

# Improved working ability in a contemporary MS population compared with a historic non-treated MS population in the same geographic area of Sweden

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## Abstract

**Background:** Multiple sclerosis (MS) often causes a reduced ability to work. Improved disease control as well as adjustment of working conditions may improve work ability in MS.

**Objectives:** The objective of this article is to compare the degree of sickness absence in two MS populations that either have or have not received disease-modifying drug (DMD) treatments or active work-promoting measures.

**Methods:** We investigated the occurrence of sickness absence in MS patients living in Västerbotten County, Sweden, in 2013, in which the majority of MS patients receive DMD treatment. The result was compared with a previous survey in the same area during a period when no DMD was available and no work-promoting measures for MS patients were practiced.

**Results:** The proportion of MS patients active in the labor market or studying increased from 38% to 70% in the contemporary compared with the historic population ( $p < 0.001$ ). The proportion of MS patients with a full-time disability pension decreased from 27% to 12% ( $p < 0.001$ ). There was a significant decrease of sickness absence in several individual EDSS grades.

**Conclusions:** Our data indicate that treatment with DMDs combined with active work-promoting measures lead to improved work ability in MS.

**Keywords:** Multiple sclerosis, work ability, disease-modifying treatments, work-promoting measures

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## Background

Multiple sclerosis (MS) typically starts in the age group 20–40 years. At disease onset these individuals are often students or have just started working life. The disease is due to a presumed autoimmune inflammation in the central nervous system (CNS) and may lead to permanent physical and cognitive dysfunction. In 2008 a total of 17,500 people with MS were estimated to live in Sweden.<sup>1</sup>

Several factors affect the work ability in MS: an active disease with ongoing inflammatory activity in the CNS providing an unstable disease difficult to cope with, impaired cognitive and physical abilities, as well as MS-related fatigue.<sup>2</sup> These factors

have different effects on ability to work, depending on type of requirements of the profession and possibility to adapt the working conditions for the individual. In general, the work ability for individuals with MS is reduced to about half compared to the general population.<sup>3</sup> With increased disability, the risk of full-time sickness absence increases significantly.<sup>4</sup> A survey based on the prevalent MS population in Västerbotten in 1997 showed that almost half (45%) of all people with MS in the age group 18–64 years had full-time sickness absence and only a third (34.5%) had no sickness absence at all.<sup>4</sup>

The first-generation disease-modifying drugs (DMDs) were introduced in Sweden during the

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mid-1990s, all reducing the number of clinical relapses by about 30%. In 2006 and 2011, respectively, natalizumab and fingolimod were approved, both offering more efficient control of inflammatory disease activity by reducing the relapse rate by 55%–70% and magnetic resonance imaging (MRI) activity by 80%–90%. Furthermore, since about 2010, rituximab has frequently been used off-label in Västerbotten County as a DMD in MS.

By using potent DMDs, the inflammation and tissue damage is effectively reduced, making the disease more stable and restricting the progression of neurological disability. In addition, we introduced in the mid-1990s a more systematic approach regarding clinical work-oriented team-based measures, and a comprehensive rehabilitation course for individuals with early MS was established in Västerbotten. The aim of the course was to increase knowledge about the disease, DMDs and factors affecting studies and work ability.

The purpose of this study was to compare sickness absence among MS patients prevalent in Västerbotten County on December 31, 1997 and December 31, 2013, respectively. For the latter population DMD had become widely available and work-related rehabilitation measures had been implemented.

## Methods

### Patients

All patients were selected from Västerbotten County, which is situated in the north of Sweden and has 260,000 inhabitants. The prevalence of MS in Västerbotten is similar to that in the rest of Sweden, which is estimated to be about one in 600.<sup>1,5</sup> In order to perform a statistically valid comparison between two populations in the same geographic area of Västerbotten County, we defined two populations that did not overlap regarding participating individuals.

1. We retrieved original data from a previous survey of sickness absence in Västerbotten analyzing the occurrence of sick leave in the prevalent MS population 1997.<sup>4</sup> These data included information on disease onset, defined as the first symptom of MS, and all patients with onset January 1, 1982 through December 31, 1997 (16 years) defined this historical MS population. The 190 patients enrolled were virtually unexposed to DMDs.

2. A new survey of work ability was performed on the prevalent MS population December 31, 2013 in Västerbotten during April–June 2014. Patients with an onset date between January 1, 1998 through December 31, 2013 (16 years) defined the contemporary MS population.

