85) (Table 7). Instead, outdoor work or combined outdoor and indoor work, compared to indoor work, was noted as a risk factor in the analysis of whole cohort (HR 1.33, 95% CI 1.11–1.60 for outdoor work, HR 1.35, 95% CI 1.17–1.55 for combined work), but these findings attenuated to non-significance when other covariates and familial confounding were taken into account.

5.4.2 Shift work and night work
Shift work, considered as work that was mainly shift work, compared to being mainly employed in regular day work, was identified as a risk factor for DP due to MSD in the analysis of the whole cohort (HR 1.24, 95% CI 1.07–1.44) (Table 7). These risk estimates attenuated to non-significance when other sociodemographic and work-related factors, or familial confounding, were taken into account.

Night work, measured as years of night work, was found to be a risk factor for DP due to MSD (HR 1.33, 95% CI 1.17–1.53 for 1–10 years of night work, HR 1.39, 95% CI 1.18–1.64 for over 10 years of night work) (Table 7). Furthermore, taking into account sociodemographic and health related factors did not have influence on risk estimates but familial confounding attenuated these associations to non-significance.

5.5 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: STRESSFUL LIFE EVENTS

Several stressful life events and their associations with DP due to MSD were analysed. Work related stressful life events, measured as the number of events including interpersonal conflicts at work, job loss, increase on work load or responsibilities at work, and change to a different kind of work, did not increase the risk (Table 8). Instead, both the total absence of these work related events (HR 0.92, 95% CI 0.81–1.05) and having many work related events (HR 0.75, 95% CI 0.60–0.94) were seen more as a protective factor, although the results were statistically non-significant for the absence of events. With respect to many work related events, after taking into account confounding due to sociodemographic and health related factors, or for familial factors, the associations became non-significant (HR 1.12, 95% CI 0.83–1.51 for discordant twin pairs).

Nonetheless, some other work related life events were seen as risk factors for DP due to MSD, i.e. several periods of unemployment, and several workplace changes (Table 8). Especially, five or more changes of workplace seemed to be an independent risk factor for DP due to MSD (HR 1.59, 95% CI 1.32–1.91). Additionally, the life event classified as “illness or injury that caused over 3 weeks” work disability” increased the risk of DP due to MSD (HR 2.25, 95% CI 1.99–2.56).
The list of stressful family related life events included 14 items (Appendix A). In the standard cohort analysis, and when taking into account confounding due to other covariates, the results were non-significant both for absence of events or having many family related events (Table 8). Instead, in the discordant twin pair analysis, the absence of events was seen to decrease the risk of DP due to MSD (HR 0.68, 95% CI 0.48, 0.95). Experiencing many (4 or more) family related events was shown to increase the risk (HR 1.63, 95% CI 1.31–2.03).

A positive change in life correlated both with family and work related events, and was found to be a protective factor for DP due to MSD (HR 0.79, 95% CI 0.68–0.91) (Table 8). Adjusting for sociodemographic and health related factors attenuated the results (HR 0.90, 95% CI 0.76–1.06), but instead, familial confounding did not affect the risk estimates.

5.6 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: STRESS OF DAILY ACTIVITIES AND BEING PROVIDER FOR THE FAMILY

Stress of daily activities was seen as an independent risk factor for future DP due to MSD (Table 9). The stress associated with daily activities was measured as stress points that were reversed for analytical purposes (range 4 to 16, 16 being lowest and 4 being highest measured levels of risk). The risk estimates were HR 1.06 (95% CI 1.04–1.09) for each unit increase in stress in standard cohort analysis (Table 9).

Not being a provider for the family displayed an increased risk of DP due to MSD (HR 1.29, 95% CI 1.11–1.50) (Table 9). The risk estimates attenuated to non-significance when other sociodemographic and work related covariates (HR 1.17, 95% CI 0.97–1.41) and familial confounding were taken into account (HR 0.99, 95% CI 0.78–1.24).

5.7 RISK OF DISABILITY PENSIONS DUE TO MUSCULOSKELETAL DIAGNOSES: OTHER FINDINGS

In the Finnish and Swedish cohorts, no major sex differences in the risk factors and their associations with DP due to MSD were found, and hence, men and women were pooled together to maximize sample size.

The few detected sex differences were as follows (unpublished data):

With respect to sociodemographic risk factors, women seemed to exhibit a slightly decreased risk for DP due to LBD (HR 0.70, 95% CI 0.60–0.83) compared to men, but this association became non-significant when socioeconomic status and health behaviour were taken into account. For DP due to MSD, no significant association with sex was found (HR 0.96, 95% CI 0.87–1.05).

With respect to the health related factors, being overweight was statistically significant risk factor among men (HR 1.47, 95% CI 1.11–1.93), although the risk estimates also pointed towards an increased risk in women (HR 1.37, 95% CI 0.98–1.91). In addition, the risk for DP due to MSD was increased for obese men (HR 2.16, 95% CI 1.33–3.52), but not for obese women (HR 0.85, 95% CI 0.43–1.71). These results showed independence from confounding due to other covariates or familial factors. The same cut-off points for BMI were used for both men and women.

With respect to the work-related factors, shift work, compared to day work, was identified as a risk factor among men, but not for women (HR 1.30, 95% CI 1.07–1.58 for men, HR 1.13, 95% CI 0.9–1.41 for women). Additionally, work that included mainly standing, was found as risk factor only for men (HR 1.35, 95% CI 1.05–1.73 for men, HR 1.02, 95% CI 0.77–1.35 for women), as was combined outdoor and indoor work versus indoor work (HR 1.43, 95% CI 1.12–1.68 for men, HR 1.14, 95% CI 0.86–1.50 for women).

With respect to stressful life events, work related events analysed separately for men and women revealed that having many stressful work related events decreased the risk in men...
(HR 0.76, 95%CI 0.61–0.95). These risk estimates for stressful work events were unaffected by other covariates, but became non-significant when familial confounding was taken into account. Among women, the results for many work related events were non-significant when the whole cohort was analysed (HR 0.93, 95% CI 0.69–1.26), and taking into account other covariates or familial influence did not influence the risk estimates (unpublished data).
Table 5. Hazards ratios (HR) with 95% confidence intervals (95% CI) for those granted a disability pension (DP) due to low back diagnoses (LBD) during follow-up from 2nd Jan 1975 until 31st Dec 2004 for sociodemographic factors.

