Multiple sclerosis and the labor market

Labor market participation, sickness absence, rehabilitation and disability pension in Norway

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Master thesis

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Abstract

Background: In young adults at the height of their economical activity, multiple sclerosis (MS) is the most common disabling neurological disease. From prior research it has been established that MS has vast effects on labor market participation. However, there is a lack of studies investigating the pattern of transitions MS patients make between labor market states.

Objective: To investigate the variation in transitions to sickness absence (SA), rehabilitation (REHAB), disability pension (DP) and return to work (RTW) relative to time with MS.

Method: A Cox proportional hazard rate model for single events is used to study the transition to DP for the Oslo cohort dataset, accounting for the relative impacts of age at onset of disease, type of MS and gender. A competing risk hazard rate model for multiple events is used to study transitions to SA, REHAB, DP and RTW for the FD-Trygd dataset, consisting of MS patients as well as matched control subjects. We account for the impact of time with MS as well as for those of age, gender, education, development over 1992-2008, seasonal dependence and duration dependence for transitions from SA and REHAB spells.

Results: MS has profound impacts on the transitions RTW, SA, REHAB and DP, which are consistently associated with poorer relative outcomes than those of controls. We find substantial effects and differences in intensity of transitions over time. After 17 years approximately 2/3rds of MS patients end up receiving DP, and only a quarter remain working. We uncover variation towards transitions in the age of the subject, the age at onset of MS (only DP), gender, education level, type of MS (only DP), and time with MS. Transition intensities also vary according to season of the year and according to duration of SA and REHAB spell. We find indication that not only onset of MS but also registration of MS with public authorities has profound impacts on the transitions to the various outcome states.

Conclusion: We find that MS patients move dynamically from a start in the state *working* towards disability pension through spells of SA and REHAB, after onset of disease. Associated with each SA and REHAB spell are the transitions back to work from where they can experience new spells. In between the starting point in the state of working and the final end-point of disability pension MS patients experience different periods that vary in transition-intensity.

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Abbreviations

MS	Multiple sclerosis
CNS	Central nervous system
RRMS	Relapse-remitting multiple sclerosis
SPMS	Secondary progressive multiple sclerosis
PPMS	Primary progressive multiple sclerosis
PRMS	Progressive relapsing multiple sclerosis
CIS	Clinically isolated syndrome
ICD-10	International Classification of Diseases, version 10
MRI	Magnetic resonance imaging
ICPC-2	International Classification for Primary Care, version 2
DSS	Disability status scale
DMD(s)	Disease modifying drug(s)
ACTH	Adrenocorticotropic hormone
IWA	Inclusive workplace agreement
MeSH	Medical subject headings
CPH	Cox proportional hazards
NPMLE	Non-parametric maximum likelihood estimator
CI	Confidence interval

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1 Introduction

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system (CNS). MS primarily affects young and middle-aged adults in the ages between 20 and 40, with peak incidence around 30 years of age (Confavreux and Vukusic, 2006). MS causes severe physical and cognitive disability. In young adults at the height of their economical activity it is the most common disabling neurological disease (Perkin and Wolinsky, 2006). With time the disease is associated with progressive disability due to nerve damage.

In this study we are reviewing what happens to MS patients in the labor market after onset of disease. Our main endpoints are the transitions that MS patients make between the labor market states of sickness absence, rehabilitation and disability pension and the transitions back to work from sickness absence and rehabilitation. In short we are looking to investigate labor market related phenomena for the MS population in Norway.

Section 1 has now introduced this study. The rest of sections 1.1 through 3 are background and theoretical chapters. In section 1.1 we review MS as a disease. We consider its risk factors, classification, development over time, treatment possibilities and the prevalence and incidence of MS in Norway. The objective of this chapter is to better our understanding of this disease. We additionally consider the structure of sickness absence, rehabilitation and disability pension and provide a summary on the framework for receiving such benefit schemes in Norway in section 1.2. In section 2 we consider previous research upon MS and the labor market and we note the focus and deficiencies of this research to date. Section 3 outlines and elaborates on the aims of the analytical sections of this study.

Sections 4 through 9 are methodological and analytical chapters where we present results and describe the methods applied to reach these. Section 4 presents the data sources used for analysis; the Oslo cohort and FD-Trygd, and presents the analytical models applied in this study. Section 5 takes a deeper tour into confronting issues that are deemed important for assessing the validity of this study, and in particular the role of confounding, measurement error, selection bias and the matching process for the FD-Trygd data.

The sections 6 and 7 present the results from this study in a descriptive and analytical manner, respectively. Section 6 describes the distribution and occurrence of labor market related

phenomena for MS patients and controls over time. Section 7 presents the results from the investigation of determinants of transitions to the various labor market states. Section 8 outlines differences and similarities between the results obtained from analysis in this study and previous investigations of MS and the labor market. Section 8 additionally deals with the drawbacks to this study. Section 9 concludes this study and gives suggestions for future research.

1.1 Multiple sclerosis epidemiology, disease classification and development over time

1.1.1 Risk factors for MS

The risk factors for getting MS are complex and have been shown to include interactions between environmental and genetic factors. According to Milo and Kahana (2010) the support for the genetic dispositional basis of MS comes from it being unevenly distributed among geographical regions and populations. MS occurs frequently in Norwegian whites, while this is not so for Norwegian Sami. The risk factors for MS include, among others, age (incidence peak around 30 years of age), gender (female/male 2:1 ratio), higher geographical latitude (the prevalence varies from <5 cases per 100,000 population in tropical areas to >100-200 cases in temperate areas such as Europe and north America) (Milo and Kahana, 2010). Behind this variation in occurrence, the climate, diet, sunlight and intake of vitamin D have been observed have an influence. MS has also been linked with Epstein-Barr virus, which among young adults increases the risk of MS in a 3 to 1 ratio. In addition some vaccines (hepatitis B, measles), family history (1 in 5 has a relative with MS) and migration (before the age of 15) have been observed with an increased risk of MS (Compston and Coles, 2008, Koutsouraki et al., 2010, Jobin et al., 2010). In conclusion the impact of modifiable risk factors that could reduce the incidence seems modest.

1.1.2 Classification of MS

According to Lublin and Reingold (1996) there are four types of MS. Relapsing-remitting (RRMS) implies relapses of and remissions from the disease. If the relapse-remitting phase is followed by a progressive phase, it is called secondary progressive multiple sclerosis (SPMS). If there is steady disease progression without relapse it is called primary progressive (PPMS).

If the progressive phase is accompanied by relapses it is called progressive relapsing (PRMS). Confavreux and Vukusic (2006, p. 606) write in their article on a unifying concept of the natural history of multiple sclerosis that the disease can be seen as the "expression of two clinical phenomena, relapses of acute neurological symptoms, which end with a partial or complete remission, and progression, which refers to the steady or irreversible worsening of symptoms and signs over ≥6 months".

80% of patients start with an clinically isolated syndrome, an attack, affecting one or several sites in the CNS (Compston and Coles, 2008). If accompanied by a second attack it fulfills the diagnostic criteria of RRMS. The diagnosis of MS requires dissemination of disease in time and space supported by clinical, and laboratory evidence (Miller et al., 2008). Patients assumed of having MS can present with neurological syndromes. Then, a MS diagnosis, calls for the ruling out of diseases also associated with the clinically isolated episode (CIS). Such CIS occurrences may present itself as diseases of the optic nerve such as optic neuritis (ICD-10 code H46), or as diseases of the brain stem such as internuclear opthalmoplegia (ICD-10 code H51.2), or of the spinal cord such partial myelopathy (ICD-code G04), to name only a few diseases that have been found to have a strong, but not necessary links with MS (Miller et al., 2008, p. 1165). A CIS can present itself with one or more lesions, in different parts of the CNS. The CIS also have a time component in that they can be either a single occurrence, relapsing (two or more) or being progressive in nature (Miller et al., 2008). This pattern can also show itself in other diseases, and it is therefore important to identify patient history prior to being diagnosed with a MS diagnosis. For example can fatigue and muscle weakness in addition to symptoms for MS also be symptoms of stroke. This example shows the myriad of symptoms that need to be taken into account when considering a MS diagnosis. Figure 1 shows different types of disease start. For the first example of MS, the disease presents itself through two clinical episodes. From the second example we see the occurrence of one clinical episode followed by magnetic resonance imaging (MRI), with identification of lesions. From the third example we see the course of diagnosis for PPMS, where one must have had one year of progressive deterioration and two of the following three categories: Either a positive brain MRI, a positive spinal cord MRI, or positive oligoclonal bands (an antibody). Patients without all the diagnostic criteria, but with an appropriate clinical presentation can be classified as having *possible multiple sclerosis* (Compston and Coles, 2008). Before the use of the McDonald criteria for definite MS, the Poser criterion from 1983 was used. One of the

major differences between the two criteria used to diagnose MS is the additional use of MRI for the McDonald criteria.

Kobelt and co-authors (2006) show the differences in age of patient from the presentation of the first symptoms to diagnosis. For a total of 13,186 patients from 9 European countries this difference was found to be in the range of 3.2 years, for the lowest average duration – to 7.3 years for the highest average duration. There is therefore considerable time that forgoes from start of disease to diagnosis is made.

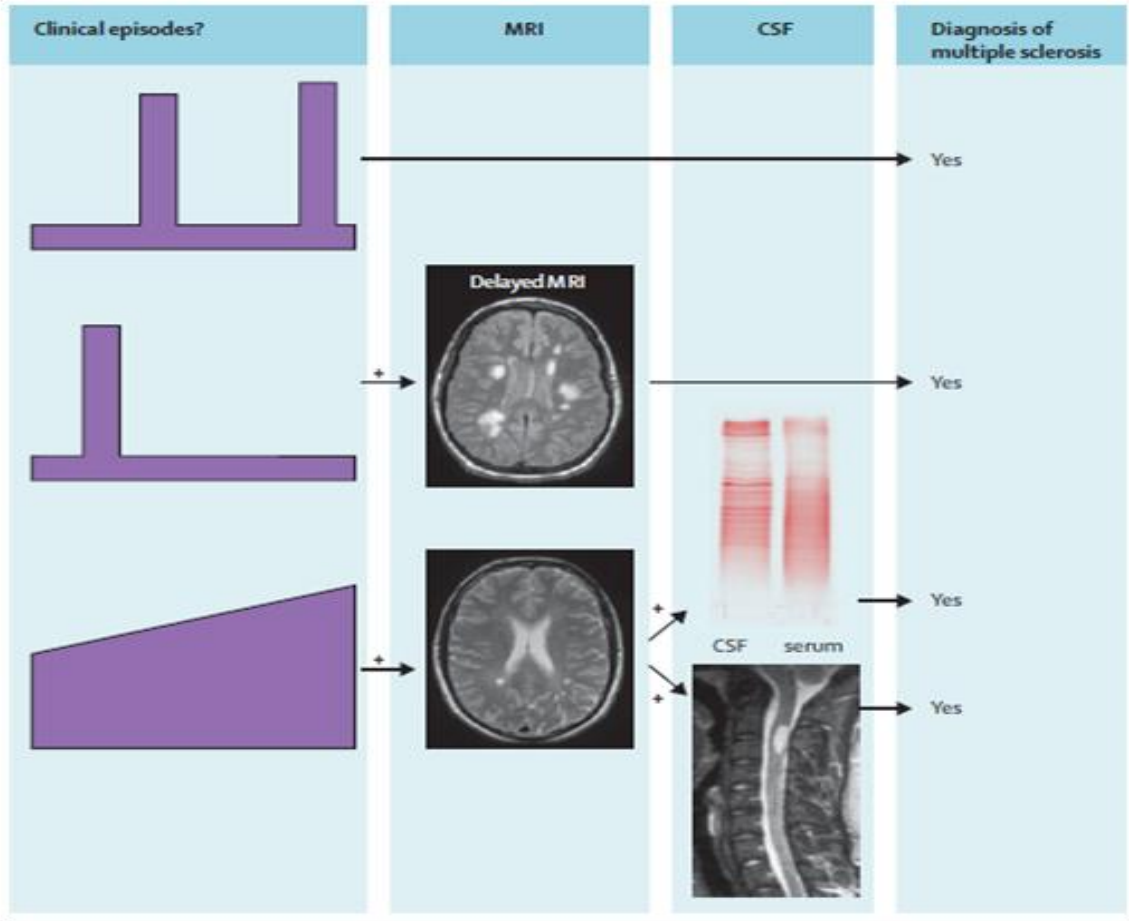

Figure 1. Criteria for the diagnosis of multiple sclerosis. From Compston and Coles (2008).

Lesion formation is a central feature of MS (sclerosis means scarring), and can happen at any place where there are myelinated nerves, within the CNS (Perkin and Wolinsky, 2006, p. 9). It is the myelinated sheaths that covers the nerves and aids the transportation of electrical signals to induce movement and speech. The nerves are able to transmit information rapidly, which is a must for efficient movement, as well as sensory perception and facile cognition.

When the nerves are damaged the electrical signals are not transported as normally. Over time the lesions will lead to an increase in the loss of motor skills. Along this there is a decrease in brain volume as seen from figure 2.

During MS attacks the nerves stop being able to transmit information across damaged segments. It is this failure that lead to the associated symptoms, such as vision disturbances, sensory disturbances (paresthesias), movement problems and fatigue. Information transmission is restored to near-normality, by regeneration of the myelinated sheaths. Following this the attack subdues (Perkin and Wolinsky, 2006, p. 13.). Schematically we can see the development of the disease in terms of figure 2, where it is the nerve losses (axonal loss) that contribute to the buildup of permanent disability. In the figure we can further see the severity of the disease on the vertical-axis and the duration on the horizontal-axis for the two distinct patterns of RRMS. In the pattern (first to the left) we see the experience of relapses with subsequent return to normal functioning. The pattern to the right is characterized by relapses without return to normal functioning. Here the pattern is for disability to increase in a stepwise manner (Compston and Coles, 2008, Perkin and Wolinsky, 2006).

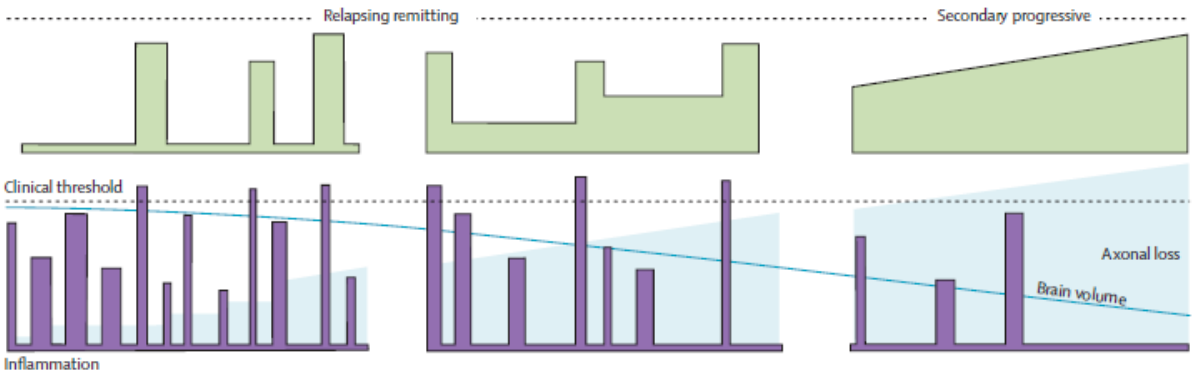

Figure 2. Inflammation, brain volume and axonal loss. From Compston and Coles (2008).

1.1.3 Development of MS

Approximately 80% of MS patients start with RRMS. The frequency of relapses has been observed to vary between an annualized rate of 0.14 and 1.1 (Compston et al., 2005). Of patients with RRMS, approximately 65-70% will develop SPMS after 10 years characterized by permanent neurological deficits and the absence of relapses (Confavreux and Vukusic, 2006, Compston and Coles, 2008). But, from the original RRMS population approximately

30% of patients will still have this form of MS 25 years after onset of disease. Within this group around two-thirds will have limited accumulated neurological findings and little actual disability, and can be seen to have benign multiple sclerosis (Perkin and Wolinsky, 2006, p. 26-7.) Some ≈15% of the patients start with a primary progressive MS without remittance and the last ≈5% develop a progressive-relapsing form of MS (PRMS), which initially simulates PPMS, but after this disease form has been established presents one or more attacks (Perkin and Wolinsky, 2006).

In MS research it is common to rely on a MS-specific disease disability scale to measure progress of disability from onset of disease. The Kurtzke Disability Status Scale (DSS) is one such instrument. The instrument returns scores between 0 and 10 with 0 indicating no neurological disability and a score of 10 being that the patient has died. In between these outer-points a score of 4 indicates limitations of walking but not requiring a walking aid or rest for a distance of 500 meters, a score of 6 indicates capability to walk with walking aid for no more than 100 meters and a score of 7 indicates a capacity to walk no more than 10 meters without having to resort to resting, leaning against a wall or the like (Confavreux and Vukusic, 2006). Progress on this scale and reaching the named outcomes are closely related with time. One criticism of the use of this scale for MS patients is that while embracing the physiological dimension of MS the DSS does not incorporate the clear cognitive dimension of this disease. However, it remains the most used instrument to measure MS-induced disability. Patients with a progressive type (PP+PR) proceed with greater intensity to an advanced stage of disease while this is not necessarily the pattern for patients starting out with RRMS and later converting to SPMS. Numbers from Confavreux and Vukusic (2006, p. 612) suggest that it takes on average 11 and a half years for patients with this latter type of MS to reach DSS 4 in which they were still just sufficiently able to walk 500 m without aid. For patients with PP or PR the same stage, for the average patient was reached in year 0. Thus, early in disease there is a big difference in disability between types of MS. To reach DSS 6 and DSS 7 took on the median 23 years and 33 years, respectively for patients with PPMS or SPMS while the same stages were reached for patients with PPMS and PRMS after only 7 and 13.5 years respectively.

1.1.4 Treating MS

Until the 1970s, treatment consisted of symptoms relief. In the 1970s intramuscular adrenocorticotropic hormone (ACTH) and intramuscular cortisone (Methylprednisolone) were introduced to shorten the duration of attacks (Soelberg Sorensen, 2010). No cure has since been discovered, but since the 1990's patients have had access to disease-modifying drugs (DMDs). The first DMD came in 1993 and now several exist (Compston and Coles, 2008). Several injection-based interferon (cytokine) (IFNs) therapies have been introduced for RRMS and early phases of SPMS. No DMD therapies are currently available for PPMS and PRMS. For RRMS and SPMS IFNs favorably affect the frequency and severity of MS attacks. This is done through immune modulation, which has an effect on the incidence of new remissions and the level of disease as measured by magnetic resonance imaging. Nowadays therapies are increasingly able to halt disease progression, in ways that are also more comfortable for the patient, with the first oral DMD coming on the market as of 2011.

1.1.5 MS in Norway and Oslo

In Norway, the prevalence, defined as the fraction with disease divided by the population total, of multiple sclerosis has been estimated to be in the order of 73-148 per 100,000 population. The annual incidence rate, defined as number of new cases per population, has equally been observed to be in the range of 3.2-8.7 per 100,000 population (Compston et al., 2005). With a population of 4,920,300 the estimated number of new cases would be in the range of 157 to 428 new cases per year. The estimated prevalence number would be in the range of 3600 to 7282 persons. However according to Myhr and co-authors (2010) the estimated actual number of MS patients in Norway was approximately 7500 in 2010. In the capital city of Oslo, the number of patients with MS has been estimated at 120 per 100,000 population (Celius and Vandvik, 2001). When excluding non-Westerners, these 1992-1996 data increases to a prevalence rate of 136 per 100,000 population. Incidence rate for the same period was according to this source estimated to be 8.7 per 100,000 population per year. Using updated data in 2005 yielded a prevalence rate of 148 per 100,000 population, with a total of 789 definite MS patients alive and resident in Oslo as of 31 December 2005(Smestad et al., 2008). According to these data the incidence of MS in the Oslo area sank somewhat to 7.2 per 100,000 population and to 6.6 per 100,000 population for the periods of 1996-2000 and 2001-2005.

1.2 Sickness, illness and disease

In this study our focus lies with studying the working life of MS patients. We are considering labor market states (working, sickness absent, on rehabilitation, or disability pensioned). By rehabilitation we focus on vocational rehabilitation, also termed the social rehabilitation executed by the Welfare Administration (Aas, 2009, p. 34). In epidemiology, as being the study of population health, one is interested in defining the population at risk of an event (Hensing, 2010). For sickness absence research the population is dividable into three denominators. The first, and most general one, is the whole population, regardless of an individual's affiliation with the labor market. The second one, and in some countries equal to the first, we have the sickness insured population. The third category makes out the sickness absent population. This the fraction of the population that is sickness insured and has made use of the right to take out sickness absence (also called sick leave). Likewise for rehabilitation and disability pension one can expect there to be a difference between people making use of such benefit schemes and those that potentially could make use of them. If large, this discrepancy can lead to biased results in the analysis as one would overestimate the use of services due to absence of a fraction of the population.

Coupled with disease, established on the basis of diagnosis, is the unique patient's experience of the symptoms of that disease, namely her illness. These two dimensions, disease and illness are linked together in the sense that they are intra-personal phenomena; they can be explained from occurrences of events inside the body. A third dimension of sickness is however to be distinguished from the latter two in the sense that this dimension is a social role (Alexanderson and Norlund, 2004). The patient who is diagnosed or the person who is ill takes a social role in society. This role for persons with diseases and illnesses tend to vary across societies, cultures and over time. The social role of sickness can be seen as a position involving rights, such as economic compensation and obligations, all varying over the social structure, time and with the establishment of a diagnosis.