The contemporary MS population was identified through a national MS register, the Swedish MS Register (SMSreg). This population included people with MS that were aged 18–64 years by December 31, 2013, registered in the SMSreg and residents of Västerbotten at the time of the survey ( $n = 416$ ). According to a recently performed study, approximately 90% of all patients in Västerbotten are registered in the SMSreg.<sup>6</sup> Of the 233 patients enrolled, 74% were treated with rituximab, 6% with natalizumab, 2% with alemtuzumab, 2% with interferons or glatiramer acetate and 1% with fingolimod by the time of the survey. Fifteen percent had no DMD treatment. Patients in the contemporary group were offered to participate in a comprehensive rehabilitation course, developed and implemented in the Västerbotten County. This course equips patients with work-promoting tools and is not practiced in a more general sense throughout the country. In total 70% of the patients in the contemporary cohort participated in the course. The demographics of the patients are described in Table 1.

### Data collection

Demographic data regarding age, gender and disease severity at the date of December 31, 2013, were collected from the SMSreg. Data on profession, degree of employment, number of hours worked per week and sickness absence were collected by the Work Ability Questionnaire-Multiple Sclerosis (WAQ-MS<sup>®</sup>, Anne Wickström 2012).<sup>7,8</sup> Patients received the questionnaire in the form of a postal questionnaire or an online survey during the period May 23 to June 30, 2014. During this period, two reminders were sent out if necessary. Supplementary inquiries by phone were performed in the case of missing or ambiguous responses.

The WAQ-MS questionnaire was primarily developed in Swedish and pretested in a pilot study and found to have high face validity and test-retest reliability. WAQ-MS has since been used in three published studies.<sup>7–9</sup> The content validity test of WAQ-MS was further evaluated by experts and lay experts to ensure that each item in the questionnaire reflected a complete range of attributes describing the concept of working ability in MS.<sup>10,11</sup> Using the content validity index (CVI), each expert

**Table 1.** Demographics for the two investigated populations 1997 and 2013 in Västerbotten, Sweden.

	1997 population	2013 population	<i>p</i> value
Identified patients (n)	202	240	
Number of respondents	190	233	
Gender, female; <i>n</i> (%)	121 (64)	161 (69)	0.284 <sup>a</sup>
<b>Age (years)</b>			
Mean (SD)	40 (9.5)	41 (11.5)	0.689
Median (IQR)	39 (33.75–47.00)	39 (31–50)	
18–34 <i>n</i> (%)	53 (28)	78 (33)	
35–44 <i>n</i> (%)	74 (39)	61 (26)	
45–54 <i>n</i> (%)	47 (25)	58 (24)	
55–64 <i>n</i> (%)	16 (8)	36 (15)	
<b>Disease duration (years)</b>			
Mean (SD)	7 (4.5)	7 (4.4)	0.991
Median (IQR)	7 (4.00–11.75)	7 (4–11)	
0–5 <i>n</i> (%)	73 (38)	86 (37)	
6–10 <i>n</i> (%)	59 (31)	81 (33)	
11–16 <i>n</i> (%)	58 (31)	66 (28)	
<b>EDSS</b>			
Median (IQR)	2.5 (1.5–5.0)	2.0 (1.0–3.0)	<0.001 <sup>b</sup>
0; <i>n</i> (%)	8 (4)	52 (22)	
1–1.5 <i>n</i> (%)	49 (26)	58 (25)	
2–2.5 <i>n</i> (%)	43 (23)	51 (22)	
3–3.5 <i>n</i> (%)	29 (15)	37 (16)	
4–5.5 <i>n</i> (%)	20 (11)	14 (6)	
6–6.5 <i>n</i> (%)	20 (11)	17 (7)	
7–9.5 <i>n</i> (%)	21 (11)	4 (2)	

Shown are numbers (*n*) with %, mean with standard deviation (SD) and median with interquartile range (IQR).  
<sup>a</sup>Pearson's Chi-squared test with Yates' continuity correction. <sup>b</sup>Wilcoxon rank sum test with continuity correction.  
EDSS: Expanded Disability Status Scale.

independently rated the relevance of each item in the WAQ-MS in four steps from not relevant to very relevant and not clear to very clear. A score of 0.80 or better indicates good content validity according to McGartland Rubio et al.<sup>11</sup> The CVI for the WAQ-MS was 0.97.