<table>
<thead>
<tr>
<th>Finnish Twin Cohort 1975</th>
<th>DP due to LBD (n=600)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age and sex-adjusted</td>
</tr>
<tr>
<td></td>
<td>HR</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.81</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Women vs men</td>
<td>0.70</td>
</tr>
<tr>
<td>Socioeconomic status 1975</td>
<td></td>
</tr>
<tr>
<td>Upper non-manual worker</td>
<td>0.41</td>
</tr>
<tr>
<td>Lower non-manual worker</td>
<td>1.00</td>
</tr>
<tr>
<td>Skilled manual worker</td>
<td>1.64</td>
</tr>
<tr>
<td>Unskilled manual worker</td>
<td>1.96</td>
</tr>
<tr>
<td>Farmer</td>
<td>1.23</td>
</tr>
<tr>
<td>Others</td>
<td>0.44</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married vs single</td>
<td>1.09</td>
</tr>
</tbody>
</table>

Full model: adjusted for sex, age, education, socioeconomic status, body mass index, presence of other diseases, pain, frequency of use of analgesics, smoking.
Discordant twin pairs: those twin pairs, where one of the twins has been granted DP due to MSD, whereas the other twin has no DP.
<table>
<thead>
<tr>
<th></th>
<th>No DP (n=19149)</th>
<th>DP due to LBD (n=600)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age and sex-adjusted</td>
<td>Full model</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck (yes)</td>
<td>14</td>
<td>34</td>
</tr>
<tr>
<td>Shoulder (yes)</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Low back (yes)</td>
<td>25</td>
<td>51</td>
</tr>
<tr>
<td>Presence of any chronic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes, at least one</td>
<td>39</td>
<td>54</td>
</tr>
<tr>
<td>Frequency of use of analgesics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than 10 days per year</td>
<td>16</td>
<td>27</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/normal (&lt;22.5)</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>Normal weight (22.5–24.99)</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Overweight (25–29.99)</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>Obese (&gt;30)</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>Occasional smoker</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Former smoker</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Current smoker</td>
<td>30</td>
<td>34</td>
</tr>
</tbody>
</table>

Full model: adjusted for sex, age, education socioeconomic status, body mass index, presence of any chronic disease, pain, frequency of use of analgesics, smoking.

Discordant twin pairs: those twin pairs, where one of the twins has been granted DP due to MSD, whereas the other twin has no DP.
Table 7. Hazards ratios (HR) with 95% confidence intervals (95% CI) for those granted disability pension (DP) due to musculoskeletal diagnoses (MSD) during follow-up.

<table>
<thead>
<tr>
<th>Finnish Twin Cohort 1975 *Swedish Twin Registry</th>
<th>No DP (n=12667, *No DP due to MSD (n=25827))</th>
<th>Age and sex-adjusted</th>
<th>Full model</th>
<th>Discordant twin pairs (n=720 pairs, *484 pairs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical work load</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sitting</td>
<td>32</td>
<td>21</td>
<td>1.00</td>
<td>1.06</td>
</tr>
<tr>
<td>Standing</td>
<td>18</td>
<td>15</td>
<td>1.19</td>
<td>0.99, 1.43</td>
</tr>
<tr>
<td>Lifting and carrying</td>
<td>41</td>
<td>49</td>
<td>1.83</td>
<td>1.58, 2.12</td>
</tr>
<tr>
<td>Physically heavy work</td>
<td>8</td>
<td>14</td>
<td>2.08</td>
<td>1.70, 2.54</td>
</tr>
<tr>
<td>Work type</td>
<td>Monotonous work vs variable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indoor or outdoor work</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indoor work</td>
<td>69</td>
<td>59</td>
<td>1.00</td>
<td>1.04</td>
</tr>
<tr>
<td>Outdoor</td>
<td>11</td>
<td>14</td>
<td>1.33</td>
<td>1.11, 1.60</td>
</tr>
<tr>
<td>Combined indoor and outdoor work</td>
<td>21</td>
<td>26</td>
<td>1.35</td>
<td>1.17, 1.55</td>
</tr>
<tr>
<td>Work type</td>
<td>Day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shift work</td>
<td>81</td>
<td>82</td>
<td>1.00</td>
<td>1.09</td>
</tr>
<tr>
<td>*Years of night work</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>66</td>
<td>69</td>
<td>1.00</td>
<td>1.09</td>
</tr>
<tr>
<td>1–10 years</td>
<td>21</td>
<td>19</td>
<td>1.33</td>
<td>1.17, 1.53</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>13</td>
<td>12</td>
<td>1.39</td>
<td>1.18, 1.64</td>
</tr>
</tbody>
</table>


Full model: adjusted for sex, age, BMI, education, socioeconomic status, marital status, provider for the family, stress of daily activities, work type (monotonous vs. variable, physical work load, work type (day, night evening or shift work), changes of work place, periods of unemployment.

*Full model: adjusted for sex, age, body mass index, children living at home, marital status, education, chronic widespread pain, tobacco use, self-rated health, severity of illness.

Discordant twin pairs: those twin pairs, where one of the twins has been granted DP due to MSD, whereas the other twin has no DP.
<table>
<thead>
<tr>
<th>Periods of unemployment</th>
<th>HR</th>
<th>95% CI</th>
<th>HR</th>
<th>95% CI</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>1</td>
<td>1.13</td>
<td>1</td>
<td>1.13</td>
<td>1</td>
<td>1.13</td>
</tr>
<tr>
<td>1-4</td>
<td>1</td>
<td>1.14</td>
<td>0.94, 1.35</td>
<td>1</td>
<td>1.14</td>
<td>0.94, 1.35</td>
</tr>
<tr>
<td>5 or more</td>
<td>1</td>
<td>1.62</td>
<td>1.26, 1.98</td>
<td>1</td>
<td>1.62</td>
<td>1.26, 1.98</td>
</tr>
<tr>
<td>Changes of workplace</td>
<td>1</td>
<td>1.30</td>
<td>1.04, 1.64</td>
<td>1</td>
<td>1.30</td>
<td>1.04, 1.64</td>
</tr>
<tr>
<td>none</td>
<td>1</td>
<td>1.17</td>
<td>0.95, 1.44</td>
<td>1</td>
<td>1.17</td>
<td>0.95, 1.44</td>
</tr>
<tr>
<td>1-4</td>
<td>1</td>
<td>1.18</td>
<td>0.95, 1.44</td>
<td>1</td>
<td>1.18</td>
<td>0.95, 1.44</td>
</tr>
<tr>
<td>5 or more</td>
<td>1</td>
<td>1.28</td>
<td>1.04, 1.56</td>
<td>1</td>
<td>1.28</td>
<td>1.04, 1.56</td>
</tr>
<tr>
<td>Stressful work related</td>
<td>1</td>
<td>1.19</td>
<td>0.95, 1.44</td>
<td>1</td>
<td>1.19</td>
<td>0.95, 1.44</td>
</tr>
<tr>
<td>events (1-5 events)</td>
<td>2</td>
<td>0.92</td>
<td>0.75, 1.12</td>
<td>2</td>
<td>0.92</td>
<td>0.75, 1.12</td>
</tr>
<tr>
<td>3 or more</td>
<td>3</td>
<td>1.24</td>
<td>1.06, 1.45</td>
<td>3</td>
<td>1.24</td>
<td>1.06, 1.45</td>
</tr>
<tr>
<td>Stressful family events</td>
<td>1</td>
<td>0.91</td>
<td>0.75, 1.10</td>
<td>1</td>
<td>0.91</td>
<td>0.75, 1.10</td>
</tr>
<tr>
<td>(1-4 events)</td>
<td>1</td>
<td>0.91</td>
<td>0.75, 1.10</td>
<td>1</td>
<td>0.91</td>
<td>0.75, 1.10</td>
</tr>
<tr>
<td>Positive change in life</td>
<td>4</td>
<td>0.62</td>
<td>0.60, 0.64</td>
<td>4</td>
<td>0.62</td>
<td>0.60, 0.64</td>
</tr>
<tr>
<td>illness or injury that</td>
<td>2</td>
<td>0.58</td>
<td>0.56, 0.60</td>
<td>2</td>
<td>0.58</td>
<td>0.56, 0.60</td>
</tr>
<tr>
<td>caused over 3 weeks</td>
<td>12</td>
<td>0.81</td>
<td>0.78, 0.85</td>
<td>12</td>
<td>0.81</td>
<td>0.78, 0.85</td>
</tr>
<tr>
<td>work disability</td>
<td>16</td>
<td>0.79</td>
<td>0.76, 0.82</td>
<td>16</td>
<td>0.79</td>
<td>0.76, 0.82</td>
</tr>
</tbody>
</table>
Table 9. Hazards ratios (HR) with 95% confidence intervals (95%CI) for those granted disability pension (DP) due to musculoskeletal diagnoses (MSD) during follow-up from 2nd Jan 1975 until 31st Dec 2004 for stress of daily activities and being a provider for the family.