These dimensions are all overlapping each other and contribute to explain why one would enter into sickness absence, or rehabilitation and disability pension. As such they can be seen as circles, with sickness absence and sickness benefits use as the smallest circle in the center. Graphically this can be presented as below as in figure 3. Note that looking upon this model in an expanded format one could easily incorporate both rehabilitation and disability pension

in the small grey circle. Ultimately it is the awareness surrounding a disease and its consequences upon capacity to work that legitimates awarding of sickness benefits or not. In today's society physicians play a major role in assessing eligibility for sickness leave. In Norway this role has also been looked upon as a gatekeeper function that the medical profession holds. It is the physician that ultimately confirms the presence of a disease such as MS, justifying the reduction of this person's time on the job and calling for social insurance economic compensation. Tellnes (1989) described the practice of sickness certification among GP's and concluded with it being one of their most common tasks.

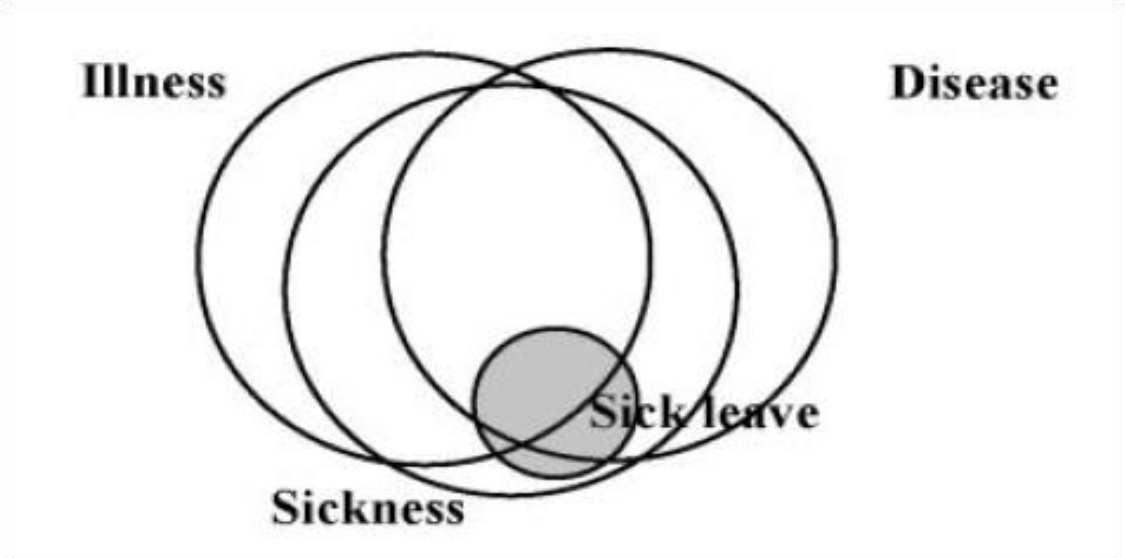

Figure 3. Ilness, disease, sickness and sick leave. From Alexanderson and Norlund (2004).

1.2.1 Sickness absence, rehabilitation and disability pension in Norway

Norwegians are paid their regular salary during sickness absence for a period of time up to one year. For the first 16 days the employer pays the sickness benefits. Hereafter the salary is paid for by the social security system. We will therefore characterize sickness absence of less than 16 days as short-term sickness absence and sickness absence of more than 16 days of absence as long-term sickness absence. As a general rule sickness absence spells, or periods, of more than 3 days must be certified by a physician. An exception from this rule is available for organizations taking part in the "inclusive workplace agreement" (IWA) between employers, employees and the state, where certification is only required after the 9th day of absence. More than 85% of sickness absence is certified by a physician (Markussen et al.,

2010). Overall, a sickness absence spell is legally limited to endure no more than 365 days. After the start and up until the 365th day there is a steady ongoing evaluation between the person on sickness absence, the employer, the government agency administering the benefit scheme and the person's general practitioner to see if a return to work is feasible either partially or fully. If the person has not recovered or has not returned fully or partially to work then it is evaluated what prevailing conditions exist and whether there exists the possibility of a successful rehabilitation stay or if the person should be transferred to a more permanent benefits scheme such as disability pension. Financially the difference between the full replacement of salary during sickness absence and benefits after moving on to rehabilitation or disability pension is 33% lower. For working persons the option of disability pension will normally only be a possibility after a period of one year of sickness absence and, following this, an evaluation for the possibility of further medical treatment or (vocational) rehabilitation. Further it is a general requirement that the "capability of earning" be reduced permanently, by more than 50%, due to the cause of illness (NAV, 2011).

In summing up the previous sections, we have now shown the complexities of MS as a disease. We have established an idea of nature of MS, and that it, among others, necessarily is a complex process from presentation and onset of disease to subsequent diagnosis. Further we have shown that variation in time to progression of disability varies according to the type of MS, and necessarily the effect of DMD's to negate progression for RRMS and SPMS patients, among others.

We have also presented the distribution of MS in Norway, and that MS as a disease takes place in a wider context where also the concepts of illness and sickness are of importance. It is the overlapping of these latter concepts that ultimately contribute to explain *why* someone would go into periods of sickness absence, rehabilitation and into the more permanent state of disability pension. We now continue with a presentation of previously conducted studies on the labor market association of MS patients in section 2.

2 Theory of labor market movement

Several studies have investigated the labor market related situation among MS-patients. The literature started focusing on employment, but later moved to include studies about disability pension and sickness absence. From figure 4 we see the 1975-2010 development in publications on labor-market related MeSH-terms for MS patients indexed in the Medline database.

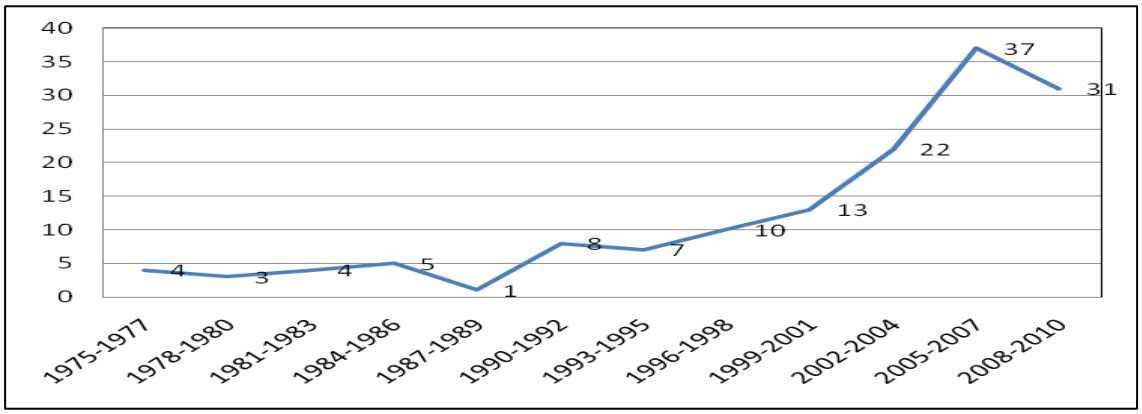

Figure 4. MS and labor-market related MeSH-terms indexed in Medline. Search (15/4/2011).

In our search[1] 145 articles were found. From small numbers in the 1970's and 80's, there was a general increase in the number of indexed articles in the 90's. From the start of the 2000's the number of articles surged, and there has been an extensive effort to expand knowledge about the subject in the previous decade.

2.1 Literature on job-related consequences of MS

Previous studies of MS and the labor market have found unemployment levels varying from 25 to 100%, with average disease duration varying from 10 to 24 years (Rozin et al., 1975, Christensen and Clausen, 1977, Johnson and Johnson, 1977, Mitchell, 1981, LaRocca et al., 1982, Kornblith et al., 1986, Genevie et al., 1987, Grønning et al., 1990, Hammond et al., 1996). Labor market status changes have been observed to vary with demographic and

[1]The search words used were ((insurance, disability. Mesh OR sick leave. Mesh OR pensions. Mesh OR absenteeism. Mesh OR employment. Mesh OR work. Mesh) AND (multiple sclerosis.tw)). Text words (.tw) means that one only searches words found in the title, abstract, and in the keywords of the article, but not in the full text of the article.

clinical measures. The disease type PPMS negatively influence labor market participation (Verdier-Taillefer et al., 1995, Sundstrom et al., 2003). Disease duration, progression (measured with e.g. DSS) have been seen to influence, and predict, labor market status (Larocca et al., 1985, Lage et al., 2006, Cervera-Deval et al., 1994, Hammond et al., 1996, Grima et al., 2000, Miller et al., 2000, Busche et al., 2003). Symptoms-activity has been seen to influence labor market status (Freal et al., 1984, Smith and Arnett, 2005, Julian et al., 2008). Entering into unemployment has been seen to vary with type of labor (manual/non-manual) (Grønning et al., 1990, Pfleger et al., 2010). Higher age and a lower educational level have also been shown to influence labor market participation (Beatty et al., 1995, Busche et al., 2003). Gender has not been observed unilaterally in favor of either males or females being more likely not to participate in the labor market (Larocca et al., 1985, Sundstrom et al., 2003, Rumrill et al., 2007, Rodriguez et al., 1994, Smith and Arnett, 2005, Simmons et al., 2010). Some studies have looked at disease-modifying drugs and work participation (Brook et al., 2009, Lage et al., 2006, Rajagopalan et al., 2011). Here patients using specific disease-modifying drugs were observed to have lower sickness absence and use of short-term disability pension.

Myhr and co-authors (2001) studied the difference in disability pension for the relapse-remitting type and primary-progressive type of MS. Patients with PPMS entered more quickly into disability pension and after 15 years after onset of disease only around 25% of this group was not disability pensioned. The similar figure for RRMS was 51.1% after 15 years.

Henriksson and co-authors (2001) investigated the cost of illness for multiple sclerosis in Sweden and gave estimates for 413 MS patients. This patient group had average disease duration of 17 years. For this population the unemployment was 60 per cent, of which this group 58% had disability pension while 11% had long-term sickness absence. Of those working full time the average no. of days per person lost in a year to sickness absence was 23, corrected for those working part-time the number was 14 days per year.

Kobelt and co-authors (2006) assessed the work capacity for 13,186 MS patients in nine European countries. The between countries age-mean and expanded DSS score was 45.1-53.4 years and 3.8-5.1, respectively. The patients had been diagnosed at averages ranging between the countries of 33 and 39.3 years of age and so the average duration of (confirmed) MS between the countries ranged from 9.7 to 16.3 years. Approximately 70% of patients were women. Between countries the proportion employed and working was in the range of 26.2 to

41.5%. The corresponding proportion of patients being on long term sick leave was in the range 0.6 to 6.7%. A large proportion of the patients, 32.9 to 44.5%, were reported to have retired early from working life due to MS.

2.2 Exiting and re-entering the work-force

Apart from the longitudinal studies (Rumrill et al., 1998, Julian et al., 2008, Pfleger et al., 2010, Rajagopalan et al., 2011), this literature has focused to our knowledge exclusively on how MS patients leave the workforce, and not how they possibly re-enter after a sickness absence or rehabilitation spell. Given the push-pull nature of the disease it should now be reasonable to believe that patients possibly exit and re-enter into the labor market in a dynamic manner.

Julian and co-authors (2008) investigated longitudinally a larger cohort of MS patients (n = 8122) for two time points over a mean interval of 1.56 ± 0.93 years. The rate of employment varied between 56-58% for these two time points. At time one unemployed patients were more likely to have a progressive disease course, longer symptom duration, and greater levels of disability. At time two it was increasing levels of MS symptoms that caused a rise in the odds of becoming unemployed.

Pfleger and co-authors (2010) looked at early pension and temporary unemployment for a complete national MS cohort, with disease onset in the years 1980-9. For early retirement 30% had left the labor market after 5 years while only 3% in the comparison group. After 20 years the corresponding figures were 78% and 14%. The authors explicitly state that until the time of their study no one had addressed the question of temporary unemployment in patients with MS. They addressed this, using a cross-sectional sub-group analysis of economically active persons at 5, 10 and 15 years after entry into the study. However, no difference between MS patients and controls was found.

Interventions available to MS patients have also been shown to have an effect on the labor market participation. The next two paragraphs demonstrate this.

Rajagopalan and co-authors (2011) looked at the effects of DMDs on direct and indirect costs among employees. They compared costs and absences from work and short-term disability for interferon therapies and glatiramer acetate before and after treatment initiation. They found

that type of DMD patients used had significantly greater reductions in sickness absence cost after treatment initiation compared with another type of interferon and glatiramer acetate. Only users of a specific type of interferon had a reduction in sick leave days.

A Cochrane review from 2009 (Khan et al., 2009) summarized the effects of different vocational rehabilitation programs on re-entry into the labor market, and among them from one controlled clinical trial (CCT). They found "insufficient" evidence for the effectiveness of such strategies to alter re-entry rates, but do provide documentation of this phenomenon. The study discussed in the Cochrane review by Rumrill and co-authors (1998) investigated the comparative effect of two vocational rehabilitation programs, in a CCT, for reentry into the labor market among 37 participants. They document that 11 of this group of 37 had reentered the labor force after 16 weeks.

In sum, the number of potentially important factors in determining a MS patient's working capability in Norway, is vast and spans over extraneous differences over time and space due to cultural and societal structures, the patient's sickness component, and differences within the patient population, the patient's disease and illness components, as to, who has had a beneficial medication treatment, more or less frequent relapses, a particularly benign form of MS, or who has had a successful rehabilitation stay. We continue now with an elaboration of the study aims in section 3 before presenting the data and methods in section 4.

3 Aims of the study

The main aim of the study was to explore movement between labor market states for patients identified with a multiple sclerosis diagnosis in Norway.

We wanted to describe level of income, labor market participation, long term sickness absence, rehabilitation use, and disability pension for MS patients and controls for the period 1992-2008 for our first data source. For MS patients we wanted to relate the level of income, labor market participation, sickness absence, rehabilitation, and disability pension in this period to the starting time in which we knew them to have MS. A secondary aim here was to describe the level of early retirement for MS patients and controls for individuals above the age of 61.

From data containing long- and short-term sickness absence spells from 2001-2006 the aim was to describe incidence of all spells. Here we wanted to investigate, the duration of spells and whether persons were fully or partially absent during their sickness absence. We wanted to compare the incidence of spells and the exit rate from spells for MS patients relative to controls.

Additionally, the main aim of our second data source was to explore how various variables such *age at onset of disease*, *gender*, and *type of MS*, influence the time from onset of disease to being awarded disability pension for the Oslo cohort. These factors are investigated to better our understanding of intra-MS group heterogeneity with respect to being awarded disability pension.

4 Data and methods

4.1.1 FD-Trygd

The first source of data for this study consists of administrative data from the event database from Statistics Norway (FD-Trygd). This database includes demographical data, use of social security services, employment, and income variables from 1992 to 2008. This data was linked with data on diagnoses from the Norwegian Labor and Welfare Administration (NAV). We included patients who had a certified sickness absence spell during the 6-year period January 2001 - November 2006 with ICD-9/10 or ICPC-2 diagnoses. This resulted in 3,518 patients with MS. We compared this group with a control group that consisted of three controls per subject, matching them on age, gender, education (using the Norwegian Standard Classification of Education), and income of more than 50,000 Norwegian Kroner in the first year they appeared in the database. This resulted in 3,367 MS patients and 10,700 controls for analysis. For 151 MS patients no controls were found and these were subsequently left out of further analysis. These differed substantially from other MS patients on age, gender and education. For the remaining MS and control subjects we have, on a monthly basis, data on income, labor market participation, rehabilitation, long term sickness absence spells (above 16 days), disability pension and early retirement from 1992-2008. In the 2001-06 data contrary to the 1992-2008 we have exact lengths of sickness absence spells, including spells of less than 16 days of duration. For 1992-2008 sickness absence rate is measured on a monthly basis only for those registered with a spell of more than 16 days. Considering this I have chosen to present the incidence rates of sickness absence spells for both kinds. In table 1 we see how MS patients compare with matched controls on age, proportion females and educational attainment.

Table 1. MS-patient inflow and general study participant characteristics from FD-Trygd data

MS patients inflow		General characteristics	MS	CONTROLS	MS patients left out
Year of registration with diagnosis	Number of subjects	Number of subjects	3367	10700	151
		Age at entry w. diagnosis	41.45		39.11
2001	964	Average age in 1992	31.75	31.34	27.73
2002	649	Average age in 2008	47.75	47.34	43.73
2003	538	% female	66.67 %	69.35 %	70.86 %
2004	445	% with college education	37.10 %	35.54 %	30.46 %
2005	427	% with highschool edu.	45.47 %	46.18 %	42.38 %
2006	344	% with middle-school edu.	17.43 %	18.28 %	27.15 %
Total	3367				

4.1.2 The Oslo cohort dataset

The second source of data in this study, consists of MS patients registered at the MS-registry that was established at the Ullevål hospital's Department of Neurology in Oslo in 1990. All patients living in Oslo have been registered retrospectively since 1972 and prospectively since 1990 (Brekke et al., 1998, Celius and Vandvik, 2001, Smestad et al., 2008). For this patient group we have data on disability pension, degree of disability pension, time at onset of disease, type of MS, age and gender. According to the administrative neurologist of this registry it is complete for the 707 subjects born after 1939 living in the Oslo area. MS disease was established using the Poser criteria. The registry is complete for this population until the end of 2005, which is also set as the end of study time. Within this cohort 18 persons had already received disability pension before the onset of MS due to other preexisting disabling diseases. Data on disability pension was furthermore missing for 93 individuals. After subtracting these we had 596 individuals left for analysis. Within this group 63.2% of individuals (*n* 377) had received disability pension with mean degree of disability pension of 93.5 (SD 18.1). Only 13 patients received disability pension after the age of 60. For a part of the individuals receiving disability pension in this cohort (n 296) we had data on the year in which they *first* received disability pension. The mean time from onset of disease to being awarded disability pension was 9.2 years (SD 8.3 / Median 7 years) for this subgroup. For the remaining 81 individuals receiving disability pension we did not have data on the year in which they *first* received disability pension, but rather whether they were registered to be on disability pension as of 31.12.2005. Mean duration from onset of disease to awarding of disability pension for this subgroup was 11.6 years (SD 7.7 / Median 11 years). Considering this difference between the two subgroups we can expect the analysis of this cohort to slightly overestimate the time from onset of disease to being awarded disability pension. General statistics and comparison between analysis- and the left out group are presented in table 2.

Table 2. General study participant characteristics for Oslo cohort.

	Analysis group (n 596)			Subjects excluded from analysis (n 111)		
	Mean	SD	Range	Mean	SD	Range
Year born	1957.6	10.81	1939-1986	1956.9	10.10	1939-1981
Age at onset	31.63	9.33	9-59	33.36	9.61	9-60
Proportion female	69 %			68.47 %		
Proportion with PPMS	15.44 %			16.22 %		
Disability pension (DP)	63.26 %			Missing		
Time from onset to DP/censoring	10.4	8.47	0-38	Missing		

4.2 Methods

In this study time until a labor market event is the outcome. This calls for the use of survival analysis or event history analysis. Some aspects of survival analysis are, firstly taking into account the problem of distribution of survival time. Individuals differ in that some experience an event late and others early. Secondly, a special problem of survival functions is the censoring of observations, meaning that for some individuals we have incompletely observed times. The causes of such censoring are that 1) the study may be terminated and not everyone experienced the event or 2) that the study participant withdraws, or exits from the study. It is the censoring of observations that precludes the use of ordinary statistical methods for longitudinal data. Thus, an assumption that is important to us is that we would like that, on the average, the individuals that get censored at any point in time do not differ from those that are under observation but not censored until the end of the study. We assume that there is no selective censoring. From Aalen and co-authors (2008, p. 376) the censoring of observations is, under the estimation process, considered a "nuisance". It is the aim of analysis to correct for its presence and to shed light on the situation surrounding a phenomenon had there been no censoring.

4.2.1 The hazard ratio as a measure of relative risk

A relative risk (RR), or incidence rate, expresses the risk, or probability, in one group over the risk in another group. The denominator in risk estimates is the number of persons initially at risk for an outcome.

The hazard rate is measure of relative risk and is the main end-point in our analysis. The hazard rate is the model counterpart of the incidence rate, which divides the number of occurrences of an event by the number of time-units (e.g. person-years, or person-months) available, or at risk, for that event to happen (Aalen et al., 2008, p. 6). The hazard function *h(time)*, is a measure of the probability of the event occurring per unit time at risk. An example of this in this context can be the change in potential of dying due to a motor-accident when crossing the street. In the moment before leaving the side-walk the hazard of dying is lower than after having walked the first steps of the crossing. Once crossed, the potential of dying sinks once again. Thus, the hazard reflects the potential of something happening at a given moment, conditional on a change in ones situation.

From Kleinbaum and Klein (2005, p. 10) the probability interpretation of the hazard function is found from the numerator to the right of the limit sign of equation 4.1. This states a conditional probability that a person's survival time *T* will lie in the time interval between *t* and *t*+ Δ *t* (increment), given that the survival time is greater than or equal to *t*. Thus the hazard rate considers the probability of persons that have still to experience an event, in a small-time interval (Aalen et al., 2008, p. 6).

$$h(t) \equiv \lim_{\Delta t \to 0} \frac{P\left(t \le T \le t + \Delta t \middle| T \ge t\right)}{\Delta t} \tag{4.1}$$

From the denominator in this equation Δt denotes a time interval of limited duration, and is the property that gives the rate interpretation of the hazard function as it is not constrained to the interval between 0 and 1 but rather can vary between 0 and infinity. It is the limit part of the equation that states that the outcome of this equation is the instantaneous potential of failing at time *t* per unit of time, the person having experienced no failure up until that time. The given sign - | - states that this is a conditional probability.