Clinical data for the historic MS population were derived from neurological examination and medical records, whereas degree of employment was retrieved from follow-up interviews. In order to compare the received data from WAQ-MS with the data of the previous study of work ability (using structural interviews) in Västerbotten,<sup>4</sup> the vocational status in the present survey was categorized in the same way as follows: i) *no sickness absence*, including full- and part-time employees, students, unemployed and individuals on parental leave, ii) *part-time sickness absence*, including partial short-term sickness benefit and partial disability pension, and iii) *full-time*

*sickness absence*, including full short-term sickness benefit and full disability pension. The data from the previous survey of working ability in Västerbotten were retrieved and used for comparison with the present data.<sup>4</sup> In this study disability pension includes activity compensation (long-term sickness compensation age 18–29 years), temporary disability pension (compensation form in 1997) and disability pension. All these types of benefit, including sickness benefit, are payable at full, three-quarters, half or one-quarter benefit rates, depending on the extent of the reduction of work ability.

The study was approved by the ethics review board at Umeå University.

#### Statistics

For statistical analyses, the program R was used. Differences in disease-related baseline characteristics between the two populations in 1997 and 2013

were analyzed with independent samples *t* test for parametric variables and with Pearson Chi-square and Wilcoxon rank sum test for the non-parametric variables. Changes of outcome variables: no sickness absence, part-time sickness absence and full-time sickness absence between the populations 1997 and 2013, were analyzed by Pearson's Chi-squared test with Yates' continuity correction or Fisher's exact test for count data. An  $\alpha$ -level of 0.05 was selected for determining statistical significance.

## Results

### *Patient identification*

We identified 416 patients with MS living in Västerbotten County as of December 31, 2013. Of these, 176 were excluded because onset of the disease was before 1998. Of the remaining 240 patients, five were excluded because of withdrawn consent and two gave no response. Thus 96% ( $n=233$ ) of the target population was enrolled in the study (Table 1).

From the prevalence population of December 31, 1997<sup>5</sup> containing 399 patients, 197 were excluded because of onset before 1982. From the remaining 202 patients, 12 were excluded because of incomplete data, leaving 190 patients enrolled in this study (Table 1).

The two populations did not differ significantly regarding basic demographic features but there was a significant difference regarding Expanded Disability Status Scale (EDSS) distribution (Table 1).

The proportion of patients with full-time disability pension decreased from 27% to 12% from 1997 to 2013 (Figure 1(a)). The proportion of people who worked, studied or were unemployed without any kind of sickness absence increased from 38% to 70% ( $p < 0.001$ ) from 1997 to 2013 and the proportion of patients with full-time sickness absence decreased from 39% to 13% ( $p < 0.001$ ; Figure 1(b)).

### *The distribution of different disease courses and sickness absence changed between 1997 and 2013*

There was a significant difference in the distribution of the disease courses relapsing–remitting (RR), secondary progressive (SP) and primary progressive (PP) MS between the 1997 and 2013 populations ( $p < 0.001$ ; Figure 2(a)). In particular, the proportion of patients in the RRMS phase increased from 60% in the 1997 cohort to 82% in the 2013 cohort. Within the RRMS and SPMS populations the sickness

absence decreased significantly from 1997 to 2013 while there was no significant change in sickness absence within the PPMS group (Figure 2(b)).