<table>
<thead>
<tr>
<th>Finnish Twin Cohort 1975</th>
<th>No DP (n=12667)</th>
<th>DP due to MSD (n=1297)</th>
<th>Age and sex-adjusted</th>
<th>Full model</th>
<th>Discordant twin pairs (n=720 pairs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>%</td>
<td>%</td>
<td>HR</td>
</tr>
<tr>
<td>Stress of daily activities (range 4–16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.06</td>
</tr>
<tr>
<td>Little (16)</td>
<td>20</td>
<td>18</td>
<td></td>
<td></td>
<td>1.29</td>
</tr>
<tr>
<td>Some (9–15)</td>
<td>72</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Much (4–8)</td>
<td>7</td>
<td>15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provider for the family</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.06</td>
</tr>
</tbody>
</table>

DP due to MSD: Those responded to be at work at baseline 1975.
Full model: adjusted for sex, age, body mass index, education, socioeconomic status, marital status, provider for the family, stress of daily activities, outdoor- or indoor work, work type, nature of work, physical work load, changes of work place and periods of unemployment.
Discordant twin pairs: those twin pairs, where one of the twins has been granted DP due to MSD, whereas the other twin has no DP.
6 DISCUSSION

This PhD thesis analysed whether there are risk factors for DP due to MSD that can be identified early during adult life course. The thesis consists of four population based prospective studies based on two large Nordic twin cohorts. Register information was available on DP due to MSD with no loss to follow-up. The follow-up time was up to three decades. The study populations of working age twins made it possible to take into account familial influence, including aspects of genetics and shared childhood environment.

6.1 SUMMARY OF THE MAIN FINDINGS

This population based study provided information on factors of importance for DP due to MSD. As in this thesis two Nordic twin cohorts with register-based information with no loss to follow-up were included, familial influence (genetics and shared, mainly childhood environment) could be taken into account. Several risk factors for DP due to MSD were identified in the substudies of this PhD thesis. These risk factors identified relatively early in the working career, were mainly unaffected by familial confounding.

The predictive factors identified for DP due to MSD included sociodemographic, health and work related factors and stressful life events. In more detail, sociodemographic factors, namely, high socioeconomic status and additional years of education, were found to decrease the risk of future DP due to MSD. With respect to the health related factors, self-reported musculoskeletal pain, the presence of any other disease, being overweight or smoker were seen to increase the risk of DP due to MSD. From work related factors, physical work load and work considered as monotonous increased the risk of DP due to MSD. With respect to the stressful life events, those with many changes of workplaces, and those with the event “illness or injury causing over 3 weeks work absence” were seen to have an increased risk of DP due to MSD. These sociodemographic, health and work related associations were unaffected by confounding due to other covariates or by familial influence. Instead, a familial influence could not be ruled out for night work. In addition, stressful family related life events were seen as risk factors among discordant twin pairs suggesting confounding due to a familial influence.

These findings for sociodemographic and health related factors are in accordance to previous findings [41, 43, 49, 51, 57-59, 63], as were the findings for work related factors, where physical work load was shown to be an independent risk factor for DP due to MSD [79, 146]. Moreover, these associations between sociodemographic, health and work related factors and DP were shown to be mainly unaffected by familial influences. Instead, the influence of familial factors was seen for stressful family related life events. This finding was supported by the known genetic influences on life events [122] and DP due to MSD [24, 25].

6.2 INTERPRETATION OF THE MAIN FINDINGS

In this thesis, the main interest was whether factors of importance for future DP due to MSD could be found even three decades beforehand. Being able to use twin data, familiar factors, including genetics and shared family environment, could be controlled for. In the Finnish twin cohort, a total of 8% of participants were granted DP due to MSD during the follow-up from 1975 to 2004 [24]. A total of 5% from the Swedish twin registry had been granted a DP due to MSD during follow up from baseline interview conducted between 1998 and 2003, until end of year 2013.
6.2.1 Sociodemographic factors
Socioeconomic status and years of education were found to influence the risk of DP due to MSD. These findings are in line with previous studies [41, 42, 49, 52], where higher socioeconomic status has been shown to decrease the risk of DP due to MSD [41, 42] and DP due to LBD [42], and with findings that years of education decrease the risk of DP due to MSD [42, 49] and DP due to LBD [52].

In this thesis, it was found that the associations between socioeconomic status and education, and future DP due to MSD, were unaffected by confounding due to other covariates, or by familial influence (substudy I). More specific, these associations were not explained by individual’s health behaviour or by family background, including genetic factors and shared childhood environment. Education was considered as an early and stable measure of attained education within the study cohort [34]. When self-reported physical loading at work was included in the same model as education and socioeconomic status (substudy II), all these three factors remained as significant factor for future DP due to MSD. This was even though socioeconomic status was considered to indicate occupational physical loading, as it reflects the social class based on the study participants’ occupation in 1975 (Finnish twin cohort) [133], and despite it has been shown, that socioeconomic status and DP due to MSD is at least partly attributed to the physical work environment, and less to health related factors [44, 147, 80]. For higher socioeconomic status and longer education, decreased risk of DP due to MSD may be at least partly attributed due to better opportunities to adjust to different life situations.