In equation 4.2 we have constructed the framework for the main outcome parameter in this study; the hazard ratio (Kleinbaum and Klein, 2005, p. 102). In this equation two persons have the same amount of time until an event but differ from each other because of the sign *, which we can think about as being some sort of trait or characteristic present with one person and absent in the next. This reduces the sum of this equation to the effect of this single trait on the hazard.

$$Hazard\ Ratio = \frac{h\,(t, X^*)}{h\,(t, X)} \tag{4.2}$$

Recalling the comparison in the form of a ratio given in section 4.1.1 we have for a hazard ratio that if this quantity in a comparison between two groups equals 1, then there is no difference. If the hazard ratio equals 5 we say that the exposed group has got 5 times the hazard of the unexposed. Reversely if the hazard equals 1/5 we say that the exposed group has got 1/5 the hazard of the unexposed group for an outcome (Kleinbaum and Klein, 2005).

4.2.1 Two methodological strategies

In this study we are using two data sources and equally applying two regression models. These are described below. They have in common that the hazard rates presented are proportional for all combinations of variables, and that on the log hazard scale we have a linear expression in the variables, where one takes the exponential expression of parameters β_i over X_i values to give the hazard ratio.

The underlying data in the two sources differ with regards to the number of events a subject can experience. In the data for the Oslo cohort we are dealing with single event data, as the event we are analyzing concerns the time to entrance into disability pension from onset of disease. In the data from FD-Trygd on the contrary we have multiple events, some of which the subjects can equally experience repeatedly. This has implications for the analysis used. We start now by describing our empirical strategy for the analysis of the Oslo cohort.

4.3 From onset of disease to disability pension

For the data from Ullevål University Hospital part of the study we have constructed a schematic model, in figure 5, for how we think MS patients enter into disability pension, with different force depending on the following effect modifiers; gender, age at onset, and whether the disease type was RRMS or PPMS. Our focus in the analysis of this data lies with investigating whether the type of MS makes a difference on the time until disability pension. Additionally we acknowledge, that the age at which the disease first became active will play a role in this relationship between time and disability pension. Furthermore, we would from divergence in theory like to investigate what differences exist between males and females. To analyze this relationship we will use the Cox proportional hazards model described below, implemented in Stata 11 statistical software package (StataCorp, 2009).

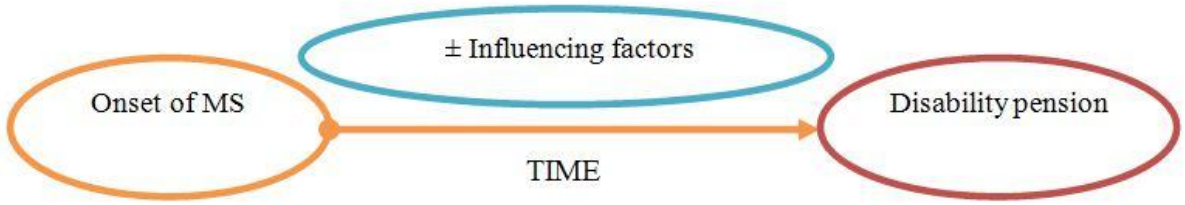

Figure 5. Time from onset of disease to being awarded disability pension.

4.3.1 The Cox proportional hazards model

In comparison with Kaplan-Meier survival analysis, which is unadjusted analysis for survival time data, the model presented here is a regression analysis adjusting for effects of other variables.

The CPH model expresses the hazard, at time *t* for an individual with a set of explanatory variables (X) (Kleinbaum and Klein, 2005). In the CPH model the hazard at time *t* is the product of two quantities, namely the hazard at time zero, h_0(t), also called the baseline hazard function. One property of this quantity is that if all the Xs were to be cero the model would reduce itself to this quantity. It is therefore that this quantity may be considered the basis of analysis as it involves *t* but not other variables (*X's*). This part is then multiplied with other variables, which are assumed to be time-independent, i.e. they contain *X's* but not *t*. A variable being time independent is thus defined to be any variable whose value does not change with time. The formula for this model is given in equation 1.4 from (Kleinbaum and Klein, 2005, p. 94).

$$h(t \mid x_i) = h_0(t) \times \exp\left(\sum_{i=1}^{n} \beta_i X_i\right) \tag{4.3}$$

The CPH model is parametric in that it is the job of the analyst to specify a functional form of the included set of variables and non-parametric in the sense that it makes no assumption about the distribution of survival time. Kleinbaum and Klein (2005) claim that the popularity of the CPH model owes itself to, despite of leaving a part of it unspecified, to produce stable results and being robust.

A special feature of the estimation of the CPH model is that when calculating the likelihood function the CPH model does this based on the order of events rather than what is normally done based on the distribution of an outcome (Kleinbaum and Klein, 2005, p. 111). The CPH model is then estimated using what is called a 'partial' maximum likelihood. This likelihood function takes the probability of the observed data as a function of the unknown parameters (β coefficients) included in the model. It is a partial rather than full likelihood function as the joint probability of the data observed considers subjects for which the failure event is recorded. If a person is censored after a failure occurring then his time in the analysis is still used to compute the likelihood function for that failure, but not after.

One important assumption in the CPH model is that of proportionality. This assumption states that the hazard ratio is consistent over time and subjects. In situations where the hazards cross this assumption is not met. Recalling equation 4.2 illustrating the hazard ratio, we can think of this assumption as being violated if the HR were to go from 2 in favor of the exposed group at time *t* and then change to 0.2 in time *t+5*. Formally we will evaluate this assumption based upon analysis of the residuals of the model. This is based on a test from Schoenfeld (Kleinbaum and Klein, 2005). The test investigates correlation between survival time and Schoenfeld residuals. If correlation is absent the proportional hazards assumption holds. The test provides a p-value, on which we will base our decision, for keeping or rejecting the assumption of proportionality.

4.4 Labor market model for movement between states

In this study we have constructed a schematic model for how most MS patients move through different states of the labor market with a multiple sclerosis diagnosis. The basic assumption of this model is that we from the theory of MS as a disease can expect progress and setbacks in an aberrant manner, but that patients will steadily deteriorate with time and as such move increasingly from being active participants in the labor market to being awarded disability pension. In between they will experience sickness absence spells and rehabilitation stays. The various states of interest, as seen from figure 6, in the labor market are (1) working, (2) sickness absence, (3) rehabilitation, and (4) disability pension. In our model individuals can go from *working* to *sickness absence* and back. From *sickness absence* they can go to *rehabilitation* and from there back to *working.* Individuals can go from sickness absence and rehabilitation states to *disability pension*, but from here they cannot go back. The circulating arrows in figure 6 for the states of *sickness absence* and *rehabilitation* are meant to signify the existence of duration dependence of spells in these states. Duration dependence considers that the intensity of transiting to other states depends on the amount of time spent in the current state. The inclusion of the control group is there to establish whether differences exist between the MS patients and another group from the general population. The focus is therefore on comparing how these groups move through labor market states.

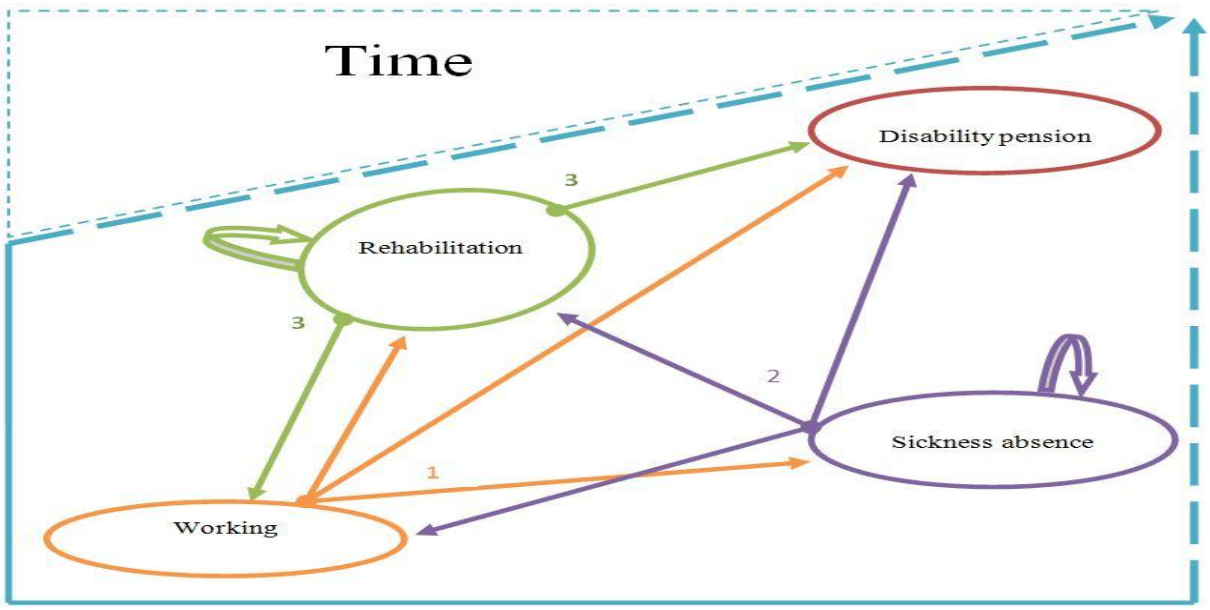

Figure 6. Labor market model for transitions between states. All subjects start in state 'Working'.

4.4.1 Competing risk hazard rate model

The following two sections build upon an analytical framework presented in the study on "The Anatomy of Absenteeism" by Markussen and co-authors (2010).

Individual sickness absence, rehabilitation, working and disability pension behavior is modeled by use of a competing risk hazard rate model for multiple events, accounting for incidence and recovery from the labor market states.

The model is estimated by means of the nonparametric maximum likelihood estimator (NPMLE) in a specialist statistical software package available at the *Ragnar Frisch Centre for Economic Research*. The benefit of this model being nonparametric is the absence of assumptions that is made on the distribution of the survival times and unobserved heterogeneity. This latter concept includes both variables not accounted for and measurement error. In estimation it is the individual propensity for any of the given states that is modeled. There are three alternative states, *k=1, 2, 3* that an individual can reside in and experience transitions to and from. These are *working (k=1), absent (k=2), rehabilitation (k=3).* Additionally subjects can enter into disability pension (*k=4),* after which they are censored. Thus, a person working is under risk of becoming absent, of going on rehabilitation and of becoming disability pension. A person on sick leave is under risk of going back to work, to rehabilitation, or to disability pension, and a person on rehabilitation is under risk for going

back to work or to disability pension. This is the competing risk aspect of the model, meaning that while residing in one state one is at risk of transiting to various others. Following the notation of Markussen and co-authors (2010) we have that K_1 is the set of possible destination states for the subjects momentarily residing in state $k=1$, and T_1 is the stochastic duration until the subject transits to state *2, 3 or 4*. The competing hazards are then defined as follows:

$$\theta_{1kit}\left(x_{it}, v_{1ki}\right) \equiv \lim_{\Delta t_1 \to 0} \frac{P\left(t_1 \le T \le t_1 + \Delta t_1, K = k \middle| T \ge t_1, i\right)}{\Delta t_1} = \exp(x_{it}\beta_{1k} + v_{1ki}), k = 2,3,4 \quad (4.4)$$

where x_{it} is the set of all the included explanatory variables assumed to affect a individual *i's* hazard rates at time *t* and(v_{12i}, v_{13i}, v_{14i}) are time-invariant unobserved individual characteristics.

Once in the state of sickness absence or rehabilitation the subjects are at risk of either returning to work, going on rehabilitation (only for sickness absent individuals) or entering into disability pension. Still following Markussen and co-authors (2010) we let T_2 and T_3 be the stochastic durations of stays in states $k=2$ and $k=3$. These two competing hazard rates are then defined as follows:

$$\theta_{jlit}\left(x_{it},, d_{it}, v_{jli}\right) \equiv \lim_{\Delta tj \to 0} \frac{P\left(t_j \le T_j \le t_j + \Delta t_j \middle| T_j \ge t_j, i\right)}{\Delta t_j} = \exp(x_{it}\beta_{j1} + d_{it}\lambda_{j1} + v_{jli}), j = 2,3 \quad (4.5)$$

where d_{it} is a set of variables describing the duration of an ongoing sickness absence or rehabilitation stay. As before (v_{2li}, v_{3li}) are the time-invariant unobserved individual characteristics for transitions from and to the respective states.

The set of variables (x_{it}) explaining the changes in hazard rates for the occurrence of a transition to a state covers *age, gender, highest attained educational level, calendar months, years* (1992-2008), *duration dependence*, whether the subject was *working*, on *sickness absence* or on *rehabilitation* before the transition was made and whether or not the subject had *MS*. The MS variable additionally contains a time coding to reflect the time before and after registration of diagnosis with the disease starting point set as the time of entrance into the study, see the year of entry part of table 1. Age covers 9 different age-groups coded in five-year intervals from *16-20* to *56-61*, education level to *college*, *high-school* and *middle-school*. Spell duration for transition from sickness absence to rehabilitation, return to work

and disability pension is binary coded to 12 variables, one for each month of possible duration. Spell duration for transition from rehabilitation to return to work and to disability pension is binary coded to 18 variables, the first 12 values on a monthly basis make out the first year, the next four values (13-16) are quarters and make out the second year, value no. 17 denotes transition dependence for subjects with duration of 3 years, and value no. 18 is the duration for subjects having been on a rehabilitation stay for more than 4 years.

So summing up this part on specification of the model I here present the final transitions that will be estimated in the model in table 3.

Table 3. FD-Trygd model transitions. Where to? where from? and in the presence of duration dependence?

Transition	Where to?	Where from?	Is there any duration dependence?
1	Work	Sickness absence, rehabilitation	Yes
2	Sickness absence	Working	No
3	Rehabilitation	Working, sickness absence	Yes; For transitions from sickness absence
4	Disability pension	Working, sickness absence, rehabilitation	Yes; For transitions from sickness absence and rehabilitation

4.4.2 Likelihood function

The likelihood function for observed data was obtained by splitting each subject's event history into components characterized by constant x_{it} and unchanged state. This means that a change in an explanatory variable, as for example a change in the time-varying age-variable, brings about a new spell-part (Markussen et al., 2010). To get the likelihood we let S_{ij}, j = 1, 2, 3, 4 be the observed spell parts in state j for individual i. We then denote l_{jis} to be the observed length of each of the spell parts $s \in S_{ji}$, and let the indicator variables (y_{12is}, y_{13is}, y_{14is}) denote if a state 1 (working) spell part ended in a transition to state 2 (sickness absence) (y_{12is}), to state 3 (rehabilitation) (y_{13is}) or was censored (disability pension), state 4 (y_{14is})). Equally let us denote (y_{21is}, y_{23is} , y_{24is}) to be whether a state 2 spell part ended in resuming work, going on to a rehabilitation stay or a censored disability pension stay and ($y_{31is,}$ y_{34is}) be whether a rehabilitation stay ended with return to work or a censored disability pension stay. Conditional on unobserved heterogeneity or variation not accounted for by the included explanatory variables we then formulate the likelihood function for subject i on the basis of (Markussen et al., 2010, p. 281):

$$L_i(v_i) = \prod_{s \in S_{1i}} \prod_{k \in \{2,3,4\}} \exp\left(-l_{1is} \left(\sum_{k \in \{2,3,4\}} \exp(x_{it}\beta_{1k} + v_{2ki}) \right) \right) \left[\exp(x_{it}\beta_{it} + v_{2ki}s) \right]^{y_{1kis}} \quad (4.6)$$

$$\times \prod_{j \in \{2,3,4\}} \prod_{s \in S_{ji}} \exp\left(-l_{jis} \left(\exp(x_{it}\beta_{j1} + d_{it}\lambda_{j1} + v_{jli}) \right) \right) \left[\exp(x_{it}\beta_{j1} + d_{it}\lambda_{j1} + v_{jli}) \right]^{y_{jlis}}$$

where we have that $v_i = (v_{12i}, v_{13i}, v_{14i}, v_{21i}, v_{31i},)$ from equations 4.4 and 4.5. The contribution to this likelihood contains unobserved variables and can therefore not be used for estimation use. To get around this a model for the joint distribution of unobserved heterogeneity is formulated where we replace equation 4.6 with its expectation. We thereby assume that the unobserved heterogeneity can be approximated without introducing unrealistic assumptions by employing a discrete distribution (Markussen et al., 2010). To do so we let Q denote the number of support points in this distribution and let, l = 1, 2, ...Q, be the associated location of the set of variables and probabilities. Following this the likelihood function for observed variables is:

$$L = \prod_{i=1}^{N} {}_{v_i} E[L_i(v_i)] = \prod_{i=1}^{N} \sum_{l=1}^{Q} p_l L_i(v_i), \sum_{l=1}^{Q} p_l = 1 \quad (4.7)$$

where $L_i(v_i)$ is taken from equation 4.6. The aim with this estimation is to maximize the likelihood function considering the model and heterogeneity parameters repetitively for alternative values of Q. The non-parametric maximum likelihood estimators (NPMLE) are obtained by initializing the estimation with Q=1. Subsequently, the model is expanded with regards to the number of support points until no further gain to the likelihood can be achieved (Markussen et al., 2010). From previous research parameters obtained this way have been shown to be consistent and approximately normally distributed (Gaure and Zhang, 2007, referred to in Markussen et al. (2010)). From this research it is also indicated that the standard errors of estimates conditional on the chosen model with Q support points are valid for the unconditional model, without support points Q. The model can therefore be used for standard inference purposes (Markussen et al., 2010).

One must appreciate that at the start of analysis time in 1992 some subjects were not in the starting state of 'Working', but absent due to sickness on rehabilitation or on disability pension. The subjects for whom this was the case were subsequently included with a new starting point in $+t$ as they were registered as working and treated equally hereafter. The

reason for this is stated in the paper by Markussen and co-authors (2010), and is that by including them from t_0 one would impose problems with regards to the initial conditions, since the initial state other than working not only make out a separate state but also a separate duration of being in this state.

In sum, we have in section 4 now described the two data sets used in this study. It is clear to us that while dealing with MS patients that are not necessarily different among themselves, that they are different according to the disease identification process resulting from the type of data. Patients in the Oslo cohort were on average traced to have disease start at the age of 31.6 while patients from FD-Trygd were recorded to have the first sickness absence with a MS diagnosis at the average age of 41.5. This is a 10 year difference.

We have learned that the analysis of the two data sets differ with regards to the number of events that MS patients can experience. For the Oslo cohort data patients can only experience one transition from onset of disease to disability pension. For the FD-Trygd data patients can experience recurrent transitions to various states. Still, the state of disability pension is the final destination.

Following this we will in section 5 deal with issues concerning the validity of this study. Section 6 is devoted the descriptive analysis and in section 7 we present the results from the models presented in section 4.

5 Validity issues with register data

This section deals primarily with an explanation of phenomena in need of attention when interpreting the validity of this study. The transferability of results, the external validity, will be dealt with in section 8. We therefore deal here with internal validity; namely with the extent to which we are measuring what we intend to measure. Here the term, internal validity, shall be understood as the degree to which our analysis is able to keep systematic error to its lowest level and give reasonable estimates of transitions to the different labor market states. In this study we are basing what we know about a phenomenon relying on the analysis of registers. National or regional registers are usually held in high esteem, with the possibility of linkage between datasets being described as one quality characteristic. Another quality characteristic from registers come from their ability to negate what primary data collection cannot; selection bias due to non-responders.

Still, we have to be aware that inferences about the causes to a given phenomenon, such as why a MS group will differ within the MS population and from a control group on entering into disability pension, face the validity problems of confounding, selection bias and measurement error. Confounding translates into the observed association being a result of something else than what is hypothesized in the study (Rothman et al., 2008, p. 128). Age is, in itself, for example, not the reason why older rather than younger people can be observed to enter into disability pension, but rather a correlate with disease progression, which is what we really think that is causing MS subjects and controls alike to go into disability pension. This is only an example, and the take away point is that there are various mentionable possible confounders within the MS group such as, whether the MS patient held a job requiring physical labor, time of onset of disease, MS type, and possible medication and risk factors differences among others that cause some individuals to progress to some states more rapidly than others. For FD-Trygd we are however able to account for unobserved heterogeneity. For the Oslo cohort, we have included no such account of unobserved heterogeneity in the analysis, and we thus face, among others, the confounding relations of intra-RRMS medications use, differences in educational attainment and whether the type of job the patient held required physical labor.

Measurement error is inherent to both data sources. For our discussion in this section we can distinguish between two types, namely theoretical and practical measurement error. Starting

with practical errors; In FD-Trygd 2001-2006 data, for example, one had, when arranging the data often several overlapping sickness absence spells at the same time. Typically three "cases" were common: 1. overlapping starting and stopping dates of multiple spells, 2. same starting but unequal stopping dates, and 3. spells within spells. The strategy is then of course to be consistent and treating everyone the same. For case no. 1 this meant taking the full length of the different spells i.e. changing the start to be the earliest observed and the stopping date to be the latest observed. For case no. 2 this meant choosing the longest spell and for case no. 3 it meant deleting the spells occurring within the observed times of other spells.

For the data from 1992-2008 from FD-Trygd many persons were registered to be on different sorts of benefit schemes at the same time, and at least with some overlap over time. However, for our analysis we wanted to permit only one state per time unit. To be consistent when arranging the data we therefore followed what we thought to be a natural hierarchy of severity among the states. This gave the hierarchy: working < sickness absence < rehabilitation < disability pension. Thus if a person was registered both to be on sick leave state and rehabilitation we dropped the observation on sick leave. Equally if the person was registered to be on sick leave, rehabilitation and disability pension we dropped the observations on the first two, coding the person to be on disability pension.