In addition, women have been shown to have an increased risk for both LBD [148] and DP due to LBD [42]. For DP due to MSD, women have either been shown to have a similar or higher risk than men [46, 70, 149]. In addition, there seem to be differences between men and women in the consequences of LBD, with women reporting more healthcare use, whereas men describe more work disability [70]. However, regarding the risk factors analysed in this thesis, no significant sex differences were detected in the risk factors of DP due to LBD or DP due to MSD.

In addition to sex, age is also to be considered when studying DP due to MSD, as the risk of DP due to MSD increases with age [5], and, at least for some of the studied risk factors, age may affect the influence on risk of DP due to MSD [96]. In this thesis, all the analyses were adjusted for potential influence of age and sex.

Previous studies have suggested an increased risk of DP among divorcees and singles compared to those who are married [46, 53]. Hence, marital status was considered for a potentially influencing factor for DP due to MSD, but no independent association was seen with future DP due to MSD or LBD. This finding was supported by a study among Swedish twins [50]. It is possible that this inconsistency in results are due to different age groups in the studies, or due to difference of DP due to any diagnoses [46] or DP due to MSD or LBD [46, 50, 53] being studied.

6.2.2 Health related factors
In this thesis, self-reported musculoskeletal pain, the presence of any chronic disease, overweight and current smoking were seen to increase the risk of DP due to MSD independently from confounding due to other covariates or by familial influence.

The findings for work impairing musculoskeletal pain as risk factors for DP due to MSD are in line with previous studies, where the presence of pain, measured either as self-reported pain [41, 57] or by the number of pain sites [55] or by diagnosed musculoskeletal disorder [51, 52] has been found to predict future DP due to MSD. Moreover, in this thesis, self-reported pain in neck, shoulder or low back area were first analysed separately, and each of these pain locations were identified equally strong risk factor for DP due to MSD. For pain, the measure used was that pain should be perceived to have affected work ability, hence reflecting pain that prevents working normally. This measure did not differentiate between acute or chronic pain.
With respect to the use of analgesics, the participants’ responses to this question were considered as an indicator of the presence of pain due to any reason, not restricted to musculoskeletal disorders. In this study, association between use of analgesics and DP due to LBD attenuated when controlling for sociodemographic and other health related factors.

The variable “presence of any chronic disease” was considered to reflect potential comorbidity with MSD. In previous studies, several comorbidities for LBD have been identified, including musculoskeletal disorders, cardiovascular diseases, and cerebrovascular diseases [67-69]. The presence of comorbidities has been found to increase the risk of future DP due to LBD [59]. These findings are considered to reflect also the situation with MSD. Furthermore, MSD appeared to have additive influence on work disability when co-occurring with other diseases [72-74]. In addition, MSD may predispose also to DP due to other diagnosis, including mental health diseases, cancer or circulatory diagnosis [77]. Furthermore, in a study of sickness absence due to back pain and its association with future DP due to MSD, it was shown that comorbidities explain partly, but not fully, the association with back pain and future DP due to MSD [56]. This is in accordance with the findings of this thesis that both musculoskeletal pain and the presence of other diagnosis have independent associations with DP due to MSD. In addition, women have been shown to have more comorbidities linked with LBD [67, 70], which may predispose them also to DP. In this thesis, comorbidities showed similar risk for both sexes. Overall, these findings suggest that there may be several potential pathways how the presence of comorbidities may contribute to risk of future DP due to MSD.

With respect to BMI, the findings of this thesis are in accordance with previous studies where being overweight or obese has been found to increase the risk of DP due to LBD [59] and DP due to MSD [61, 62], and LBD [150, 151]. In this thesis, being overweight increased the risk of DP due LBD. Moreover, for both DP due to LBD and DP due to MSD, each unit increase in BMI was seen to increase the risk.

With respect to smoking, our findings are also in accordance with previous studies, which have found smoking to be an independent risk factor for DP due to LBD [52, 63] and DP due to MSD [41, 57, 63], and identified smoking also as a risk factor of LBD [64, 152].

There are genetic influences identified in health related risk factors associated with DP due to MSD, such as BMI [120, 121] and smoking [119]. In addition, genetics are known to have a relatively important role in the pathology of LBD [71, 110-113, 153]. Furthermore, also DP due to MSD is shown to have a moderate genetic component [24, 25]. The finding of this thesis that there was no familial influence between health related factors and future DP due to MSD, despite these known genetic influences, adds to the current knowledge, and shows preventive potential to reduce number of DP due to MSD.

Moreover, as familial confounding did not explain the associations between health related factors and being granted a DP due to MSD, this points more towards causal relationship rather than an association through mediating factors. This causal relationship seems possible at least for smoking, as it has been shown to be a risk factor both for MSD [64, 152] and DP due to MSD [57, 63], and was shown to be a strong and independent risk factor DP due to MSD also in this thesis.

Altogether, these results suggest that several health related factors potentially play roles both in the development of MSD, and in the consequences of MSD, such as DP. Self-reported musculoskeletal pain, the presence of any chronic disease, overweight and current smoking were seen as independent risk factors of DP due to MSD.

### 6.2.3 Work related factors

This PhD thesis evaluated work-related factors as possible predictors for DP due to MSD among individuals who were at work at the baseline in 1975. Many factors reflecting different aspects of work load, especially the physical work load, confirmed findings in the literature [79, 79, 80, 82, 146, 146] and suggest that several work-related factors are potentially...
associated with permanent work incapacity and, furthermore that these factors can be identified early in the adult life course.

Moreover, many of the work-related questions were the participants’ own reflections, for example, does the participant regards his/her work as physically heavy. These questions are considered to offer a crude but reliable and relevant estimation of the potential association between work load and DP due to MSD. Furthermore, these results are applicable also in today’s work life which still involves relatively often physically loading work [13]. However, some of the queried items may have been influenced by changes in working life, for example, the question of whether work is considered monotonous may nowadays reflect more diverse work environment than in the 1970s.

For DP due to MSD, lifting and carrying at work and monotonous work seemed to have a direct effect on the susceptibility to DP due to MSD, as their effects were found to be independent of familial effects. The other associations between DP and work-related factors, including outdoor work, were in a similar direction and magnitude in the discordant pair analyses, pointing to independence from familial effects. These findings are in accordance with the current literature, as it has been shown that an unfavourable ergonomic situation (such as heavy lifting) [79], and cumulative work exposure to lifting, increase the risk of DP in general [83]. Moreover, physical work load, low job control and occupational class have been identified as risk factors for future DP due to MSD [80].

To clarify the role of work-related factors for DP, socioeconomic status and education were included as confounders in the model. With all these factors in the same model, it is possible to obtain more conservative estimates for work-related factors and their associations with future DP due to MSD. In the previous research, it has been shown that socioeconomic status and education both play a role in MSD [154] and in DP due to MSD [41, 44], and also in work-related factors [155, 156]. These previous findings, together with the results of this PhD thesis, showed that although socioeconomic status and education partly represent similar factors than direct work related measures, they are all unique contributing factors as they all showed a strong association with DP due to MSD.

Overall, these results show that a single question assessment of individuals own perception of work load offers valuable information regarding risk of future DP due to MSD. In addition, they showed that physical work load, especially being in work involving lifting and carrying, independently increases risk of DP due to MSD, as does work that is considered as monotonous.

**Shift work and night work**

With respect to shift work, the associations between DP due to MSD were in a similar direction and magnitude in the standard cohort analysis and in the discordant pair analyses, pointing towards independence from familial effects, although attenuated to statistical non-significance. For night work, both 1–10 years and more than 10 years of night work were significant predictors of future DP due to MSD independently of health and lifestyle factors. These results for night work are in line with previous findings on the risk of night work for DP in general [53] but not with studies concentrating on musculoskeletal pain and night work that either found no association [85] or found an association with only long (over 16h) working hours [86]. Moreover, the results for night work and its association with DP due to MSD differed from shift work, as after adjusting for familial confounding (genetics and shared family environment), the association between night work and DP due to MSD attenuated, suggesting that familial factors might be of importance.

Several possible pathways were considered through which shift and night work could be associated with DP due to MSD, including the stress attributable to the psychosocial, behavioural, and physiological factors, including work stress and health behaviour [157]. Hence, for shift work, sociodemographic and work related factors were considered as potential confounders and they appeared to play a role, as the risk estimates became attenuated. For night work, sociodemographic and health related covariates were considered
most likely to explain the potential association, including musculoskeletal pain at baseline, but they seemed to exert no effect on the association.

The findings of this thesis for night work and DP due to MSD are supported by a previous Danish study showing that night work was a risk factor of DP due to any reason independently of sociodemographic factors [53]. In that study, marital status, socioeconomic status, and health related factors including leisure-time physical activity, alcohol use, smoking and BMI, and physical working conditions were included as covariates [53].

Moreover, for shift work, the risk estimates, although attenuated, pointed more towards independence of familial factors. However, the small number of discordant pairs means that conclusions should be drawn with caution. Instead, for night work and DP due to MSD, these risk estimates attenuated after controlling for familial factors. Hence, one cannot rule out familial influence. Furthermore, the results of this thesis do not point to a causal relationship for night work and DP due to MSD, as besides that the association was not independent from confounding, no accumulation of risk was seen for those with over 10 years of night work compared to those with 1 to 10 years of night work.

It is possible that the difference in our findings regarding shift and night work is due to the fact that different phenomena was being studied, i.e., the difference of working mainly shift work at baseline, and between years of exposure to night work during working years. Further studies are needed to clarify if the difference between these studies is due to shift and night work having different influence on DP due to MSD.

Moreover, time or timing of exposure to shift/night work may have an influence, as age has been shown to be rather influential factor especially for shift and night work. Not only can age affect adaptation and tolerance to night work [97, 98], but there may be differences in health consequences related to the age when the first exposure to night work takes place [96] and to the length of exposure to night work [136]. In addition, a healthy worker effect may be involved in the pathway between night work and DP due to MSD, as it is possible that those unable to adapt to night work change to day work instead [98, 158]. This probably apply also for shift work, as shift work usually involves also night work. In this thesis, we were not able to assess this potential healthy worker influence.

Overall, it was shown that shift work and night work differ in their association with DP due to MSD. Night work was identified as a risk factor for future DP due to MSD with potential familial confounding playing a role, whereas for shift work, confounding due to other factors seemed more evident. As lifetime night work experience was queried, it is considered that within both cohorts, a similar time in the individuals’ working life was under study, i.e. that differences in working life do not explain the difference in these results.

6.2.4 Stressful life events

In this thesis, stressful life events, divided into work and family related events, were analysed for their association with DP due to MSD. Information gathered at baseline 1981 was limited to life events occurring within the past five years. Participants were at time of this questionnaire between 23 to 64 years of age. The potential association between life events and DP due to MSD was analysed taking sociodemographic and health related factors into account as potential confounders, as well as the familial influence. In addition to stressful work and family events, also individual life events were analysed, including periods of unemployment, changes of working place as well as life event “positive change in life”.

Stressful work related life events, measured as the combination of events, showed that having many work events seemed to be protective against the risk of DP due to MSD, but this association was influenced by familial confounding. The absence of stressful work events showed no significant association with DP due to MSD. These results differ from previous findings where stressful work related events have been shown to associate with poorer general health among male industrial workers, independently of being manual or non-manual worker [159].
Moreover, periods of unemployment and changes of work place were associated with a higher risk of DP due to MSD in this thesis. These life events may have a direct effect on the susceptibility to DP, as in previous studies, unemployment has been seen to increase risk of DP due to RA [105] and to predict limited work capacity [160], and it is also recognised as risk factor for DP in general [17]. Instead, no association has been found for short-term unemployment, lasting between 1 to 12 months, and DP due to MSD [161]. In this PhD thesis, when analysing the association between unemployment and changes of work place, the selection criterion of being at work at baseline was used. As despite this selection criterion, changes of workplace and times of unemployment prior to baseline in 1975 were significant factors for DP due to MSD baseline, these findings are pronounced.

A single life event, “Illness or injury causing over 3 weeks work disability”, was recognised as a direct risk factor for DP due to MSD. This was an expected finding, as long-term sickness absence is a general requirement for being eligible for DP [5].

With regard to stressful family events, the absence of family events decreased the risk of DP due to MSD, whereas many family events increased the risk, when accounting for familial confounding. In the standard cohort analysis, these risk estimates were not significant. Health or socioeconomic status at baseline had no major influence on these associations. This independence of health related confounding has been shown also in an earlier study of stressful family events and risk of sickness absence [103].

Also, for family events, as well as for work events, the absence of events may represent a different life situation than having many events within five years. The study population was, on average, in their 40s at the time of questionnaire, and may be considered to have already established a steady work or family life. The absence of family related events may reflect not only individual choices but also chance events, as some events are uncontrollable, for example, the health of a family member [162]. Having many work or family events may be considered to reflect high overall stress in life. Furthermore, genetic component has been identified for the frequency of life events, including both family and work related stressful life events [122].

Besides work and family related events, a single item, “Positive change in life” was analysed separately. Previous findings of health and positive life events are scarce, but support the finding of this thesis that a positive life event may decrease the risk of DP due to MSD [163, 164]. The life event “positive change in life” was analysed separately, as the correlation between single stressful life events showed equal correlations both with work and family events.