"Theoretical" measurement error is a form of validity problem. In the FD-Trygd data this deals, mainly, with identification of disease start and the time from this point until making transitions from the various labor market states. This problem stems from a limited observation window stretching over the 6 year period from 2001-2006 and from the type of data. Hereby it is expected that we therefore "mix" in the study population both new and older patients, and as a result the timeline of disease will be inaccurate. The difference in disease identification between our two data sets exists for a disease that we from previous discussed literature know to have its peak incidence around 30 years of age (cf. sections 1, 4.1.1 and 4.1.2). This imposes limitations to our interpretation of time lines in FD-Trygd. What we do have, in terms of variables, is the month in a given year (for example January 2002) in which the authorities got a notification of a person having MS; this being the first sickness absence spell accompanied by information on disease. We also know from the type of data (sickness absence) that the MS patient was economically active prior to this point in time. Using this information we have constructed theoretical periods of when we think the disease actually "starts" relative to when the authorities got a notification of this.

Measurement error from the Oslo cohort deals mainly with absence of information of disability pension from 93 MS patients and absence of year in which disability pension was first received from another 81 MS patients. One outsider would perhaps intervene that such a group will also contain patients both receiving and not receiving disability pension, but that on the average it is possibly skewed towards more people *not receiving* than receiving. For the 81 patients receiving disability pension but without registration of when they started doing so, their inclusion into the study have probably introduced "light" selective censoring of survival time. I have referred to it as "light" in the sense that it only occurred for patients that *did* receive disability pension. We learned from the difference in survival time between these 81 patients and the majority of 296 patients that the effect of including the former inflates overall survival time somewhat. Exact calculation of survival times from onset of disease to disability pension for this cohort should therefore be interpreted cautiously.

Selection bias is differences in effects that result from how the study participants, or the origin of the effects, entered into the study (Rothman et al., 2008). Selection bias in FD-Trygd will be dealt with in greater length in the section 5.1.1. Selection bias in the Oslo cohort should, due to it being complete for all MS patients in Oslo, be reduced to a minimum. This is of course a statement that is subject to the analysis group (n 596) not differing from the 93 individuals that had missing data on disability pension.

5.1.1 Matching in cohort studies

Matching in cohort studies is as done with respect to the participant's characteristics (age, gender, and education), and without considering events that occur during follow-up (Rothman et al., 2008). It is important to notice that the matching categories are far from exhaustive of what could be relevant for this study. Reviewing the goal of this study, which is to compare labor market movement for MS and control group; the exposure that separates the study groups, with regards to reaching different labor market states, is appearing with a MS diagnosis in the time period 2001-2006. This definition of the study aim involves a view of MS as the 'exposure' which separates the two study groups, namely MS and control. In this study we matched in a constant ratio of three controls per case for individuals in the year of registration with annual income surpassing NOK 50,000. According to Rothman and co-authors (2008, p. 174) matching unexposed subjects (non-MS and non-sickness absence) to exposed (MS and sickness absence) "can prevent confounding of the crude risk difference and

ratio by the matched factors because such matching prevents an association between exposure and the matching factors among the study subjects at the start of follow-up". This means that we can compare results from the descriptive part of the study without worrying that the differences observed are due to underlying differences in age, gender or educational structure.

Study subjects were matched in the period of identification of MS patients (2001-2006). We selected controls not on grounds of sickness absence, which is how we came to know about the cases of MS, (although every control had at least one sickness absence spell), but on grounds of registration of participation in the labor market in the period 2001-2006. Overall, it is assumed that this matching strategy overestimates the association between MS and poor labor market outcomes, in comparison with the reverse case of matching the controls on having had a sickness absence spell in the period 2001-2006. Ultimately, our matching strategy "left out" 151 MS patients, due to the income requirement in the *first* year with a sickness absence spell with MS diagnosis, and the validity of this study should be judged against this group having been left out, as they differed from the analysis group on key characteristics; being younger when study started and ended, and in between these outer points being younger when they were registered with disease.

6 Descriptive analysis

6.1 Descriptive analysis of disability pension in the Oslo cohort

In table 4 some of the general categories of analysis in the Oslo cohort have been presented. For each category (e.g. male/female) we have the number of events and subjects, the number of years at risk before the event or censoring occurred and the resulting incidence rate per person per year. Furthermore the survival time of the 25th 50th and 75th percentile is presented. We see that females have higher incidence of entering into disability pension than males. Being of higher age when disease struck, with age measured both continuously[2] and categorically, leaves the patient at higher risk of entry into disability pension according to the CPH model hazard ratio[2] and survival time. Age, measured categorically is however not significantly different according to the log-rank test that compares survival curves[2] (p-value 0.46). We will therefore treat age as continuous in further analysis of these data in section 7. The previously schematized difference in survival times due to the censoring problem of 81 patients is substantial, when looking at differences in survival time and incidence rate. The resulting hazard ratio from a CPH model is, however, not statistically significant, and neither is the log-rank test for equality of the survivor function (p-value 0.1). We therefore leave this matter and concentrate on how disease type affects time until disability pension, well knowing that we have allowed some selective censoring into the analysis (cf. section 4.1.2. and 5.).

Table 4. Descriptive statistics for survival time until disability pension for Oslo cohort

		Incidence rates for Oslo cohort			Survival time in years		
Variable	Events observed	Subjects	Time at risk*	Incidence rate**	25 %	Median	75 %
Disease type; RRMS	299	504	5423	0.055	6	14	24
Disease type; PPMS	78	92	774	0.101	3	7	14
Males	103	185	2278	0.045	9	17	30
Females	274	411	3919	0.070	4	12	20
Age at onset of MS 9-25	152	153	2267	0.038	11	20	30
Age at onset of MS 26-40	176	335	3245	0.065	5	12	21
Age at onset of MS 41-59	49	108	685	0.117	2	7	12
Male and RRMS***	71	144	1860	0.038	10	18	33
Time of disability unknown	81	81	936	0.080	5	11	15
Time of disability known	296	296	2719	0.098	2	7	14

* Time at risk in total person-years

** Per person-year. Calculated as; number of events / years at risk

*** Later Cox proportional hazards reference categories

[2] Results not shown.

We additionally see a substantial difference between MS patients with RRMS and PPMS, in both the incidence and the survival time in years after onset of disease. In terms of the incidence rate presented we saw that after 5 years time we can expect 24.6% (= 1-(1-0.055^5) and 41.3% to be on disability pension in the RRMS and PPMS group, respectively. In addition to the information provided in the table we have estimated a Kaplan-Meier survival curve in figure 7 with median survival on the vertical axis. Here, one orders the survival time(s) by increasing length starting with the shortest one. We start out with 100% (RRMS *n* 504 & PPMS *n* 92), and then as time goes the proportion not on disability pension decreases. It is decreasing only for events and not for censored observations (Swinscow and Campbell, 1997). If a censored observation occurs the survival curve will not change at the time this happening, but afterwards the number of people "at risk" for leaving the working state is reduced by the number of censored observations between the two time points. Summing up the tabular and graphical evidence we have strong indications of a difference between RRMS and PPMS patients in the time until disability pension is awarded.

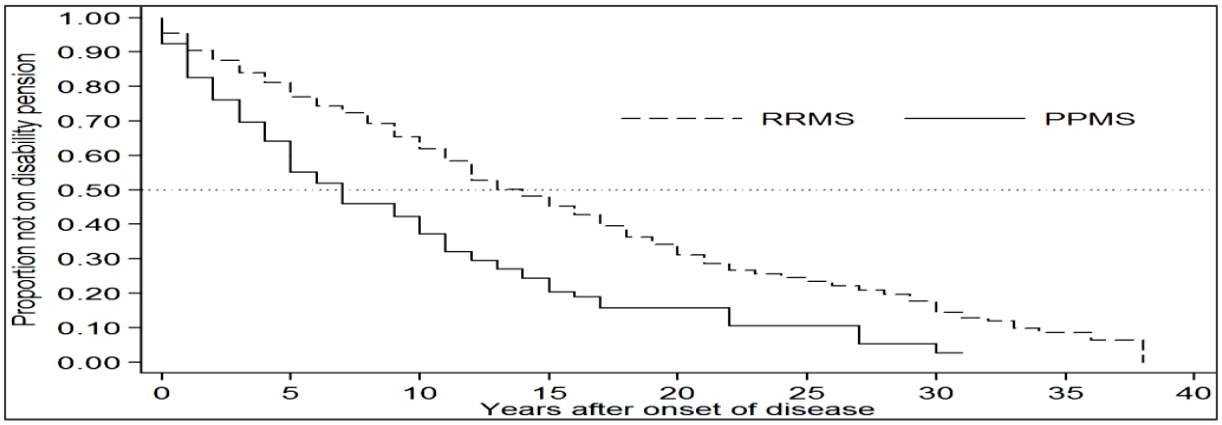

Figure 7. Kaplan-Meier plot of comparison between PPMS and RRMS in time to disability pension.

6.2 Descriptive statistics from the data on certified sickness absence spells

In figure 8 we see a Kaplan-Meier plot of the average duration in days of an average spell for the 2001-2006 data from FD-Trygd. The figure tells us the different patterns of duration in the average time for an initiated sickness absence spell to end. When nearing the 365th day we see the remaining MS patients "rush out" as this is the legal limit for sickness absence spell durations. Overall there is a big difference whether the spell is started by either a MS or

control subject, with MS patients having spells of much greater duration when first on sickness absence, in comparison with the control subjects who on the other side had a higher incidence of new spells, also when adjusting for spent in other states in the MS patient population. According to the monthly incidence rates presented here in table 5 we would expect 54.2% of MS patients to have a sickness absence spell of either long or short duration in a year (= 1-(1-0.063^12). Equally 58 % of controls can be expected to have a sickness absence spell within one year. Duration of control spells was shorter than that of MS patients as seen from duration and daily exit rate. The effective length of spells when accounting for part-time work is to be adjusted down 11% for MS patients and 5% for controls as seen from the *degree of spell*. This part concludes our analysis of long and short term sickness absence. In future result sections we will only deal with long-term absences.

Table 5. Incidence of short- and long-term sickness absence spells in time period 2001 - 2006 for FD-Trygd

	MS	Controls		MS	Controls
Total number of sickness absence spells	7975	44617	Number of spells	2.37 (2.6)	4.17 (3.58)
Number of subjects	3367	10700	Mean duration of spells in days	113 (134)	43 (79)
Total follow-up time*	235690	749000	Mean degree of spell	0.89 (0.2)	0.95 (0.14)
Time spent in sickness absence spells*	29184	59129			
Time spent in rehabilitation spells*	8412	15696			
Time spent in disability pension*	71064	38004	Percentile duration of spell (in days)		
			25% duration of spell	15	7
Monthly incidence rate**	0.063	0.070	Median duration of spell	39	13
Daily exit rate from spell	0.0088	0.0226	75% duration of spell	199	36

* In person-months

** Per person-month. Calculated as; number of events / (total time - time not in working state)

*** Numbers in brackets are standard deviations

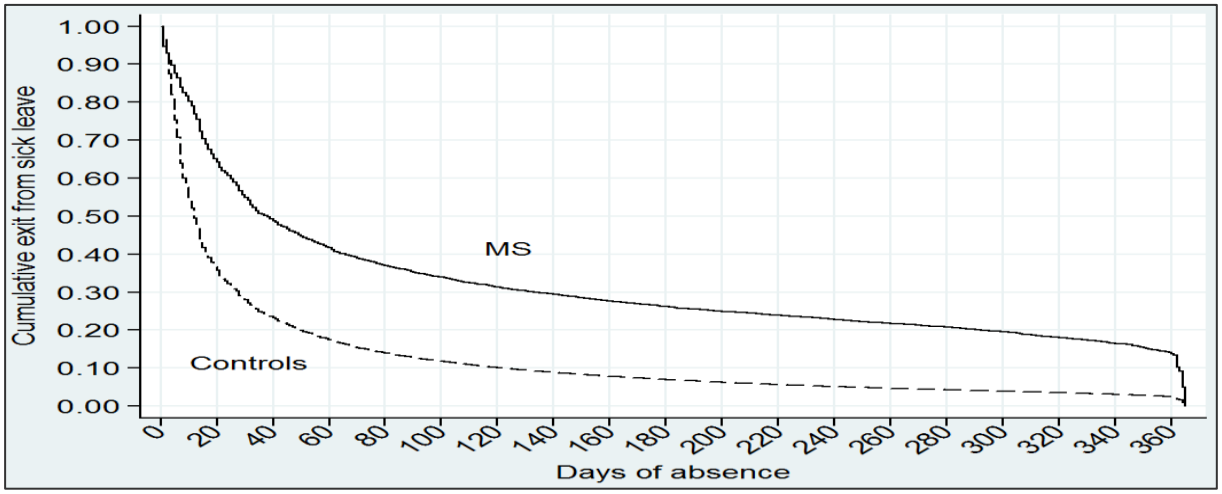

Figure 8. Cumulative exit from sick leave after start of spell.

6.3 Descriptive statistics from data on labor market participation income, and early retirement

Below we look at general descriptive statistics for labor market participation, income, and early retirement. For all endpoints but income we are looking at the number of persons making use of a service divided by the total number of persons per year. This returns the prevalence rate for the outcome. For income we are looking at the average income per person per year. For all endpoints except for early retirement, the interpretation of the timeline t_{-9} to t_{+7} is as follows: t_0 denotes the year of entrance into the study (see table 1. above) and $t_{\pm}$ are years relative to this point in time. For a subject entering in 2004 (t_0) year t_{-9} is 1996, for a subject entering in 2005 year t_{-9} is 1997 and so on. Our follow-up stops in 2008. This means that we have only got full follow-up (t_{+7}) for those entering the study in year 2001. For subjects entering in later years we have follow-up until $t_{+6,5,4,3,2}$ This implies that we have increasing statistical uncertainty the further we look into the future relative to t_0.

From figure 9 we see the yearly crude rate of employment for MS and control group. It is crude in that the real proportion of MS and controls is not adjusted for time spent in the other states of sickness absence, rehabilitation and disability pension. From the start the MS group had a higher, crude, participation rate in the labor market than that of controls. From year t_0 however, the difference in labor market participation widens dramatically from 0.6% to 22.4% at the end of follow-up.

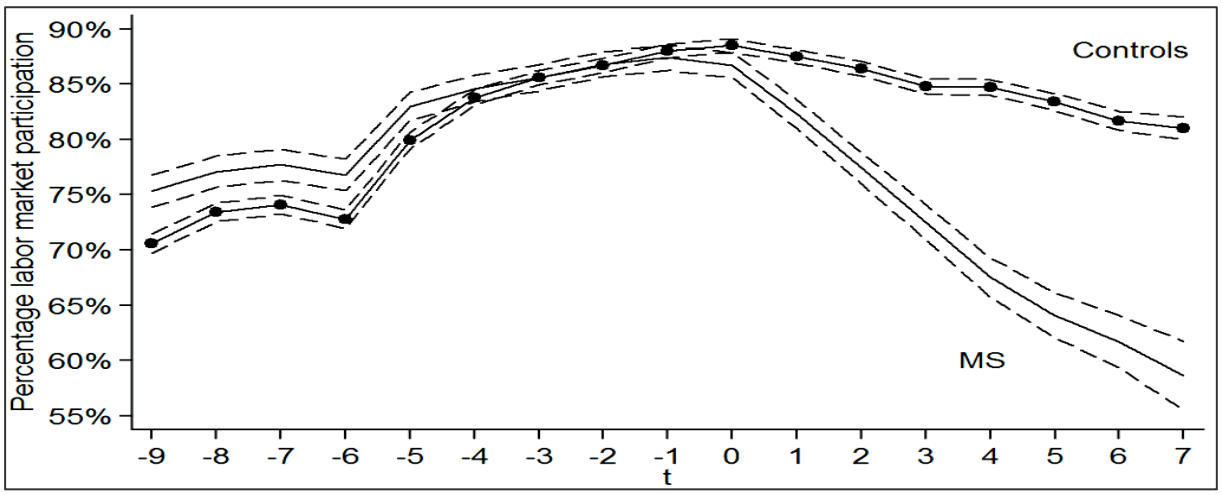

Figure 9. Rate of labor market participation with 95% CI. t=0 denotes year of notification of MS diagnosis for MS patients and year of first sickness absence in period 2001-2006 for controls.

From figure 10 we see yearly income averages from labor for MS and control group. From the start until year t_0 the MS group average income from labor was higher than that of controls. After year t_0 the difference in income for the two groups widens dramatically, from MS earning 368 NOK more to 113,000 NOK at the end of follow up.

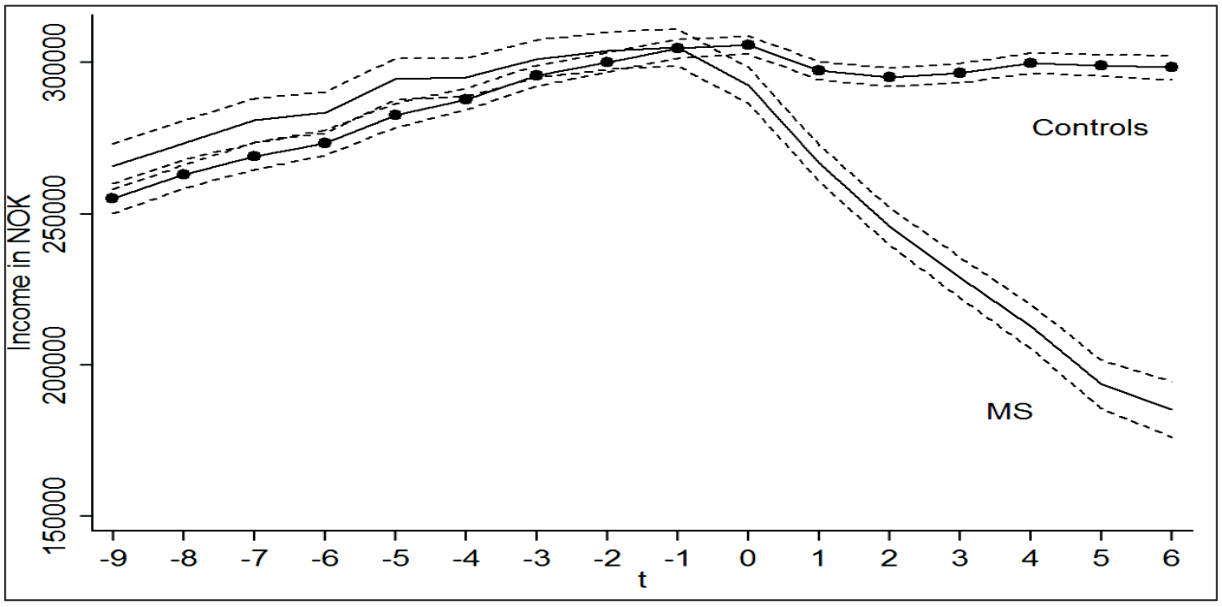

Figure 10. Income level indexed according to the basic amount of the National Insurance Scheme (year 2007) with 95%CI. t=0 denotes year of notification of MS diagnosis for MS patients and first sickness absence in period 2001-2006 for controls.

From figure 11 we see the yearly prevalence rates of early retirement for the persons born in the birth cohort 1940-45, which is the group of people at risk for entering into this benefits scheme. In Norway this scheme is known as 'AFP' and concerns persons above 61 years of age that are working within areas where the wage rate is set collectively according to sector-specific agreements between the employee(s) and employer(s). According to this we see that the curves for MS and controls starts to rise around year 2000, which in this case corresponds with the age at which the oldest subjects start to qualify for taking out early retirement. At the end of follow-up approximately 4 % of MS patients qualifying with regards to their age made use of this scheme while almost 16% doing so in the control group, leaving this group almost 4 times as likely to make use of this welfare scheme.

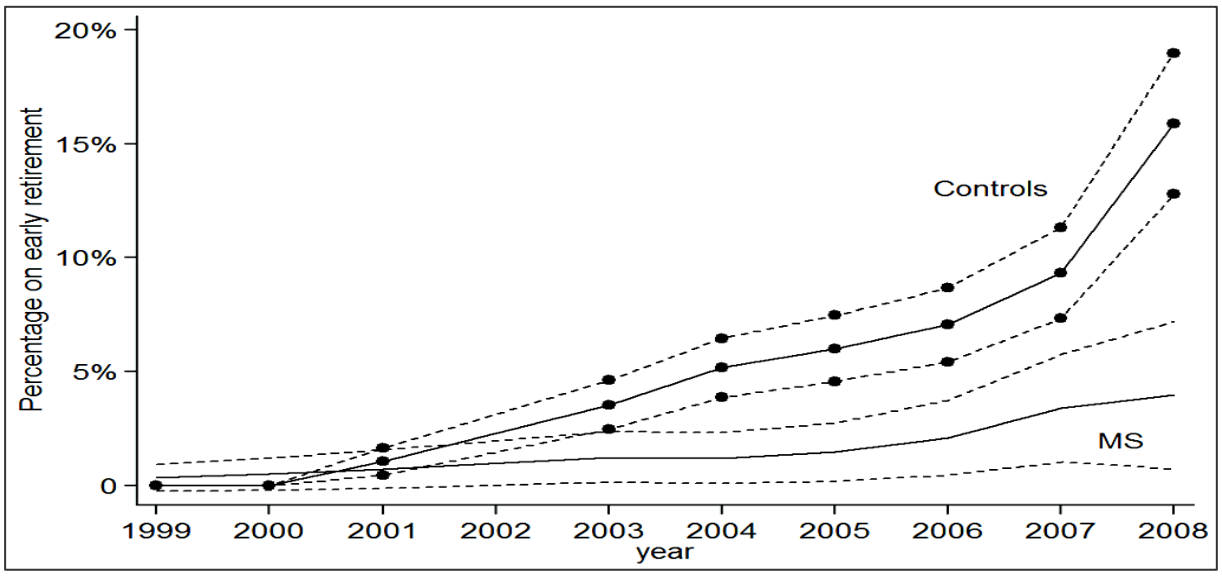

Figure 11. Rates of early retirement for the birth cohort 1940-45 from 1999 to 2008 with 95% CI. MS (n 390) Control (n 1148).