Overall, this approach of analysing stressful life events divided as work and family events provided new information compared to analysing all life events together. As work and family events are often connected to each other, for example, changing work place may lead to a change of residence, the finding that the correlations between single stressful life events supported the categorizing of events to stressful family and work related life events is of significance, as it captured the actual living experiences of people.

Moreover, based on these findings, it seems that stressful work and family related life events exert different influences with respect to the risk of DP due to MSD, as does having an absence or experiencing many of these events. In contrast to previous studies [102, 103, 165], no independent association was found between having many stressful work or family related life events and DP due to MSD. Instead, the results in this thesis indicate that familial confounding influences these associations, a finding supported by other reports separately for stressful life events [122] and DP due to MSD [24, 25]. A single item “Positive change in life” seem to capture a different phenomenon than stressful life events, as it was found to be independent from familial confounding.

6.2.5 Stress of daily activities and being a provider for the family

This thesis also examined the perceived overall stress of daily activities reflecting several dimensions of life, that is, every day hassles including family and work life, that may be
related to an excessive work load or a way to react to daily stress. For DP due to MSD, if daily activities evoked high levels of stress, this was shown to increase susceptibility to DP and furthermore, this association was unaffected by other covariates or familial influence. This effect of stress of daily life for future DP due to MSD adds to the rather limited prior knowledge on the association between stress and future DP due to any diagnosis [48, 166], and is supported by finding that increased stress of daily activities, measured six years apart, has been shown to be an independent risk factor for DP due to MSD [81]. Moreover, those not providing for the family were shown to have an increased risk of DP due to MSD, but this association attenuated to non-significance when confounding due to other factors or due to familial influence was taken into account, and hence not having independent association with DP due to MSD.

6.3 METHODOLOGICAL CONSIDERATIONS

This thesis had an advantage of having access to two large population based Nordic twin cohorts. Both cohorts have comprehensive baseline information combined with register information on DP events during follow-up. This means that there was complete data on cases of DP due to MSD during three decades of follow-up.

Potential risk factors of DP due to MSD or LBD were examined in detail as we had the opportunity of using three models. First, a standard cohort analysis with optimal age and sex adjustment due to the fact that twin pairs were evaluated. Second, a model taking into account other covariates was conducted in order to provide statistical evidence for the independent contribution of a risk factor even when known confounders had been taken into account. Third, the co-twin model was able to take into account shared environmental factors, including genetic factors and shared childhood factors, by demonstrating that the association also was evident when environmental factors not measurable otherwise, were controlled for. With these three models, the identified risk factors, that were unaffected by confounding due to other covariates and by familial factors, can be considered as strong and independent risk factors. Furthermore, as follow-up was up to three decades, possible causal associations can be considered for such strong risk factors for DP due to MSD or LBD.

Moreover, when interpreting the influence of familial confounding, the analysis where twins are analysed as singletons (standard cohort analysis) is used as the reference in the comparisons. If the risk estimates attenuate when the analyses are restricted to discordant twin pairs, i.e. where one of the twin in a pair, but not the other, have been granted a DP due to MSD, this would be indicative of familial confounding. Nonetheless, when interpreting the differences between discordant twins, the possibility of a limited number of cases needs to be taken into consideration.

The final sample, depending on selection criteria, ranged from 16 028 to 27 165 working age twin individuals. Among Finnish twins, the baseline information originated from the years 1975 and 1981. Among Swedish twins, the lifetime experience of night work was queried at the baseline interview, which occurred between the years 1998 to 2003. Hence, the information extracted from these two Nordic cohorts captures a similar period in society and work life developments. Moreover, as same sex twin siblings were studied, the changes in society are expected to have similar impact on both twin siblings.

In this PhD thesis, several potential risk factors for DP due to MSD were analysed, that were selected based on the previous knowledge of factors important for MSD/LBD and for DP, separately, and of factors of importance for DP due to MSD. Both individual questions and combined information from multiple questions were used to gain better understandings of the risk factors of importance for DP due to MSD. In general, the risk factors included in this thesis are considered reliable and stable measures [134, 167]. With respect to stressful life events, the previous knowledge on significance to MSD was limited, but there are a few studies indicating that they are associated with a risk of future DP in general [17, 102, 103].
Limitations of this thesis include that the comprehensive baseline data was self-reported and thus affected by possible recall bias. In addition, a possible source of bias in this thesis could have been drop-out due to those not responding. However, this is considered small as the response rates were high for all the baseline questionnaires (89% for questionnaire 1975, and 84% for questionnaire 1981 in Finnish twin cohort, and 66% for Swedish twin cohort). Other limitations include a small sample size, i.e. for some observations, no firm conclusions could be drawn. In addition, for each specific risk factor selected in this PhD thesis, the estimates used were rather crude. Further, it may be problematic that the influence of socioeconomic status, education was included in the same models, since they are mutually associated. As these correlations were only moderate (ranged from 0.23 to -0.38) and did not suggest strong collinearity, socioeconomic status and education were included in the same model. Moreover, in substudy II, also self-reported physical work load was included, which had a correlation coefficient of 0.39 with socioeconomic status when the whole cohort was evaluated. Based on the results obtained in this study, these factors seem to measure different, possibly complimentary, sociodemographic aspects, perhaps reflecting different aspects of physical work load during working careers.

Other potential sources of multicollinearity could be discerned from responses to questions of pain location and use of analgesics. In this study, it was concluded that each pain location (back, shoulder, neck) had an independent yet similar association with future DP due to MSD. To test for potential multicollinearity, correlations between pain locations and use of analgesics were tested among those individuals being granted a DP due to LBD during follow-up (substudy I). The highest correlation of pain and use of analgesics (0.15–0.41) was found in woman who were 36 to 45 years of age, with the highest correlation found for the association between neck pain and the use of analgesics, whereas back or shoulder pain displayed low correlations with analgesic use. Hence, it was concluded that the use of analgesics captures different information than a question inquiring about work impairing pain.

Other limitations of this thesis include age of the study cohorts. The Finnish twins were between 18 to 64 years of age at baseline, which may have diluted some of the effects and caused an underestimation of the associations. This is especially evident as the majority of the sampled individuals were under 35 years of age (n=15 172). In contrast, the number of those over 55 years of age was small (n=1345). When the age of received DP due to MSD was considered, it was noted that the cases of DP were most prevalent among those in the age bracket 36 to 55 years (n=7525, including 1152 cases of DP due to MSD out of a total 1829 DP due to MSD cases in the cohort). Moreover, the mean age of the cohort was 32 years of age, and at end of the follow-up, they were 55 years of age. To maximize the sample size, also those close to retirement age were included as in the pre-analysis conducted within Finnish twin cohort. This decision was supported by finding that no real difference in risk estimates were shown, when follow-up time was limited to start six years after baseline for a purpose of testing influence of follow-up time.

The study sample of Swedish twins consisted of adults aged between 41 to 64 years, and hence, does not cover the whole working age population as the Finnish twin cohort. However, in the Swedish twins, night work history and its association with DP due to MSD were studied as the years of night work experience up until the time of the baseline interview. Due to this research question, and the fact that average age of this cohort was over 50 years at baseline, age of cohort was also seen as strength. This is because it may be assumed that workers over 50 years of age would be unlikely to start night work, and therefore, those individuals with a work history involving night work were considered to be relatively well captured within this study setting.

In this thesis, those individuals not granted DP due to MSD/LBD (but may have been granted DP for some other reason) were used as the reference group. The use of those individuals without DP due to MSD/LBD as the reference group may lead to an underestimation of the real risk, as conversely using those without any DP may cause an
overestimation of true effect. However, when testing for the effect of reference class, no real difference in risk estimates was seen. To maximize sample size, those with no DP due to MSD or LBD were used as the reference class in this thesis.

Additionally, the effects of time and back pain at baseline were analysed. These additional analyses were conducted in substudy I, where DP due to LBD was measured as an outcome event. Limiting the follow-up time to begin from 1981 instead of 1975 had no real influence on the risk estimates. This test was conducted to examine whether the changes in the granting of a disability pension had influence on the association between selected factors of interest and DP due to MSD. Additionally, this limiting of the follow-up time also excluded those who may have already been in the process of being granted a DP due to MSD, i.e. on sick leave due to MSD but not yet fulfilling the criteria for being granted a DP. Additionally, there was no change in the risk estimates when those having back pain at baseline were excluded. It was therefore concluded that although work-impairing back pain at baseline increases the risk of DP due to MSD and LBD, it does not modify the risk of future DP due to MSD or LBD.

As Nordic countries have similar working environments and social security systems, findings among Finnish and Swedish cohorts are expected to be complimentary. Furthermore, as twins have been demonstrated to be representative of standard national population [125, 168], these findings are considered to apply to similar aged populations in both countries.

Overall, this thesis had several strengths, including the use of two large population based twin cohorts of men and women. The cohorts provided a powerful opportunity to control for genetic factors and for shared childhood environment, use of longitudinal study designs with a long follow-up time and high quality registry data with no drop-out in the outcome information, that is, all individuals could be followed up. The high-quality registry data included dates and diagnosis for DP occurring during follow-up for all individuals. Moreover, the results regarding the association between sociodemographic, health and work related factors and stressful life events, and DP due to MSD, are considered more likely to be an under- rather than an over-estimation of the long-term health effects in terms of DP due to MSD.
7 CONCLUSIONS

In this PhD thesis, it was found that several sociodemographic, health and work related factors, and stressful life events, predict future DP due to MSD. These risk factors can be identified early in the adult life course. Furthermore, these risk factors were shown to be mainly independent from familial influence, even though a moderate genetic influence has been recognised for DP due to MSD [24, 25, 124]. The framework of the study, modified life course approach, included being able to consider genetics and shared childhood environment, education reached relatively early in life, and factors of early working years and their association with later life work capacity being the main interest, to answer, if factors of early adulthood influence risk of later life DP due to MSD.

The following conclusions were proposed on the basis of the present study:

1. From sociodemographic factors, high socioeconomic position as well as additional years of education decreased the risk of future DP due to MSD. Lower socioeconomic position increased the risk of DP due to MSD. These associations were unaffected by confounding due to other covariates or by familial influence.

2. From health related factors, musculoskeletal pain, presence of any chronic disease, overweight and smoking were found as strong and independent risk factors for DP due to MSD.

3. From work related factors, monotonous work and physically heavy work were recognised as strong and independent risk factors for DP due to MSD. Night work increased the risk of future DP due to MSD, but familial confounding could not be ruled out for this association.

4. With respect to stressful life events, illness or injury causing over three weeks of work disability, and having experienced many changes of workplaces, increased the risk of future DP due to MSD independently from confounding due to other covariates or by familial influence. A single life event “positive change in life” decreased the risk of DP due to MSD. This association was unaffected by familial confounding. Family related life events were identified as risk factors among discordant twin pairs.

7.1 IMPLICATIONS AND FUTURE PERSPECTIVES

As DP due to MSD incurs severe losses both for individuals and society, it would be of importance to clarify the pathway leading to DP due to MSD. In this thesis, several risk factors for DP due to MSD were found. These were identified up to three decades beforehand mainly with a single question. Moreover, the risk factors found in analysis of this thesis are considered to be strong and early predictors for future DP due to MSD, as they were mainly independent from confounding due to other covariates of by familial influence. In general, findings of this points towards the possibility of implementing early preventive actions to reduce the burden caused by DP due to MSD.

Moreover, in this thesis, possible causal links were identified between health behaviour and risk of DP due to MSD. Furthermore, it was observed that DP due to MSD is a multifactorial phenomenon, with sociodemographic, health and work related factors, and stressful life events, all exerting predictive roles. During life course, many factors naturally co-occur, and may lead to accumulation of risk. Hence, it would be of importance to be able to identify persons at increased risk for DP due to MSD early in working years for preventive actions. Furthermore, as only minor sex differences were shown in risk factors for DP due to MSD, findings of this thesis implicate that to promote musculoskeletal health throughout working years, similar recommendations apply for both men and women. Findings for
family related stressful life event being potentially a risk factor for future DP due to MSD implies that making work life more flexible could help decrease risk of DP MSD. From a methodological point of view, the results of this thesis are in line with previous knowledge regarding MSD [71, 110-118] and DP due to MSD [24, 25, 124], that the potential role of familial confounding is to be considered while studying the risk factors of DP due to MSD.

The policy implications of the findings emerging from this study suggest that in occupational health care, early identification of persons at risk is possible. In addition, in order to reduce the incidences of DP due to MSD, it is important to recognize those occupations where physical or working hours related work environment may cause later-life health problems and advice about current best practices should be provided to support good working capacities. For work places, this study highlights the importance of considering the health of their employees early and throughout their working careers. Supporting the health of employees could include promoting healthy habits (i.e. a non-smoking work environment), and working together with occupational health care in arranging an optimal physical work environment to support long term work capacity. With respect to the individual, the results of this thesis stress the value of adopting positive health behaviours throughout life, to avoid a premature exit from working life due to MSD.

In conclusion, many of the identified risk factors in this thesis seem amenable to preventive actions in occupational health care, and by adjustments at work places, or by individual life style choices. These preventive actions to reduce incidences of DP due to MSD should be in place early in working life. At societal level, these actions would benefit the efforts to prolong working careers.

The results of this thesis obtained by analysing Finnish and Swedish twins are probably generalizable to the Nordic countries with similar social welfare systems, but they are probably less generalizable to other countries.