In further analysis we will not be dealing at length with early retirement as this scheme applies only to a small number of MS patients and controls. We will however illustrate in figure 12 the effect of adjusting for people in the birth cohort 1940-45 already on disability pension, as these are no longer at risk of early retirement. When removing the contribution from this group to the population at risk, the rate of MS patients making use of the scheme jumps up to around 10 percent. Removing the ones already on disability pension has removed confounding from the rate, but the estimate is fairly uncertain as witnessed from the wide confidence interval.

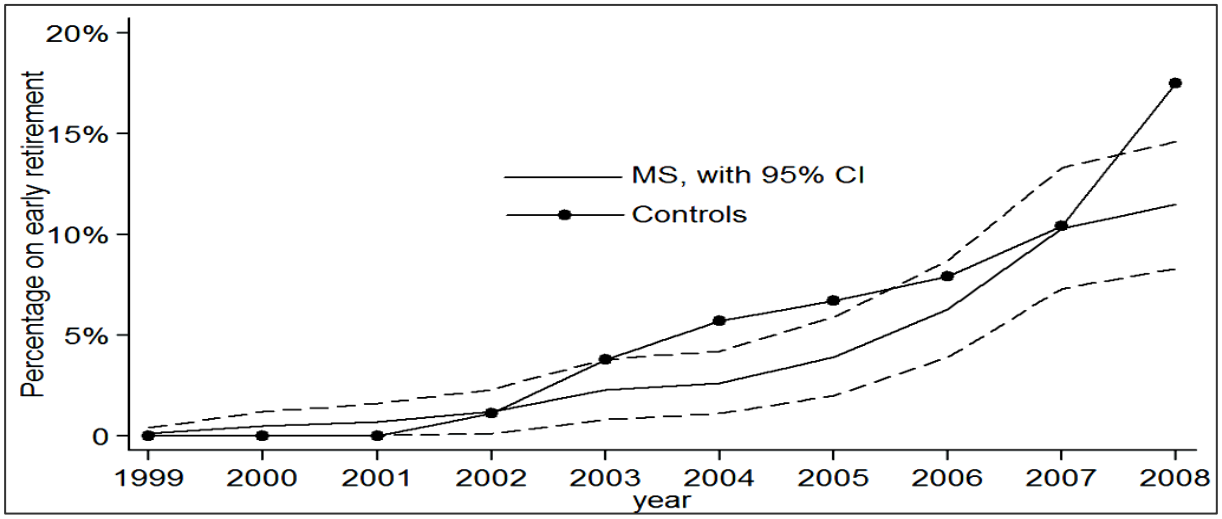

Figure 12. Early retirement rate after removing persons on disability pension.

6.4 Descriptive analysis of transitions and time spent in states

From table 6 we see the transitions to and from all states with observed frequencies and the time spent in each state in months for MS patients and controls. Overall each subject has 204 observations in person-months, equaling 17 years of follow-up. This table serves as a cross-sectional analysis of differences between the groups. The table describes the number of transitions observed in each group and the differences in incidence according to the total contribution in person-time per group. For example the number of people transiting from 'Working' to sickness absence was relatively higher in the MS group. Here the MS group transited between these states 60% more than the control group relative to their time at risk for making this transition. A reminder to the here is that sickness absence here refers to long-term sickness absence of more than 16 days.

Table 6. Transitions during follow-up 1992-2008 for FD-Trygd

Transition		MS		Controls		Incidence rate ratio (IRR)		
From state	To state	Time at risk*	Transitions	Time at risk*	Transitions	95% CI Lower b.	IRR	95% CI Upper b.
Working	Sickness absence	457489	12090	1906314	31466	1.58	1.60	1.62
Sickness absence	Working	55502	10750	111222	29589	0.71	0.73	0.75
Working	Rehabilitation	457489	937	1906314	2379	1.58	1.64	1.71
Rehabilitation	Working	21250	684	41561	1535	0.80	0.87	0.95
Sickness absence	Rehabilitation	55502	836	111222	1319	1.20	1.27	1.34
Rehabilitation	Sickness absence	21250	22	41561	35	0.81	1.23	1.65
Working	Disability pension	457489	950	1906314	559	7.02	7.08	7.15
Sickness absence	Disability pension	55502	477	111222	115	8.22	8.31	8.40
Rehabilitation	Disability pension	21250	558	41561	394	2.69	2.77	2.85
Disability pension	Sickness absence	132571	19	65635	17	0.10	0.55	1.00
Disability pension	Rehabilitation	132571	8	65635	9	0.00	0.44	1.13
Disability pension	Working	132571	196	65635	142	0.54	0.68	0.82
Working**	Early retirement**	7964	20	44541	262	0.00	0.43	0.87
Total follow-up in months***		666812		2124732			1	

*Time at risk refers to person-months of observation.
** Transition to early retirement. Calculated for people over 61 years of age, not already on disability pension.
*** Excludes people above 61 years of age

From table 7 we see the resulting states, with percentage transitions of total time, according to the model we represented schematically in figure 8. The observation time is thus the same, only presented in percentages instead of person-months as above. Here we see a simplification of what we learned from table 6. One quick observation is that we have left out the small amount of transiting subjects from 'Rehabilitation' to long-term 'Sickness absence'.

These were instead coded to have made the transition to 'Working', to keep them in the analysis. 'Early retirement' is left out from further analysis and so are the transitions occurring starting out from 'Disability pension'. Observations are therefore treated as censored when a subject has first been observed to make a transition to 'Disability pension'. All subjects entering into disability pension are therefore denied a reoccurrence of entrance into other states, even though that we learned from table 6 that 338 such transitions were observed just for subjects returning to work.

Table 7. Transitions during follow-up after arranging the data for FD-Trygd

Group	Origin state	Months with no transition	Months with transition to				
			Working	Absence	Rehab.	Disability p.	Total
MS	Working	96.76 %		2.89 %	0.15 %	0.20 %	100 %
	Absence	74.00 %	23.86 %		1.35 %	0.79 %	100 %
	Rehabilitation	91.93 %	5.03 %			3.04 %	100 %
Controls	Working	98.11 %		1.78 %	0.08 %	0.03 %	100 %
	Absence	62.48 %	36.36 %		1.07 %	0.09 %	100 %
	Rehabilitation	91.86 %	6.98 %			1.16 %	100 %

To avoid complications with people remaining at risk for early retirement and other pension schemes, subjects were treated as censored as they turned 61 years of age. This applied only to 1% of the observations in person-month time. We also note that the number of person-months remaining for analysis has decreased from a steady follow-up time per person of 204 months (17 years) to an average of 169 months. This is due to the requirement of the analysis, that everyone 'starts' in the 'Working' state. Thus, if a person was not registered as either sickness absent, on rehabilitation or on disability pension in January 1992 ($month_1$) she was registered in the analysis with full follow-up until the end of 2008 ($month_{204}$). In the setting of being registered as sickness absent, on rehabilitation or on disability pension from the start in January 1992 ($month_1$) until May 1993 ($month_{17}$) this person will only be registered in the analysis with 187 months of follow-up, and consequently have her first months left-censored. Say that a person enters into disability pension in December 2005 ($month_{168}$) she will be subsequently right-censored.

In table 8 we see the resulting development over time after having imposed that everyone starts in the state of working. The table shows movement to and from the states and the proportion of time spent in each state in the years proceeding and exceeding entry into the study (cf. table 1), along with income development and average age. The variable "Year" in

this table was generated subtracting the difference between the notifications of disease and preceding analysis time. This created a variable whose maximum preceding years before notification and "entry" was -13 (for those entering with a diagnosis in late 2006), and where the maximum exceeding years after notification and "entry" was 8 (for those entering with a diagnosis in early 2001. The validity of imposing this start in the state of working can be assessed by comparing the unconditional development over time, which can be found in the Appendix table 12. Generally, this requirement does not seem to have distorted the underlying structure of movement through states, with the proportions corresponding with each other to a great extent. One consequence of this coding is, however, the slight loss of continuity when calculating the average age in a given year relative to MS time (cf. table 12). On the left side of the table one will also find how time was coded in the analysis presented in section 7. Years -13 through -10 was subsequently coded to be the same for the MS group and controls. Years -9 through -6, years -5 through 0, years +1 through +4, and years +5 through +8 was subsequently coded as time 1, 2, 3 and 4, respectively. Time was coded this way in analysis due to data limitations, and to restrict the loss of information and create meaningful categories. One implication of this is that development over time for the control group is given by the ordinary *year* variable ranging from 1992 to 2008.

Table 8. Development over time relative to notification of MS disease and suspected disease start for FD-Trygd

After conditioning on start in state 'Working'			MS population						
	Coding in		Proportion of total population time spent in state				Income**	Income relative	Age
Terming of period	analysis	Year	***working***	***absent***	***rehab.***	***disability p.***	in NOK	to entry level	average
	0	-13	97.1 %	2.7 %	0.3 %	0.0 %	299482	94.2 %	32.0
Disease "free"	0	-12	96.7 %	2.9 %	0.2 %	0.2 %	303507	95.5 %	32.6
population	0	-11	95.9 %	3.2 %	0.4 %	0.6 %	304696	95.8 %	33.2
	0	-10	95.7 %	2.9 %	0.6 %	0.8 %	308760	97.1 %	33.8
	1	-9	94.8 %	3.7 %	0.6 %	0.9 %	315376	99.2 %	34.3
Some "early movers" suffer	1	-8	93.0 %	4.6 %	1.0 %	1.4 %	321234	101.0 %	34.9
consequences of MS	1	-7	91.1 %	5.1 %	1.8 %	2.0 %	324798	102.2 %	35.5
	1	-6	89.0 %	5.8 %	2.4 %	2.8 %	328057	103.2 %	36.3
	2	-5	86.4 %	6.5 %	2.8 %	4.3 %	329949	103.8 %	37.1
Disease "starts" for majority	2	-4	82.8 %	8.0 %	3.2 %	6.0 %	330688	104.0 %	37.9
and period ends with	2	-3	80.1 %	8.1 %	3.5 %	8.2 %	328819	103.4 %	38.9
notification of this	2	-2	77.1 %	8.7 %	3.5 %	10.7 %	328367	103.3 %	39.8
	2	Entry -1	73.5 %	9.9 %	2.8 %	13.7 %	328732	103.4 %	40.8
	2	**Entry year***	**74.1 %**	**7.0 %**	**1.9 %**	**16.9 %**	**317945**	**100.0 %**	**41.7**
	3	Entry +1	38.3 %	41.5 %	1.5 %	18.7 %	258412	81.3 %	42.7
Disease has consequences	3	2	47.5 %	10.3 %	10.4 %	31.8 %	224205	70.5 %	43.7
for majority	3	3	43.2 %	8.4 %	6.1 %	42.3 %	211777	66.6 %	44.7
	3	4	39.2 %	6.9 %	2.6 %	51.4 %	198164	62.3 %	45.8
Disease "progresses"	4	5	35.0 %	6.6 %	2.2 %	56.2 %	186477	58.7 %	46.8
and only a few	4	6	32.7 %	5.5 %	1.9 %	59.9 %	173539	54.6 %	47.8
remain working	4	7	30.1 %	4.0 %	1.6 %	64.3 %	162015	51.0 %	48.7
	4	8	25.0 %	4.5 %	2.2 %	68.3 %	146710	46.1 %	49.4

* Entry refers to the month in year of entry into the study, see table 1.

** Income adjusted for the 2007 basic amount of the National Insurance Scheme

Especially interesting in this table is the development relative to the “entry” year. From year 0, when the patient “entered”, to the next year 1, the proportion of time spent in the state “working” drops dramatically from 74% to 38%, a 50% decrease. Correspondingly, the proportion of time spent in the state of sickness “absent” increases from 7% to 42% in these two years. One year after this in year “2” we see a 10% return to work, and additional 10% remaining with sickness absence, a big jump in the proportion of time spent in rehabilitation (goes from 1 to 10%), and a relative increase of 70% in the time spent in the state “disability pension” (goes from 18.7% to 31.8%). Equally, the effects of these movements after entry with a diagnosis on income are substantial. One year after entering for the first time with a MS diagnosis a person earns only 81% of what he did in the previous year from work. After 8 years he can expect to earn only half of what he did in the “entry” year.

7 Results

7.1 Oslo cohort

We now start presenting the results from the analysis of the Oslo cohort dataset with the CPH model. From table 9 we see the different hazard ratios for time from onset of disease to being awarded disability pension. MS patients with PPMS type of disease proceed statistically significant faster to disability pension than patients with RRMS (HR 95% CI 1.27-2.15). This relationship holds also when having included the other variables in the model. Females are equally more likely than males (HR 95% CI 1.37-2.18) to proceed faster to being awarded disability pension. Age is also associated with proceeding faster to disability pension, a relationship that augments the HR with 1.05 per additional year of age at onset of disease (HR 95% CI 1.03-1.06). All three variables satisfy the CPH model assumption of proportionality as witnessed by the large p-values under '*PH test'*, and thus fail to reject the hypothesis of proportionality. The conclusion is therefore that disease type PPMS is associated with less time from onset of disease until disability pension is awarded.

Table 9. Analysis of time until disability pension for Oslo cohort.

Cox regression - Efron method for solving ties

No. of subjects	596	LR chi-square (3 DF)	100.11
No. of transitions to disability pension	377	Log likelihood	-2020.377
Time at risk (years)	6197	Prob > chi-square =	<0.0001

	Haz. Ratio	S.E.	z-value	P-value	95% CI for Haz. Ratio	PH test* Prob>chi2
Disease type; RRMS (ref.)	1					
Disease type; PPMS	1.66	0.22	3.73	<0.001	1.27 - 2.16	0.68
Males (ref.)	1					
Females	1.73	0.20	4.64	<0.001	1.37 - 2.18	0.20
Age at onset	1.05	0.01	7.36	<0.001	1.03 - 1.06	0.49
					Global test	0.52

* Test of proportional hazards assumption

** S.E. denotes standard error

Finally, our interest lies with predicting the proportion of MS patients surviving until year *t* after onset of disease on the basis of our chosen model. In figure 13 we have plotted the cumulative survival function for patients with PPMS and RRMS. It took around 9 years for

the first 50% of the PPMS group to be awarded disability pension while it took almost another 4 years before this percentage was reached for patients with RRMS.

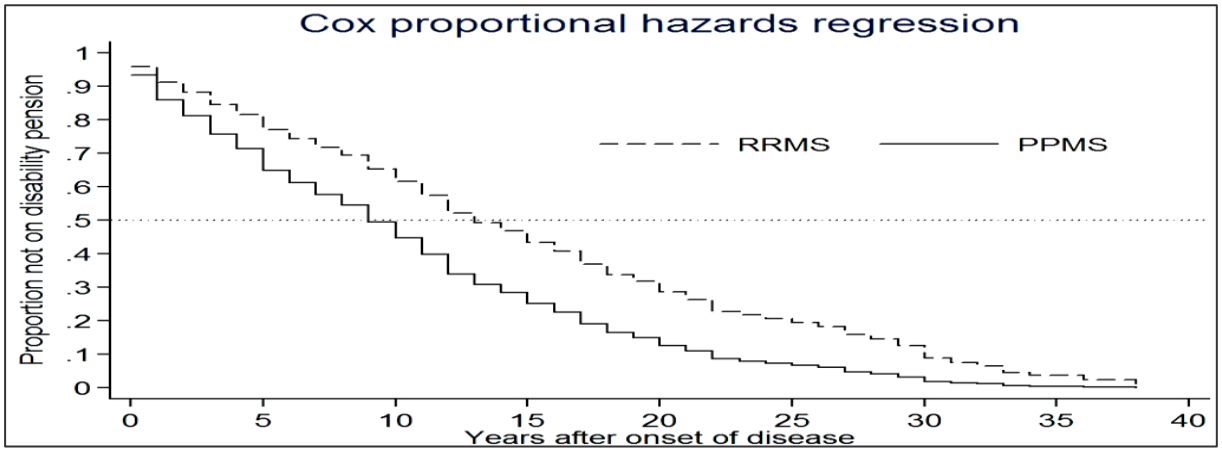

Figure13. Comparison between patients with PPMS and RRMS with median survival on the vertical axis.

7.2 FD-Trygd

In this section the results from the NPMLE is presented. The chosen mixture model had 13 support points for the unobserved heterogeneity distribution. In total this model had 311 parameters to estimate. Estimates of hazard ratios and 95% confidence intervals are presented. Note that the reference category for some of the variables has been arbitrarily selected. For example for the *month in year* variable to investigate seasonal dependence January has been set as the reference. Coefficient values, standard errors and t-values for this model are presented in the Appendix table 13. A reminder is that everyone started in the state of *working*. All transitions to work are therefore *return to work* transitions. Another reminder is that all transitions to sickness absence are to *long-term sickness absence*.

The starting point of our presentation of the results is the empirical reference category rates of making a given transition to any of the four states, which is the selected way of translating the theoretical concept of hazard ratios into conditional probabilities. These rates were found from tabular analysis of transitions for males aged 36-40, who had completed high school and did not have MS in 2008. The denominators for these rates are person-months. The hazard ratios are to be seen in reference to these rates. Thus, the reference hazard rate of moving to long-term sickness absence, rehabilitation and disability pension was 0.01585, 0.00114 and 0.00014, respectively. The reference hazard rate of making the transition from long-term

sickness absence to return to work was 0.1974. These reference values can be multiplied with the hazard ratios presented in the model, and are alone to be seen as hazards, or conditional probabilities of a transition occurring (cf. section 4.2.1). The hazard ratios are presented in table 10.

Reviewing the resulting hazard ratios we see that transitions from rehabilitation to work have a hazard ratio that is only 31.7% (i.e. 1/3rd) of the one seen for transitions from long-term sickness absence to return to work. Hence the hazard rate changes from 0.1974 per month to 0.0626. Transitions to rehabilitation from long-term sickness absence are 55.5% of the hazard ratio for transitions from work. This translates into a change in the hazard rate from 0.00114 to 0.00063. The hazard ratio for transitions to disability pension is not different between transitions from work and rehabilitation. It is less likely that it comes from long-term sickness absence with a hazard ratio being only 11% that of the reference rate *from working*.

7.2.1 Relative impact of gender, education and age

Gender has a relative effect on the various hazard rates. Women rather than men are more likely to leave the work-force and have higher entry rates to any of the other three states of sickness absence, rehabilitation and disability pension. Compared with men, women have a hazard rate that is 4% smaller for return to work from rehabilitation and sickness absence. This would change monthly conditional probability of making the transition from 0.197 to 0.189 Women are 43% more likely to transit to long-term sickness absence and 19% more likely to enter into rehabilitation and 74% more likely to enter into disability pension as seen from table 10.

Educational attainment also has a relative impact on the hazard of making the various transitions. Persons with middle-school have a hazard rate for returning to work from long-term sickness absence or rehabilitation that is 5.1% smaller than people with high-school education and 9.2% (= HR 0.949/ HR 1.031) smaller than people with college education. Likewise we see the protective association of higher education relative to individuals whose highest attained educational level is high- or middle school for transitions to long-term sickness absence, rehabilitation and disability pension.