7.1.1 Future perspectives

Future studies with even larger sample sizes, for example, by pooling existing twin cohorts, could be one way to confirm these findings. More studies are needed to determine if these Nordic twin cohort findings also reflect the situation in other western countries.

With respect to the risk factors identified in this thesis, stability or a change in risk factors during life course would add to knowledge gained in this thesis. These have already been studied for several health and work related factors [54, 63, 81], but for example for stressful life events, limited information is available.

In addition, a potential causal influence seems plausible for some of the studied risk factors, and DP due to MSD, most strongly for smoking. This warrants further research, to identify specific pathways contributing to this association, as well as to add to the current knowledge on development of MSD.

More research is needed to understand why night work seems to increase risk of DP due to MSD. One way to gain more knowledge would be repeated measures of pain and sleep among those doing night work. Moreover, there is a very limited scientific literature investigating night work and stressful life events as risk factor for DP due to MSD. Hence, findings of this PhD thesis need to be interpreted with caution until confirmed in further epidemiological studies. Studying the effect of individual family related life events instead of combining the events together might provide useful information for reducing future incidences of DP due to MSD. In addition, more knowledge is needed about whether work place interventions aimed at increasing flexibility at work are beneficial in reducing the potential harms related to working hours and having many stressful family related life events in terms of a future DP due to MSD.

One aspect of future studies would be linkage of twin cohorts, not only to enhance findings of this thesis, but to allow analyses separately for DZ and MZ twin pairs. This would allow to clarify further the role of genetic and shared familial environment in associations between potential risk factors and future DP due to MSD. For example, for some of the factors
analysed in this thesis i.e. night work and stressful life events, potential confounding due to familial factors was observed with respect to their association with DP due to MSD. If one wishes to confirm these findings and gain a better understanding of these associations, either another twin cohort could be examined, or alternatively existing twin cohorts could be pooled. Furthermore, it might be beneficial to study if age influences some of other risks also, for example, if physical loading at work is a similar risk factor in both young and older workers. Besides allowing to analyse more closely specific age groups or occupational groups, linkage of data would make it possible to study also subclasses of MSD, such as LBD, OA and RA.

From specific risk factors, knowledge on the role of stressful life events in relation to future DP due to MSD is scarce. In this thesis, the stressful family and work events were seen to be relatively complex in their associations with DP due to MSD. Not only are stressful work and family related life events influenced differently by familial confounding, but it also seems that those individuals not experiencing these events differ from those with many stressful life events in terms of their association with DP due to MSD. Moreover, the finding that positive life events seem to decrease the risk of DP due to MSD, needs more clarification. Particularly, these findings require further investigation to in means of preventing future incidence of DP due to MSD.

Furthermore, in this PhD thesis, the psychosocial work environment was not investigated and this aspect should be included in future studies on risk factors of DP due to MSD.
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Appendices

Appendix A. Stressful life events divided to work and family related events.

Appendix B. Baseline characteristics with means (standard deviations) and percentages a) for those responded questionnaire 1975 and granted disability pension (DP) due to low back diagnoses (LBD); b) for those at work in 1975 and granted DP due to musculoskeletal diagnoses (MSD); c) DP due to MSD for those responded questionnaire sent in 1981; d) for those granted DP due to MSD during follow-up in Swedish twin registry. Baseline for a) and b) is 2nd Jan 1975, c) 1st Jan 1982, d) baseline interview 1998–2003.
**Appendix A. Stressful life events divided to work and family related events.**

<table>
<thead>
<tr>
<th>Family related events (14 questions)</th>
<th>Work related events (5 questions)</th>
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<tr>
<td>Death of spouse</td>
<td>Loss of a job</td>
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<tr>
<td>Death of friend</td>
<td>Change to different kind of work</td>
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<tr>
<td>Change in health of family member</td>
<td>Interpersonal conflict at work</td>
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<tr>
<td>Sexual difficulties</td>
<td>Increase in responsibilities at work</td>
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<tr>
<td>Financial problems</td>
<td>Increase in amount of work</td>
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<td>Gain of new family member</td>
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<td>Divorce or separation</td>
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<td>Interrupted pregnancy in family</td>
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<td>Change in residence</td>
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<td>Family member leaving home</td>
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<td>Serious conflict in close relationship</td>
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<td>Change in number of arguments with spouse</td>
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<td>Taking a loan (more than half of yearly income)</td>
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<td>Living away from spouse due to work</td>
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</table>
Appendix B. Baseline characteristics with means (standard deviations) and percentages a) for those responded questionnaire 1975 and granted disability pension (DP) due to low back diagnoses (LBD); b) for those at work in 1975 and granted DP due to musculoskeletal diagnoses (MSD); c) for those responded questionnaire sent in 1981 and granted DP due to MSD; d) for those granted DP due to MSD during follow-up in Swedish twin registry. Baseline for a) and b) is 2\textsuperscript{nd} Jan 1975, c) 1\textsuperscript{st} Jan 1982, d) baseline interview 1998–2003.

<table>
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<tr>
<th>Baseline characteristics (Studies I-IV)</th>
<th>Finnish Twin Cohort</th>
<th>Swedish Twin Registry</th>
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<td>a)</td>
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<td></td>
<td>DP due to LBD</td>
<td>DP due to MSD</td>
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<tr>
<td></td>
<td>(n=600)</td>
<td>(n=1297)</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>39 (10)</td>
<td>39 (9)</td>
</tr>
<tr>
<td>Follow-up time</td>
<td>16 (8)</td>
<td>15 (7)</td>
</tr>
<tr>
<td>Education in years</td>
<td>7 (2)</td>
<td>7 (1)</td>
</tr>
<tr>
<td>% Compulsory</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>More than compulsory</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sex</td>
<td>Women</td>
<td>42</td>
</tr>
<tr>
<td>Socioeconomic status 1975</td>
<td>Upper non-manual</td>
<td>3</td>
</tr>
<tr>
<td>worker</td>
<td>Low non-manual</td>
<td>20</td>
</tr>
<tr>
<td>worker</td>
<td>Skilled manual</td>
<td>38</td>
</tr>
<tr>
<td>worker</td>
<td>Unskilled manual</td>
<td>13</td>
</tr>
<tr>
<td>worker</td>
<td>Farmer</td>
<td>11</td>
</tr>
<tr>
<td>Others</td>
<td>Marital status</td>
<td>Married</td>
</tr>
</tbody>
</table>

Note: The percentages for each category add up to 100%.
Musculoskeletal diagnoses account the most of the disability pensions along with mental diagnoses. This follow-up study of Finnish and Swedish working age twins investigated various sociodemographic, health and work related factors as predictors of disability pension due to musculoskeletal diagnoses. The findings indicate that negative health behaviours and physically heavy work might be potential targets for interventions to prevent early exit from working life due to musculoskeletal diagnoses.