Variable	Hazard ratios for transitions to											
	Work			Sickness absence			Rehabilitation			Disability pension		
	Lower HR	HR	Upper HR	Lower HR	HR	Upper HR	Lower HR	HR	Upper HR	Lower HR	HR	Upper HR
From state												
Working				Only transitions from working state possible				1			1	
Sickness absence		1					0.409	0.555	0.753	0.060	0.110	0.202
Rehabilitation	0.282	0.317	0.356							0.689	1.014	1.493
Gender												
Males (ref.)		1			1			1			1	
Females	0.932	0.960	0.988	1.379	1.429	1.481	1.086	1.191	1.307	1.530	1.736	1.970
Educational attainment												
Middle-school	0.916	0.949	0.983	1.137	1.188	1.241	1.361	1.523	1.704	1.278	1.479	1.712
High-school (ref.)		1			1			1			1	
College	1.001	1.031	1.062	0.774	0.802	0.832	0.616	0.680	0.751	0.440	0.501	0.570
Age-group												
16-20	1.016	1.196	1.409	0.196	0.222	0.251	0.164	0.295	0.533			
21-25	1.078	1.144	1.214	0.652	0.687	0.724	0.633	0.759	0.910	0.081	0.130	0.208
26-30	0.985	1.027	1.070	0.922	0.957	0.994	0.741	0.847	0.969	0.169	0.227	0.305
31-35	0.996	1.033	1.072	0.976	1.008	1.041	0.778	0.878	0.991	0.464	0.564	0.684
36-40 (ref.)		1			1			1			1	
41-45	0.964	0.999	1.035	0.940	0.971	1.002	0.867	0.971	1.087	1.298	1.517	1.772
46-50	0.912	0.948	0.986	0.998	1.034	1.071	0.785	0.888	1.005	1.647	1.947	2.300
51-55	0.815	0.851	0.890	1.096	1.143	1.192	0.932	1.069	1.226	2.921	3.485	4.157
56-61	0.707	0.745	0.786	1.271	1.343	1.419	1.029	1.212	1.427	6.506	7.903	9.600
Group membership												
Controls (ref.)		1			1			1			1	
MS baseline	0.772	0.861	0.959	1.340	1.468	1.607	1.213	1.941	3.106	7.52	16.55	36.45
9 to 6 years before MS (time 1)	0.711	0.752	0.796	1.396	1.476	1.560	1.797	2.213	2.727	7.15	10.17	14.45
5 to 0.1 years before MS (time 2)	0.709	0.740	0.772	2.097	2.199	2.305	1.801	2.092	2.431	15.84	19.78	24.69
0 to 4 years after MS (time 3)	0.428	0.447	0.466	2.799	2.955	3.120	5.535	6.461	7.542	99.09	129.35	168.86
5 to 8 years after MS (time 4)	0.533	0.579	0.628	2.174	2.369	2.582	3.300	4.378	5.809	62.49	88.39	125.02
Year												
1992	1.501	1.635	1.781	0.494	0.531	0.571	0.047	0.077	0.126	0.008	0.018	0.042
1993	1.481	1.602	1.732	0.469	0.504	0.542	0.176	0.239	0.326	0.025	0.049	0.099
1994	1.422	1.534	1.654	0.553	0.593	0.636	0.228	0.304	0.405	0.093	0.144	0.223
1995	1.380	1.482	1.591	0.591	0.632	0.676	0.289	0.378	0.495	0.107	0.162	0.245
1996	1.309	1.400	1.498	0.598	0.636	0.677	0.280	0.360	0.462	0.081	0.116	0.168
1997	1.232	1.316	1.405	0.662	0.703	0.748	0.401	0.501	0.625	0.144	0.198	0.273
1998	1.125	1.201	1.281	0.680	0.723	0.768	0.436	0.540	0.670	0.240	0.322	0.434
1999	1.056	1.125	1.197	0.793	0.841	0.892	0.491	0.611	0.761	0.377	0.498	0.657
2000	1.042	1.108	1.178	0.943	1.000	1.060	0.605	0.750	0.928	0.395	0.520	0.685
2001	1.129	1.196	1.267	1.078	1.138	1.201	0.590	0.726	0.892	0.264	0.344	0.448
2002	1.117	1.181	1.250	1.057	1.116	1.178	0.728	0.876	1.054	0.401	0.505	0.636
2003	1.038	1.099	1.164	1.155	1.218	1.284	0.782	0.947	1.146	0.478	0.595	0.742
2004	1.066	1.129	1.196	1.043	1.102	1.166	0.926	1.110	1.330	0.662	0.813	0.999
2005	1.045	1.108	1.174	1.157	1.221	1.290	0.815	0.991	1.204	0.861	1.046	1.270
2006	1.086	1.149	1.215	1.089	1.151	1.216	1.020	1.232	1.487	0.745	0.898	1.082
2007	1.154	1.222	1.295	1.012	1.072	1.135	0.996	1.205	1.458	0.747	0.906	1.097
2008 (ref.)		1			1			1			1	
Seasonal dependence												
January (ref.)		1			1			1			1	
February	0.970	1.019	1.071	0.800	0.838	0.878	0.849	1.003	1.185	0.673	0.807	0.968
March	1.102	1.157	1.215	0.811	0.850	0.891	0.848	1.003	1.186	0.597	0.721	0.871
April	1.020	1.072	1.127	0.777	0.814	0.854	0.826	0.980	1.162	0.611	0.738	0.891
May	1.204	1.264	1.327	0.770	0.806	0.845	0.948	1.119	1.321	0.667	0.804	0.970
June	1.404	1.473	1.546	0.465	0.490	0.517	1.103	1.303	1.538	0.729	0.876	1.052
July	1.247	1.312	1.381	0.889	0.930	0.973	0.830	0.980	1.156	0.621	0.749	0.903
August	0.968	1.020	1.074	0.941	0.984	1.029	1.001	1.175	1.380	0.666	0.801	0.964
September	0.974	1.025	1.078	0.944	0.987	1.032	0.963	1.135	1.339	0.829	0.990	1.182
October	0.930	0.978	1.028	1.005	1.050	1.098	1.050	1.238	1.460	0.855	1.019	1.214
November	0.871	0.916	0.963	0.715	0.750	0.788	1.021	1.201	1.413	0.714	0.861	1.038
December	1.114	1.170	1.230	1.003	1.049	1.096	0.855	1.007	1.188	0.772	0.925	1.109
Duration dependence from rehabilitation												
1st month	1.172	1.529	1.994							0.116	0.193	0.321
2nd month	1.092	1.425	1.858							0.135	0.220	0.359
3rd month	0.787	1.036	1.365							0.202	0.323	0.516
4th month	0.699	0.931	1.240							0.219	0.351	0.561
5th month	0.645	0.860	1.146							0.189	0.309	0.505
6th month	0.598	0.805	1.083							0.216	0.351	0.572
7th month	0.633	0.853	1.150							0.252	0.406	0.655
8th month	0.527	0.724	0.995							0.217	0.359	0.595
9th month	0.705	0.952	1.285							0.255	0.418	0.686
10th month	0.739	0.998	1.349							0.321	0.517	0.835
11th month	0.655	0.895	1.223							0.394	0.629	1.006
12th month	0.848	1.156	1.576							0.538	0.839	1.310
1st quarter, 2nd year	0.711	0.936	1.233							0.511	0.756	1.120
2nd quarter, 2nd year	0.626	0.834	1.111							0.564	0.844	1.264
3rd quarter, 2nd year	0.618	0.837	1.135							0.809	1.213	1.818
4th quarter, 2nd year	1.097	1.465	1.955							1.118	1.693	2.564
3rd year	0.713	0.941	1.240							0.927	1.357	1.987
>4 years (ref.)		1									1	
Duration dependence from sickness absence												
1st month	0.233	0.247	0.261				0.002	0.003	0.004	0.002	0.004	0.007
2nd month	0.184	0.195	0.207				0.002	0.002	0.004	0.001	0.002	0.005
3rd month	0.139	0.148	0.157				0.003	0.004	0.006	0.001	0.002	0.006
4th month	0.109	0.117	0.125				0.004	0.005	0.007	0.001	0.003	0.006
5th month	0.097	0.105	0.113				0.004	0.005	0.007	0.004	0.008	0.013
6th month	0.089	0.096	0.104				0.005	0.007	0.009	0.003	0.006	0.012
7th month	0.082	0.089	0.097				0.005	0.007	0.010	0.004	0.007	0.012
8th month	0.071	0.077	0.085				0.006	0.008	0.011	0.002	0.004	0.009
9th month	0.067	0.074	0.081				0.008	0.010	0.014	0.008	0.012	0.020
10th month	0.081	0.090	0.099				0.012	0.015	0.019	0.012	0.018	0.028
11th month	0.140	0.153	0.166				0.046	0.054	0.063	0.063	0.080	0.102
12th month (ref.)		1						1			1	

Table 10. Hazard ratios for FD-Trygd model. Lower and upper HR denotes lower and upper bound for 95% confidence interval of the hazard ratio (HR)

Still for education, we see for transitions to sickness absence that persons with middle-school have a hazard rate for going that is 18.8% higher than those with high-school and that is 39.4% (= HR 1.188/ HR 0.802) higher than persons with college education. For transitions to rehabilitation persons with middle-school have 52.3% higher hazard rate than persons with high-school and 123.9% (= HR 1.523/ HR 0.68) higher than the hazard of persons with college education. For transitions to disability pension persons with middle-school had a hazard rate that was 47.9% higher than those with high-school and 195.2% (= HR 1.479/ HR 0.501) higher than persons with college education.

From table 10 we see that the hazard ratio for transiting to return to work decreases steadily over age. The youngest age group has a 60% higher hazard of making this transition than do people in the oldest age group (= HR 1.196/ HR 0.745). For transitions to long-term sickness absence, rehabilitation and disability pension the hazard ratio shows that increasing age is generally associated with a poorer labor market outcome. The young-old comparison leaves the youngest with a hazard rate that is only 16.5% of the hazard for the oldest for making the sickness absence transition. For rehabilitation young people have only 24.4% of the hazard that people in the oldest age-category do, and for disability pension this figure is only 1.6% for those in the youngest age-group. This relationship can be represented terms of development in hazard rates as in figure 14.

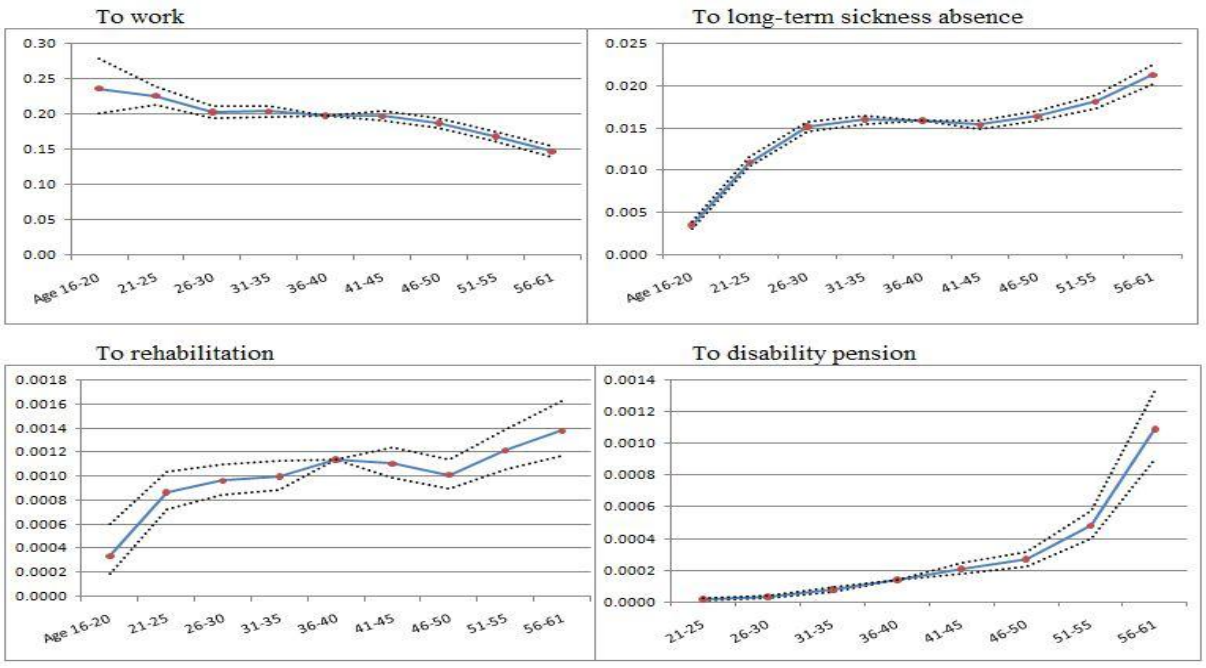

Figure 144. Development in hazard rates over age with 95% CI. Monthly probabilities. Note the difference in scales on vertical axes.

7.2.2 Variation over the years 1992-2008 and months within years

From the variable year in table 10, we saw the development in hazard ratios over the period 1992-2008 for controls. Generally this illustrates the relative impact of an ageing and more diseased control population over the period. At the start of this period, in 1992, the hazard of transiting from to return to work was 63.5% higher than in 2008. Equally the hazard of transiting to long-term sickness absence was 88.3% higher in 2008 than in 1992 (HR = HR 1/ HR 0.513). More dramatic however, were the increases in hazards of transiting to rehabilitation and disability pension, which at the start of this 17 year period was only 7.7% of the 2008 hazard for rehabilitation and 1.6% of the 2008 hazard for disability pension. From figure 15 we see these hazard ratios in relation with the reference hazards from section 7.2.

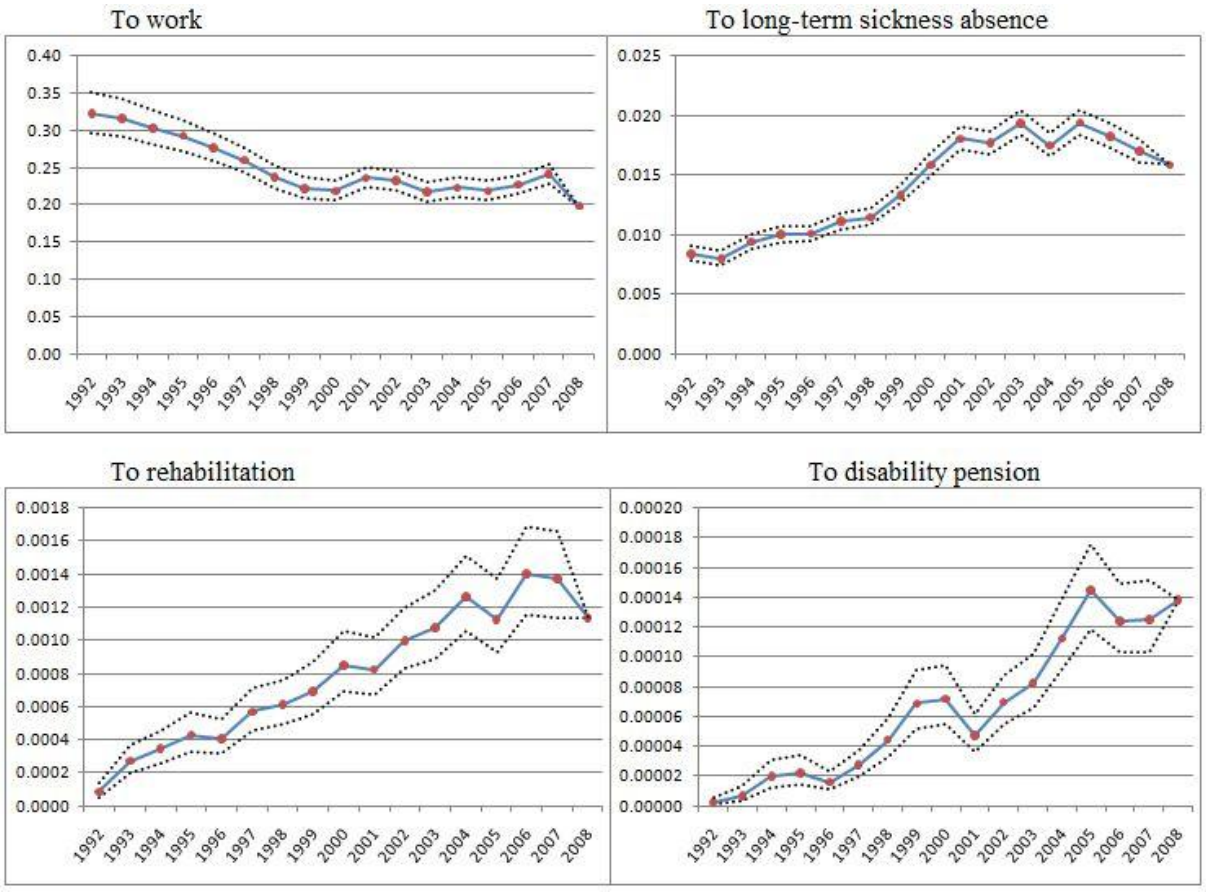

Figure 15. Development in hazard rates over 1992-2008 with 95% CI. Monthly probabilities. Note the difference in scales on vertical axis.

From figure 16 we see the seasonal dependence of transitions to the states in the form of hazard ratios with January as the reference with 95% confidence intervals. We see that the

seasonal dependence is very much present for movement to work and to long-term sickness absence. Return to work transitions becomes more likely in the "spring- and summer months" of March, April, May, June and July compared with the reference month of January. There is also a significant increase in the hazard rate for return to work in December. For transitions from work to long-term sickness absence the reverse pattern is shown. Here hazard rates are lower than reference of January in the early spring and summer months until July when it stabilizes to the same level as January. In the second half of each year it becomes less likely again in November before returning to normal in December. Movement to rehabilitation and disability pension has not got the same seasonal dependence, and estimates are not as certain as for movement to work and to sickness absence from work, as seen from the relatively wide confidence intervals. However one could perhaps interpret a pattern being that relatively more people transit to a rehabilitation stay and disability pension during the 2nd half of each year.

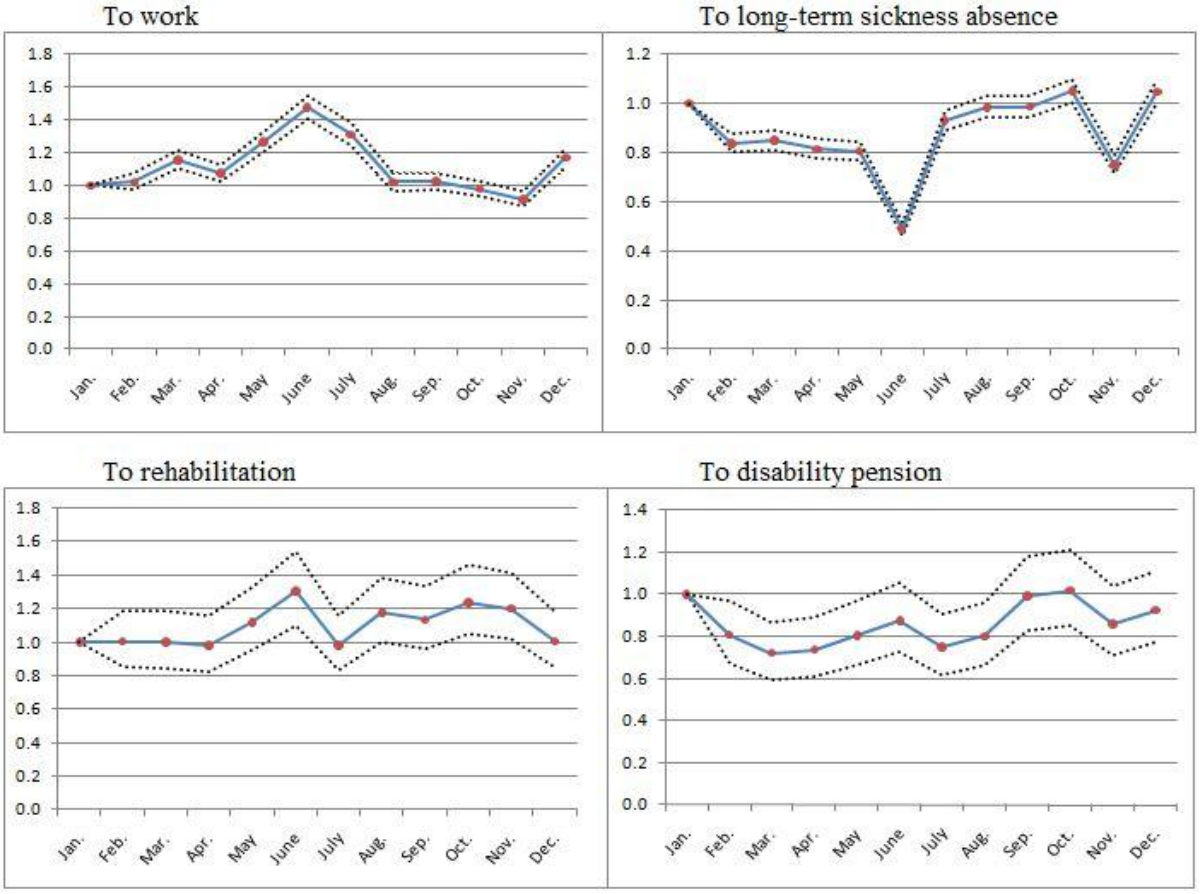

Figure 16. Relative impact of calendar month on the hazard rates of making the four transitions with 95% CI. Note the difference in scales on vertical axis.

7.2.3 Duration dependence

Figure 17 demonstrates the various duration dependencies involved with stays in either rehabilitation or long-term sickness absence with 95% confidence intervals. The reference category hazards for transitions from rehabilitation to work and disability pension are 0.0565 and 0.0157, respectively. The reference category hazards for transitions from long-term sickness absence to return to work, to rehabilitation and to disability pension are 0.4983, 0.2987 and 0.0797, respectively. For return to work there is a slight negative duration dependence in hazards during the first couple of months before leveling off at conditional probabilities of around 5% until a jump is seen in the 4th quarter of the second year of stay on rehabilitation where approximately 8% returns to work. For transitions made to disability pension from rehabilitation there is positive duration dependence. The probability of making this transition increases steadily, although remaining at low levels, throughout the two first years before dipping slightly from the peak in the 4th quarter of year 2 in years 3 and 4.

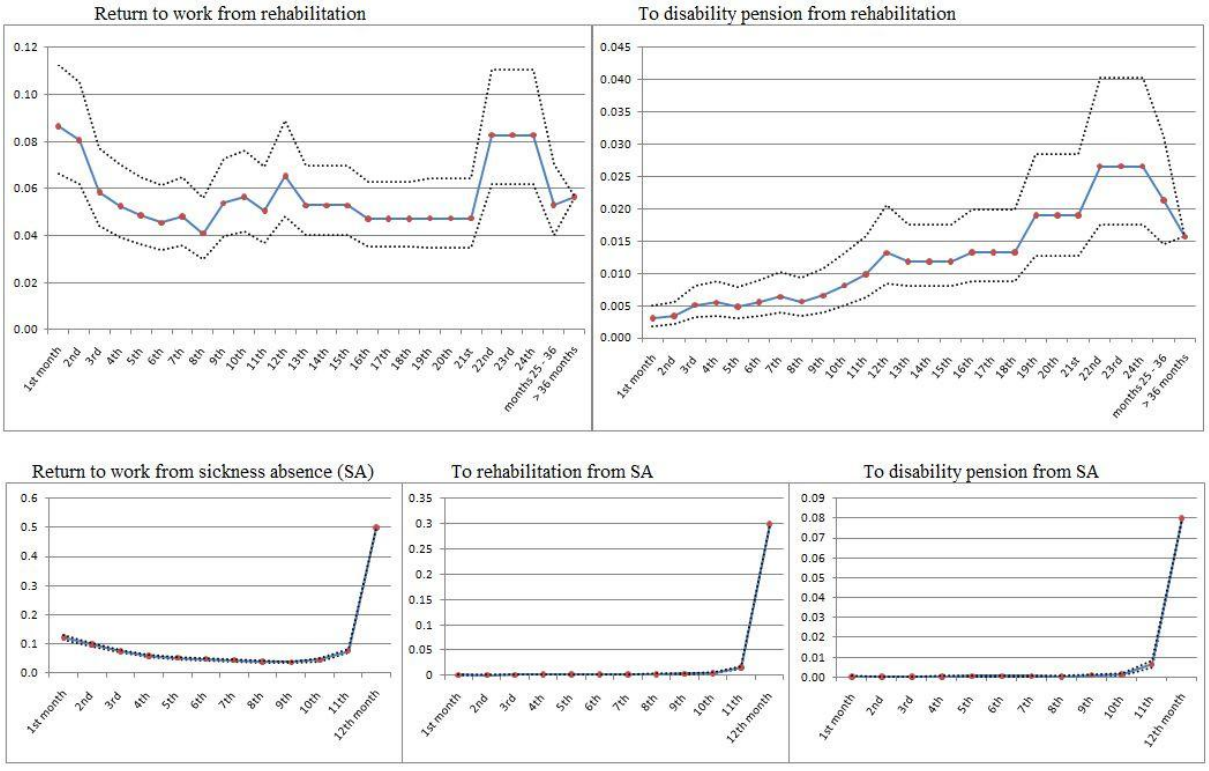

Figure 17. Duration dependence in recovery hazards from rehabilitation and sickness absence with 95% CI. Monthly probabilities, given no recovery up until this month.

Duration dependence for transiting from sickness absence to work, to rehabilitation, and disability pension are negative. Transitions from long-term sickness absence are extremely

low in the first 11 months before increasing to very high probabilities in the 12th month. Overall the pattern of duration dependencies for long-term sickness absence spells reflects the legal limit for spell duration, set at 365 days. When reaching the 12th month of a spell subjects are forced either to return to work, go on rehabilitation or on disability pension. Overall this presentation reflects the pattern we saw from figure 8, only differing in that figure 18 deals with the transition pattern for long-term sickness absence only.

7.2.4 Relative impact of MS on hazard rates

In table 10 we have presented the hazard ratios for the relative impact of MS and how this impact develops in time before and after a diagnosis. The categories MS time 1 and 2 denote the discrete periods of 9 to 6 years and 5 to 0.1 years before registration with diagnosis. Categories MS time 3 and 4 refer to the discrete periods of 0 and 4 years and 5 and 8 years after diagnosis, respectively. We saw that in comparison with the controls that MS patients have, consistently, from start to the end of study, a higher risk of experiencing some adverse outcome on the labor market. For instance the hazard ratio for returning to work decreases throughout the period for MS patients relative to controls. In the years 0 to 4 (MS time 3) after registration with diagnosis controls had a hazard that was 124% higher than that of MS (HR = HR 1 / HR 0.447). For the same time period MS patients transited to long-term sickness absence with a hazard ratio that was 3 times as large as for controls. For rehabilitation it was 6.5 times as large in this period while it was 130 times as great as that of controls. Some of the presented hazard ratios in table 10 were indeed very large, and it is therefore important to relate these hazard ratios to the reference category hazards as discussed in section 7.2. In figure 18 we see the resulting monthly probabilities for the various transitions for MS patients.

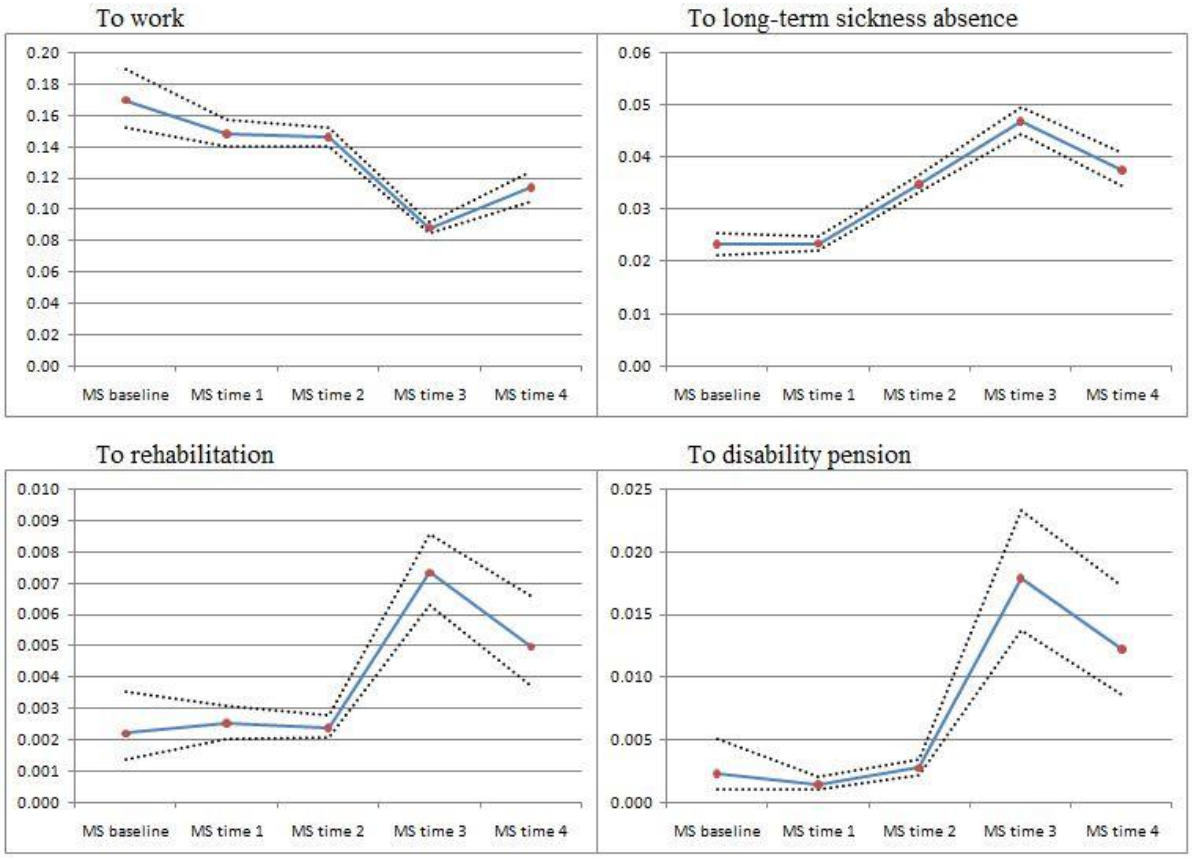

Figure 18. Development in hazard rates over time for MS patients with 95% CI. Monthly probabilities. Note the different scales on vertical axes.

We note from figure 18 that it is not until time 2 that the sickness absence rate increases vastly from the baseline and time 1 measure. This tendency tops in time 3 before slowing somewhat in time 4. For return to work rates there is throughout the study period a lower rate for MS patients. From baseline to time 2 this rate does not change dramatically when considering the intra-MS situation. In time 3 and 4 MS have a return to work rate of around 0.09-0.12 per month in sickness absence. Looking at the monthly probabilities for rehabilitation spells there is no substantial change for MS patients until time 3 when it jumps up to a rate of 0.0073 from 0.0022 (a HR of 3.1 over the MS time 2 level). In time 4 this hazard decreased somewhat, but is still higher than before registration with diagnosis. For MS patients the monthly probability for transitions to disability pension, while always higher than that of controls, stays practically unchanged until time 3 just after being registered with a diagnosis. Here it increases to a monthly probability of 0.0179, reflecting a very high transition rate in those years as seen from table 7. The hazard of MS in time 4 decreases somewhat relative to the peak in time 3.

7.2.5 Unobserved heterogeneity

Underlying what we have observed from the results section on the dataset from FD-Trygd until now is the unobserved heterogeneity. Recall from section 7.2 that this model had 13 support points for the unobserved heterogeneity distribution. In table 11 we examine the correlation between the four unobserved intercepts in the above model. This is done by estimating Kendall's τ, which varies between 1 for full positive correlation and -1 for full negative correlation, for all possible pairs of persons that can be formed from the heterogeneity distribution (Markussen et al., 2010). People with a high probability of working (1) subsequently, and unsurprisingly, have a lower rate of entering into sickness absence (corr -0.44), rehabilitation (corr -0.84) and disability pension (corr -0.64). People with a high probability of sickness absence (1) have higher entry rates into rehabilitation (corr 0.60) and disability pension (corr 0.74) but lower rates of going back to work (corr -044). People with a high probability of going on rehabilitation (1) have subsequently lower rates of going back to work (corr -0.84) but a high entry rate into sickness absence (corr 0.60) and disability pension (corr 0.78).

Table 11. Unobserved heterogeneity in FD-Trygd. Kendall's (T) for rank correlation between unobserved intercepts.

	Working	Sickness absence	Rehabilitation	Disability pension
Working	1	-0.444	-0.843	-0.643
Sickness absence		1	0.599	0.741
Rehabilitation			1	0.778

8 Discussion and limitations

The purpose of this study was to investigate MS patients and the relationship this patient group has with the labor market. We wanted to investigate development over time with regards to income development, use of sickness absence rights, development in rehabilitation stays and how this patient group exits the labor market due to being awarded disability pension. In this regard, we have constructed two main models for the analysis of transitions between the labor market states; *working, long-term sickness absence, rehabilitation and disability pension.* We have dealt with analysis of income development, use of short- and long-term sickness absence combined and use of the early retirement scheme descriptively. The aim of studying transitions to the various states has been to fill a gap in existing research on MS and the labor market.

To analyze this phenomenon we have made extensive use of survival analysis, both in its simple form of life-table analysis (Kaplan-Meier survival curves), over the more complicated modeling of hazards through Cox Proportional Hazards regression for the study of single events and a competing hazard rate model for the study of competing, and recurring events. The main outcome in this study has been hazard rates and ratios. What we have gained by modeling is compressed analysis where we are able to consider the relative importance of the various aspects. These aspects, in addition to having MS and the time a subject has had MS, range from the relative importance of demographic characteristics, development over the 17 year period 1992-2008, the within-year seasonal dependence of transitions, and the duration dependence for transiting from sickness absence and rehabilitation stays to other states.

8.1 Findings from descriptive analysis

Starting with the findings from the descriptive statistical analyses provided in section 6 we can discuss some of the findings that we did not follow-up with further determinants analysis in section 7. Starting with the incidence of sickness absence; while we learned from the analysis in section 7 that MS and control populations are different when it comes to incidence of long-term sickness absence, this is not necessarily the case when we also include short-term sickness absence spells. Results from table 5 indicate that when adjusting for time spent in other labor market states during the 2001-2006 period, controls still have a slightly higher or at least a rate that is at the same level when it comes to frequency of sickness absence

spells. MS patients have vastly longer sickness absence spells, but the control group by far exceeds the MS patients in the number of spells per person during this period. On the basis of this, accounting for the assumed time spent in other states the yearly incidence rate of MS patients was found to be 54.2% while it was 58.2% for controls. When it comes to exiting from sickness absence controls are however different from MS patients. Generally, MS patients exit the sickness absence spell at a rate of 0.88% per day, while 2.26% of controls do the same. Moreover, we learned that when in a sickness absence spell, approximately $1/5^{th}$ of MS patients seem to hold on until forced over into other benefit schemes (cf. figure 10).

Comparing with Henriksson and co-authors (2001) who found that for Sweden the number of days lost per person in a year to sickness absence to be 23 for full-time workers and 14 for part-time workers, we find that for Norway such a figure could be found in the region of 21 days for those working full time (= 54.2% with sickness absence in a year × 39 days of median duration of spell) and 19 days when correcting for the proportion working part-time within the time of the spell. We are thus able to produce similar figures for sickness absence for MS patients in Norway.

Considering the early retirement scheme available to Norwegian workers we have in this study found an indication that MS patients make less use of this scheme than do corresponding controls. The relationship between MS patients making use of this scheme is to some degree confounded by the fact that many by the time that they will reach the qualifying age of 61 years will have made use of disability pension. Removing subjects already on disability pension removes some of the confounding associated with this estimate of both incidence rate (cf. table 6) and prevalence rate (cf. figures 11 and 12) of MS patients on early retirement. However, some confounding could be expected to remain under the assumption that if a person has a MS disease then it is fairly unreasonable (in comparison with population average numbers) that she would stay in the labor market until her 61^{st} birthday. MS patients remaining in the labor market until that age could therefore be interpreted to be a selected group in the first place.

One thing that we could have done differently in the analysis of FD-Trygd (cf. section 7.2), with regards to early retirement, would have been to include early retirement as a form of disability pension, and just combine these categories. This could be reasonable under the assumption that there is selection to different benefit schemes which depends on whether or not one has got a diagnosis to accompany one's illness. From the interpretation of this

argument one could state that the reason why this early retirement discrepancy between MS patients and controls exists; being due to fewer controls being found a diagnosis of disease to accompany their illness. This could lead to more controls (with an illness) rather than MS patients (with a disease) to make use of early retirement as a substitute for disability pension. If so, then we are indeed perhaps overestimating relationship between MS patients going on disability pension in comparison with control subjects.

Looking at income development we saw that income adjusted for the basic amount of the National Insurance Scheme to 2007 values of NOK differed widely between MS patients and controls in the years after the first sickness absence spell with a MS diagnosis (cf. figure 10). We showed, however, that income levels between MS patients and controls did not differ in the years before being registered with a diagnosis for the sickness absence spell. In fact, our estimates show that the income level of MS patients was slightly higher than the corresponding controls estimate. Thus, this *first* sickness absence spell registered with a MS diagnosis is the start of a serious decline in income for this patient group, and must count as important when judging the social consequences of this disease in Norway. Exploiting the relative time differences between start of follow-up in 1992 and year in which registration with diagnosis took place (cf. table 8 and 12) the income development for MS was truly dramatic. Eight years after registration with diagnosis in a sickness absence spell, MS patients earned only around half of what they did in the one-year interval preceding this incident.

Relative to income development we also considered the time spent in the various states before and after being registered with a sickness absence spell with MS diagnosis. From tables 8 and 12 we saw the continuous decline of time available for work relative to time spent in the states of sickness absence, rehabilitation and most dramatically disability pension. Both for the unconditional tabular analysis and the tabular analysis after imposing that everyone starts in the working state the percentage on disability pension at year 8 was in the lower region of 70%. Previous to this we had dramatic movement between the states in the two year period after the sickness absence spell registered with a MS diagnosis. As such, the percentage working decreased from 72% to 37% within one year (unconditional table). Corresponding with this figure the percentage on sickness absence increased from 6.8% to 40.5%. In year two after the start of the sickness absence spell the percentage working had increased temporarily to 46%, the percentage on sickness absence was now 10%, the percentage on rehabilitation and disability pension had increased greatly from 1.4% to 10.2% and 21% to

33.8%, respectively. Over time from entry year to year 8 the proportion on disability pension increases from 19.4% to 69.7%, a truly dramatic enlargement.

8.2 Findings from model analysis

Some of the findings of this study include that there is an association between demographic variables and intensity of transitions to all of the states. MS patients, and controls, with higher education are less likely to leave the labor market in favor of long-term sickness absence, rehabilitation and disability pension, and are in turn more likely to return to work from sickness absence and rehabilitation that patients with lower levels of educational attainment. Age is equally a factor that facilitates higher entry rates to long-term sickness absence, rehabilitation and disability pension and that complicates the chances of returning from either rehabilitation or sickness absence when in a spell. All of this agrees well with the theory outlined in section 2.1. From a previous study Myhr and co-authors (2001) found that the age at onset of MS is deemed of statistical importance. Data from the Oslo cohort supports this, in line with what was hypothesized in section 2.1. In the study by Myhr and co-authors the hazard ratio of age at onset was increasing at two percent per year for both RRMS and PPMS (HR 1.02, with 95% CI 1.00-1.05) which is in the low end of the observed relative impact of age in the Oslo cohort dataset, with an increase in the hazard rate of 5% (95% CI 1.03-1.06) per extra year of age at onset. Previously we had named a range of studies that were torn about the association between gender and association with the labor market (Smith and Arnett, 2005, Sundstrom et al., 2003, Simmons et al., 2010, Rumrill et al., 2007, Rodriguez et al., 1994, Larocca et al., 1985). In our study gender is throughout associated with a poorer relative outcome for females. Women are, in both the Oslo cohort and in the FD-Trygd data, estimated to have higher intensity of entering into disability pension, rehabilitation and long-term sickness absence. When sickness absent or on rehabilitation women also have poorer recovery prospects than their male counterparts.

Regardless of group affiliation there is a development over time in the hazard rates of transiting to the various states as shown by figure 15. The associated probability of transiting back work decreases steadily over the period. Transitions to long-term sickness absence, rehabilitation and disability pension show the reverse pattern. In general this can be thought of as the effect of an ageing control population, which together with the MS patient population becomes more at risk of poorer labor market outcomes.

Within each year we have also considered the impacts of seasonal dependence on the hazard rate. This seasonal dependence seems strong when we consider movement to long-term sickness absence and return to work from sickness absence and rehabilitation. For movement to rehabilitation and disability pension from either work or disability pension, this pattern fades out, and although we notice some variation throughout the year, this variation seems modest and insecure as witnessed from the relatively wide confidence intervals.

In our FD-Trygd model we are also capturing aspects of the duration dependence of long-term sickness absence and rehabilitation spells (cf. figure 17). For duration dependence for transition from rehabilitation to return to work we saw how the probability of returning went from 0.086 and 0.08 in the two first months before stabilizing in the range between 0.041 and 0.065 from the 3rd month of rehabilitation onwards to the end of the 3rd quarter of the second year when it rises to levels before only seen at the start for the 4th quarter. For duration dependency from rehabilitation to disability pension we saw how the probability of making this transition increased, reasonably, throughout the 4 year period with, also here, a spike in the 4th quarter of year 2. Thus we could characterize the duration dependency for making the transition from rehabilitation to return to work as negative and the duration dependency for transitions to disability pension as positive. We are from the presentation of this relationship able to say more about the pattern of return to work transitions from rehabilitation and document the rate of this movement in the labor market. We therefore find support to the theory outlined in section 2.2 on return to work from rehabilitation from both descriptive analysis in section 6 and from the model analysis in section 7.

Duration dependence for transitions from long-term sickness absence to return to work, to rehabilitation and disability pension all start out at very low probabilities and then have very strong spikes in probabilities of transitions in the 12th month. Generally we are seeing a resemblance of the pattern observed in figure 8, where we considered a combination of long- and short-term sickness absence spells. In the duration dependency pattern disclosed in figure 17 we are seeing where the individuals transit after ending their long-term sickness absence spell. Transitions back to work have a comparatively higher probability throughout the sickness absence spell. For transitions to both rehabilitation and disability pension the probability is virtually zero up until the 12th month. A general interpretation of this duration dependence could be the reluctance to give up the relatively higher replacement ratio of the salary.

One assumption invoked by the model is that duration dependence, once within a long-term sickness absence or rehabilitation spell, and seasonal dependence, is the same for both MS patients and controls. The validity of making this assumption is questionable. Then it could only be valid on the assumption that once in a long-term sickness absence or rehabilitation spell, controls will have some illnesses or disease that we have not accounted for.

For MS patients both the models and previous descriptive statistics show interesting aspects of labor market movement. Recapitulating, we saw an increasing risk of relatively poorer labor market as time with MS increased for both FD-Trygd and the Oslo cohort. For FD-Trygd we have witnessed a comparison between MS patients and controls that by far show the darker prospect of MS patients on the labor market. Looking more closely at the sickness absence pattern observed in tables 8 and 12, we can say that the FD-Trygd model with its discrete time periods for MS patients, to some degree, fails to fully capture the explosiveness in developments in sickness absence around the year of registration. This is due to the hazard rate in time period 3 being aggregated over a four year period. The observed hazard rate therefore does not show the same intensity as one would expect from these previously mentioned tables. However, still the general pattern throughout the study period is for MS patients to increase their transition intensity to long-term sickness absence.

For both transitions to rehabilitation and disability pension the FD-Trygd model captures the relative increases in years after entry with a diagnosis (cf. tables 8 and 12) rather well with both increasing dramatically in the four year period. With time it also becomes increasingly less likely that MS patients will return from sickness absence and rehabilitation stays, which is not surprising when taking the progressive nature of the disease into account. The development of transitions to all labor market states as of time 3 (just after registration with disease) can therefore under the *disease*, *illness*, and *sickness* framework put forward in section 1.2 be understood as the relative impact of finding a disease to accompany one's illness, which results in a more clearly defined social role (sickness) for the patient. On the basis of this it can be argued that it is the registration with a disease that, partially, legitimizes these transitions.

For all four transitions there is the pattern of moving towards less dramatic labor market outcomes in MS time 4. This could very well be due to sorting in and out of the labor-market, with a selected group of individuals remaining in the labor market and the majority of MS patients already having transited to disability pension and thus not remaining at risk of

returning either back to work, of going to long-term sickness absence or to rehabilitation. This fits well with what was outlined in the theory section on the development of MS with a group of RRMS patients ending up having benign multiple sclerosis with limited accumulated disability even after more than 20 years of disease.

Intra-MS in the Oslo cohort we have observed a difference between disease type and the time until disability pension is awarded. This is in line with what was previously found from Myhr and co-authors (2001) and in line with other previous work (Verdier-Taillefer et al., 1995, Sundstrom et al., 2003). Estimates from analysis of the Oslo cohort provide us with figures that resemble those of Myhr and co-authors to a great extent (cf. figure 7 and 13). Myhr and co-authors found the 15 year proportion on disability pension for PPMS patients to be around 75% and around 50% for RRMS patients. For data from the Oslo cohort these percentages at year 15 were slightly more than 75% for PPMS and slightly more than 50% for RRMS.

Comparing the results with those of Pfleger and co-authors (2010), and Henriksson and co-authors (2001), for which we have general study results linking the proportion not in work and disease duration, the results from this study seem plausible. Recapitulating the results from Pfleger and co-authors some 78% had left the labor market for early retirement after 20 years time. In the study of Henriksson and co-authors some 60% had done so after average disease duration of 17 years. Contrasting the results from these two studies from respectively Denmark and Sweden, we found in our study this percentage to be 65% after 17 years and 75% after 22 years for the Oslo cohort and approximately 70% for data from FD-Trygd after 17 years (cf. table 8 and 12). We therefore do encounter support for aspects uncovered in this study, in particularly those pertaining to sickness absence and disability pension. External validity therefore seems present with regards to the basic structure of labor market related phenomena for MS patients, considering both what was discussed with regards to disability pension and sickness absence.

Looking at the time until disability pension for our two study datasets, we are thus able to produce comparable figures with the studies conducted in Denmark and Sweden as well as with the study conducted by Myhr and co-authors (2001) (see above). Differences within our two study datasets, and between these and the others that have been mentioned, can possibly be attributed to measurement error on the outer points of the dimension *time at onset of MS - time at outcome*. For the data from the Oslo cohort we can argue that they are specific when it comes to determining the *time at onset of MS* but not so when it comes to determining the

time at disability pension. For FD-Trygd the opposite is the case; here we are not (necessarily) in possession of data that are specific when it comes to determine when MS was first onset, rather we are here in possession of data that allows us to determine with great precision the time at which an outcome occurred (long-term sickness absence, return to work, rehabilitation and disability pension). It is probable that the two datasets thus are biased in one direction or the other, and that the *real* time-sequence from onset of disease to occurrence of events are to be found between the ability to produce accurate estimates of onset of disease and accurate estimates of labor market outcome. A result of this relationship would be the necessity for future research, using public administrative data, on labor market outcomes and chronic diseases with complex incubation processes to more accurately link the time at onset, established on the basis of professional diagnosis, with the time of the outcome. One suggestion on how to accomplish this would be to extend the number of years of patient identification (cf. table 1).

In comparing the two datasets used in this study we uncover some relationships for FD-Trygd that is not accounted for in the Oslo cohort and vice-versa. For FD-Trygd we have uncovered the relative importance of elements, such as education level, duration dependence and seasonal dependence, in addition to the dynamics of transitions between a set of labor market states and the comparison with a control group from the general population. An element important in FD-Trygd is the high specificity with regards to when the outcomes occur. Elements only present in the Oslo cohort covers, among others, finer "optics" on time of onset of disease and the end-point of disability pension, access to information on the disease type of the patient, access to patients not discovered in our 6-year window from 2001-2006 for FD-Trygd. Additionally we had the ability in the Oslo cohort of drawing upon a full cohort for a geographically restricted area as we in FD-Trygd cover only those with a sickness absence spell in combination with a diagnosis.

With regards to the difference in age at registration with disease between the two study data sets we still end up with similar results with regards to the proportion on disability pension after end of follow-up. The proposed categories, for FD-Trygd, describing the time periods therefore gain some face validity (cf. *terming of period* in tables 8 and 12). Despite of being an inaccurate representation of time with disease, FD-Trygd manages to uncover dramatic developments after registration, with regards to transitions to all of the outcome states, that augments its credibility.

Other limitations to this study are the limit to the number of states that an individual can reside in at any given time for FD-Trygd. This means that we are not distinguishing between patients that are either fully or partially sickness absent not those that are registered under a partial disability pension.

For the Oslo cohort it is a limitation that the year in which 81 patients first got disability pension is not visible to us. We have previously argued that this inflates survival time from onset of disease to disability pension. It is a further limitation that we do not gain any knowledge about what happens in between the onset of disease and disability pension for these patients. Ultimately, we are analysis dependent on a limited number of variables, which puts a limit to the relationships studied for both data sets.

For both data sets we are missing potentially important relationships related with the work-place. For instance both the dimension physical/ non-physical labor and private/public sector could prove to be a source of variation in transition intensity to the various outcome states. Another relationship that could be of importance could be the patient's general practitioner. For FD-Trygd data one could look for variation in transition intensities towards sickness absence, rehabilitation, return to work and disability pension and see if male or female doctors or doctors with and without specialization would be associated with increasing or decreasing degrees of good or poor labor market outcomes.

9 Conclusion

This is to the author's knowledge the first study investigating movement between a set of labor market states for a multiple sclerosis patient population. The results presented in this study shed light on the complex phenomena of MS and movement between labor market states. MS as a disease has vast impacts on the use of social security benefits in comparison with a matched control group from the general population. After registration with MS, patients usually stop working and enter into a long period of sickness absence before transiting to rehabilitation and on to disability pension. In between these outer points MS patients experience recurrent return to work transitions, long-term sickness absence and rehabilitation spells. Over a follow-up period of 17 years approximately 2/3rds of MS patients will end up with disability pension, according to analysis of the Oslo cohort and FD-Trygd datasets.

MS patients have consistently poorer relative labor market outcomes than controls that only deteriorate with time. Some factors not pertaining to the disease itself also modify the intensity of transitions to the various labor market states. We have identified such variation in the intensity of transitions to sickness absence, rehabilitation, and return to work from these states, that depend on age, gender, educational attainment, time, seasonal dependence and duration dependence within the sickness absence and rehabilitation spells. In addition to the above mentioned moderating factors we have identified, for transitions to disability pension, that the intensity also varies with age at onset of disease and whether the disease type is relapsing-remitting or primary progressive.

Implications for involved parties in the treatment of and interaction with MS patients, both in the medical community, in public authorities and at the workplace, could be to more closely integrate their follow-up of MS patients. Special attention can be given to the relative risks uncovered in this study. Accommodating that MS patients retain their working life after onset of disease is important, and valuable both to the patients themselves and to society at large.

Future research on the intersection between MS and the labor market using labor- and welfare-registers should make use of longer periods of case-identification to better assure separation between old and new cases. Studies considering other diseases for which complex diagnostic processes exist should equally do so, although the for-how-long question remains

case-specific. The possibility of linking data from various sources such as disease records and other registers containing information on vocational rehabilitation and health services use could add to the level of knowledge describing the relation between MS patients and their connection with the labor market. Ultimately, and in the long run, studies in the area of comparative effectiveness research should also draw upon data concerning the labor market to comprehensively evaluate treatment benefits, and the ability of these to enable patients to remain in work after onset of disease and initiation of treatment.

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Appendix

Table 12. Before conditioning on start in working state. Development over time relative to notification of MS disease and suspected disease start for FD-Trygd

Before conditioning on start in state 'Working'			MS population						
	Coding		Proportion of total population time spent in state				Income**	Income relative	Age
Terming of period	in analysis	Year	***working***	***absent***	***rehab.***	***disability p.***	*in NOK*	to entry level	average
	0	-13	93.8 %	2.5 %	1.5 %	2.2 %	241893	77.5 %	28.8
Disease "free"	0	-12	93.6 %	2.9 %	1.5 %	1.9 %	252099	80.8 %	29.9
population	0	-11	92.6 %	3.1 %	1.8 %	2.5 %	260085	83.3 %	31.0
	0	-10	92.0 %	2.9 %	2.0 %	3.1 %	268706	86.1 %	32.1
	1	-9	90.9 %	3.5 %	1.8 %	3.7 %	280534	89.9 %	33.2
Some "early movers"	1	-8	89.1 %	4.2 %	2.5 %	4.2 %	291208	93.3 %	34.1
suffer consequences of MS	1	-7	87.8 %	4.5 %	2.9 %	4.8 %	302810	97.0 %	35.1
	1	-6	85.9 %	5.4 %	3.1 %	5.7 %	311208	99.7 %	36.1
	2	-5	83.5 %	6.2 %	3.3 %	7.1 %	316939	101.5 %	37.1
Disease "starts" for majority	2	-4	80.1 %	7.5 %	3.4 %	9.0 %	320211	102.6 %	38.1
and period ends with	2	-3	77.6 %	7.7 %	3.5 %	11.2 %	320335	102.6 %	39.1
notification of this	2	-2	74.7 %	8.3 %	3.4 %	13.6 %	320911	102.8 %	40.1
	2	Entry -1	71.3 %	9.6 %	2.7 %	16.5 %	322451	103.3 %	41.1
	2	**Entry year***	**72.0 %**	**6.8 %**	**1.8 %**	**19.4 %**	**312181**	**100.0 %**	**42.1**
	3	Entry +1	37.0 %	40.5 %	1.4 %	21.0 %	253092	81.1 %	43.1
Disease has consequences	3	2	46.0 %	10.0 %	10.2 %	33.8 %	219218	70.2 %	44.1
for majority	3	3	41.7 %	8.1 %	6.1 %	44.1 %	206620	66.2 %	45.1
	3	4	37.7 %	6.6 %	2.6 %	53.1 %	193067	61.8 %	46.1
Disease "progresses"	4	5	33.7 %	6.3 %	2.1 %	57.9 %	181230	58.1 %	47.2
and only a few	4	6	31.3 %	5.4 %	1.8 %	61.5 %	168631	54.0 %	48.2
remain working	4	7	28.9 %	3.9 %	1.5 %	65.7 %	156956	50.3 %	49.0
	4	8	23.9 %	4.4 %	2.1 %	69.7 %	142204	45.6 %	49.7

* Entry refers to the month in year of entry into the study, see table 1.

** Income adjusted for the 2007 basic amount of the National Insurance Scheme

Graphical presentation of table 12 in figure 19. Percentage working, sickness absent, on rehabilitation and on disability pension relative to year of entry.

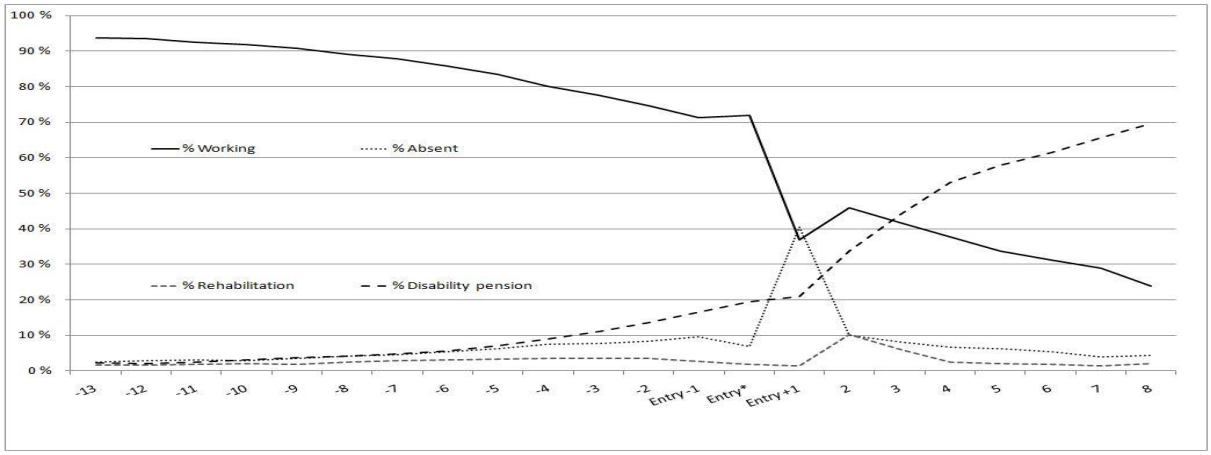

Figure 19. Development over time for MS patients without conditioning on start in the "working" state.

Variable	Transitions											
	To work			To sickness absence			To rehabilitation			To disability pension		
	β-value	S.E.	t-value	β-value	S.E.	t-value	β-value	S.E.	t-value	β-value	S.E.	t-value
From state												
Working							Ref.			Ref.		
Rehabilitation	-1.148	0.059	-19.382	Only transitions from						0.014	0.198	0.071
Sickness absence	Ref.			working state possible			-0.589	0.156	-3.780	-2.203	0.308	-7.161
Gender												
Males	Ref.			Ref.			Ref.			Ref.		
Females	-0.041	0.015	-2.751	0.357	0.018	19.720	0.175	0.047	3.693	0.552	0.064	8.562
Educational attainment												
Middle-school	-0.053	0.018	-2.922	0.172	0.022	7.736	0.421	0.057	7.353	0.392	0.075	5.248
Highschool	Ref.			Ref.			Ref.			Ref.		
College	0.031	0.015	2.023	-0.220	0.019	-11.895	-0.386	0.051	-7.624	-0.692	0.066	-10.481
Age-group												
16-20	0.179	0.084	2.148	-1.505	0.063	-23.756	-1.220	0.301	-4.049			
21-25	0.135	0.030	4.467	-0.375	0.027	-14.098	-0.276	0.093	-2.983	-2.042	0.240	-8.515
26-30	0.026	0.021	1.253	-0.044	0.019	-2.256	-0.166	0.068	-2.424	-1.483	0.150	-9.857
31-35	0.033	0.019	1.758	0.008	0.016	0.490	-0.130	0.062	-2.109	-0.573	0.099	-5.788
36-40	Ref.			Ref.			Ref.			Ref.		
41-45	-0.001	0.018	-0.061	-0.030	0.016	-1.857	-0.030	0.058	-0.514	0.417	0.079	5.255
46-50	-0.053	0.020	-2.698	0.033	0.018	1.859	-0.119	0.063	-1.881	0.666	0.085	7.823
51-55	-0.161	0.022	-7.184	0.134	0.022	6.203	0.067	0.070	0.958	1.248	0.090	13.867
56-61	-0.294	0.027	-10.813	0.295	0.028	10.458	0.192	0.083	2.306	2.067	0.099	20.831
Group membership												
Controls (ref.)	Ref.			Ref.			Ref.			Ref.		
MS baseline	-0.150	0.055	-2.722	0.384	0.046	8.280	0.663	0.240	2.764	2.807	0.403	6.967
9 to 6 years before MS (time 1)	-0.285	0.029	-9.916	0.389	0.028	13.693	0.795	0.106	7.468	2.319	0.179	12.930
5 to 0.1 years before MS (time 2)	-0.301	0.022	-13.818	0.788	0.024	32.629	0.738	0.077	9.645	2.985	0.113	26.348
0 to 4 years after MS (time 3)	-0.806	0.022	-36.555	1.083	0.028	39.087	1.866	0.079	23.646	4.863	0.136	35.763
5 to 8 years after MS (time 4)	-0.547	0.041	-13.189	0.863	0.044	19.678	1.477	0.144	10.237	4.482	0.177	25.332
Year												
1992	0.492	0.044	11.239	-0.634	0.037	-17.125	-2.565	0.251	-10.206	-3.998	0.417	-9.587
1993	0.471	0.040	11.757	-0.684	0.037	-18.583	-1.429	0.157	-9.112	-3.009	0.356	-8.458
1994	0.428	0.038	11.125	-0.522	0.035	-14.774	-1.191	0.147	-8.117	-1.936	0.223	-8.679
1995	0.393	0.036	10.836	-0.459	0.034	-13.350	-0.972	0.137	-7.091	-1.823	0.213	-8.567
1996	0.337	0.034	9.780	-0.452	0.032	-14.221	-1.022	0.127	-8.031	-2.150	0.188	-11.452
1997	0.275	0.034	8.182	-0.352	0.031	-11.314	-0.692	0.113	-6.117	-1.617	0.163	-9.907
1998	0.183	0.033	5.495	-0.325	0.031	-10.502	-0.616	0.110	-5.614	-1.132	0.151	-7.491
1999	0.117	0.032	3.672	-0.173	0.030	-5.797	-0.492	0.112	-4.412	-0.698	0.141	-4.931
2000	0.102	0.031	3.262	0.000	0.030	-0.012	-0.288	0.109	-2.647	-0.654	0.141	-4.651
2001	0.179	0.029	6.091	0.129	0.027	4.705	-0.321	0.105	-3.043	-1.067	0.134	-7.950
2002	0.167	0.029	5.815	0.110	0.028	3.964	-0.132	0.094	-1.404	-0.684	0.118	-5.796
2003	0.095	0.029	3.248	0.197	0.027	7.247	-0.055	0.097	-0.561	-0.518	0.112	-4.618
2004	0.122	0.029	4.146	0.098	0.029	3.421	0.104	0.092	1.132	-0.207	0.105	-1.972
2005	0.102	0.030	3.455	0.200	0.028	7.197	-0.009	0.100	-0.093	0.045	0.099	0.455
2006	0.139	0.029	4.806	0.140	0.028	4.999	0.208	0.096	2.170	-0.107	0.095	-1.131
2007	0.201	0.029	6.838	0.070	0.029	2.383	0.187	0.097	1.920	-0.099	0.098	-1.014
2008	Ref.			Ref.			Ref.			Ref.		
Seasonal dependence												
January	Ref.			Ref.			Ref.			Ref.		
February	0.019	0.025	0.757	-0.176	0.024	-7.383	0.003	0.085	0.039	-0.214	0.093	-2.308
March	0.146	0.025	5.896	-0.162	0.024	-6.793	0.003	0.086	0.033	-0.327	0.096	-3.402
April	0.070	0.026	2.734	-0.206	0.024	-8.535	-0.020	0.087	-0.231	-0.304	0.096	-3.154
May	0.234	0.025	9.445	-0.215	0.024	-9.021	0.112	0.085	1.324	-0.218	0.096	-2.276
June	0.387	0.024	15.835	-0.713	0.027	-26.204	0.264	0.085	3.112	-0.132	0.094	-1.415
July	0.272	0.026	10.401	-0.073	0.023	-3.174	-0.020	0.084	-0.240	-0.289	0.096	-3.025
August	0.019	0.027	0.728	-0.016	0.023	-0.724	0.162	0.082	1.974	-0.222	0.094	-2.353
September	0.025	0.026	0.956	-0.013	0.023	-0.572	0.127	0.084	1.506	-0.010	0.091	-0.114
October	-0.022	0.026	-0.868	0.049	0.023	2.179	0.214	0.084	2.541	0.019	0.090	0.208
November	-0.088	0.026	-3.431	-0.287	0.025	-11.662	0.183	0.083	2.210	-0.150	0.096	-1.569
December	0.157	0.025	6.260	0.048	0.023	2.103	0.007	0.084	0.088	-0.078	0.092	-0.845
Duration dependence from rehabilitation												
1st month	0.424	0.136	3.131							-1.646	0.260	-6.320
2nd month	0.354	0.136	2.611							-1.514	0.250	-6.061
3rd month	0.035	0.141	0.252							-1.130	0.239	-4.721
4th month	-0.071	0.146	-0.488							-1.048	0.240	-4.374
5th month	-0.151	0.147	-1.031							-1.175	0.251	-4.678
6th month	-0.218	0.152	-1.433							-1.046	0.249	-4.207
7th month	-0.159	0.152	-1.044							-0.900	0.244	-3.696
8th month	-0.323	0.162	-1.991							-1.023	0.258	-3.973
9th month	-0.049	0.153	-0.321							-0.871	0.252	-3.453
10th month	-0.002	0.154	-0.010							-0.659	0.244	-2.698
11th month	-0.111	0.159	-0.695							-0.463	0.239	-1.936
12th month	0.145	0.158	0.917							-0.175	0.227	-0.771
1st quarter, 2nd year	-0.066	0.140	-0.468							-0.279	0.200	-1.394
2nd quarter, 2nd year	-0.181	0.146	-1.239							-0.169	0.206	-0.823
3rd quarter, 2nd year	-0.178	0.155	-1.145							0.193	0.207	0.934
4th quarter, 2nd year	0.382	0.147	2.591							0.526	0.212	2.485
3rd year	-0.061	0.141	-0.433							0.305	0.195	1.568
>4 years	Ref.									Ref.		
Duration dependence from sickness absence												
1st month	-1.399	0.029	-47.509				-5.838	0.157	-37.113	-5.553	0.313	-17.762
2nd month	-1.633	0.031	-53.508				-6.015	0.190	-31.726	-6.160	0.464	-13.263
3rd month	-1.913	0.032	-59.160				-5.447	0.163	-33.417	-6.042	0.459	-13.164
4th month	-2.145	0.035	-61.068				-5.321	0.163	-32.627	-5.960	0.464	-12.835
5th month	-2.255	0.037	-60.413				-5.303	0.169	-31.293	-4.885	0.284	-17.215
6th month	-2.343	0.040	-59.107				-5.014	0.158	-31.797	-5.080	0.317	-16.033
7th month	-2.422	0.043	-56.571				-4.957	0.160	-31.068	-5.003	0.316	-15.844
8th month	-2.558	0.047	-54.461				-4.779	0.151	-31.729	-5.436	0.394	-13.809
9th month	-2.607	0.051	-51.302				-4.573	0.145	-31.580	-4.393	0.245	-17.943
10th month	-2.411	0.049	-48.873				-4.202	0.127	-33.023	-3.996	0.210	-19.022
11th month	-1.880	0.044	-42.773				-2.919	0.080	-36.672	-2.525	0.125	-20.219
12th month	Ref.						Ref.			Ref.		

Table13. Model coefficients for FD-Trygd model. Beta-coefficients, standard errors and t-values