### *Sickness absence in relation to age, disease duration and sex*

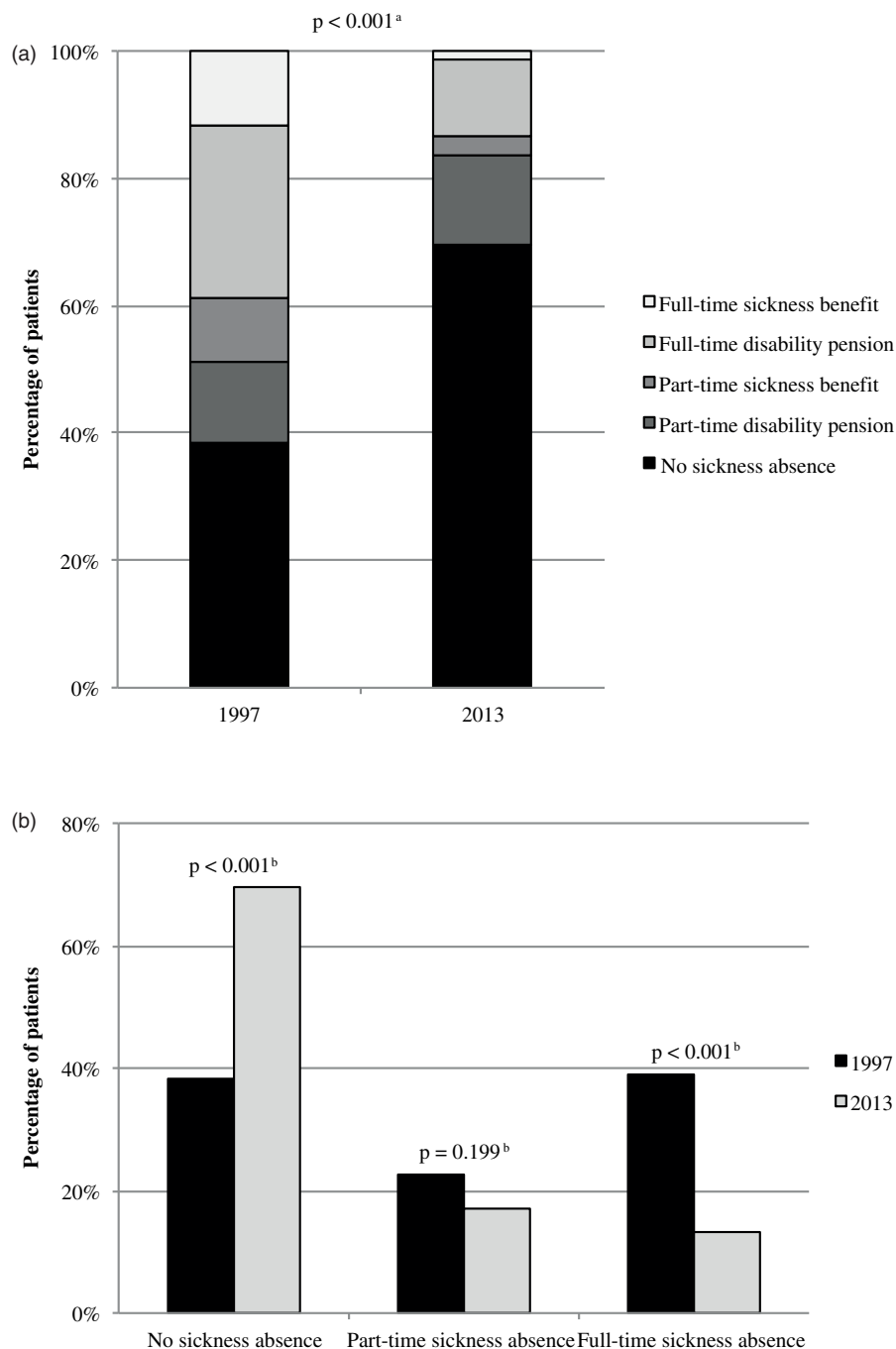
We also analyzed the degree of sickness absence as a factor of age, disease duration and sex (Figure 3). Focusing on full-time sickness absence, either short- or long-term, it could be seen that only 5% of the patients aged 18–34 years in the 2013 population had full-time sickness absence compared with 40% in the 1997 population ( $p < 0.001$ ). Likewise, the proportion of patients aged 45–54 years with full-time sickness absence were 16% in the 2013 population compared with 47% in the 1997 population ( $p < 0.001$ ). Similarly, 8% of patients in the 2013 population with disease duration of 0–5 years had full-time sickness absence while the corresponding value for the 1997 population was 30% ( $p < 0.001$ ). Even in the group of patients with disease duration 6–10 years this proportion was changed from 49% in the 1997 population to 10% in the 2013 population ( $p < 0.001$ ). Men and women both showed lower sickness absence in the 2013 population compared to the 1997 population.

### *The change of sickness absence in different EDSS levels*

EDSS changed from a median (interquartile range (IQR)) of 2.5 (1.5–5.0) points in the 1997 population to 2.0 (1.0–3.0) points in the 2013 population ( $p < 0.001$ ), affecting all age groups (Table 1). Within several EDSS groups, the proportion of full-time sickness absence was lower in 2013 than in 1997 (Figure 4). Full-time sickness absence decreased between 1997 and 2013 in the EDSS group 2–2.5 from 26% to 6% ( $p = 0.009$ ), in the EDSS group 3–3.5 from 38% to 16% ( $p = 0.045$ ), and in the EDSS group 6–6.5 from 85% to 47% ( $p = 0.032$ ). There was no reduction of the proportion of full-time sickness absence in the EDSS group 4–5.5 between the two populations. In the highest EDSS group 7–9.5, the number of patients was too small for reliable statistical calculation.

## Discussion

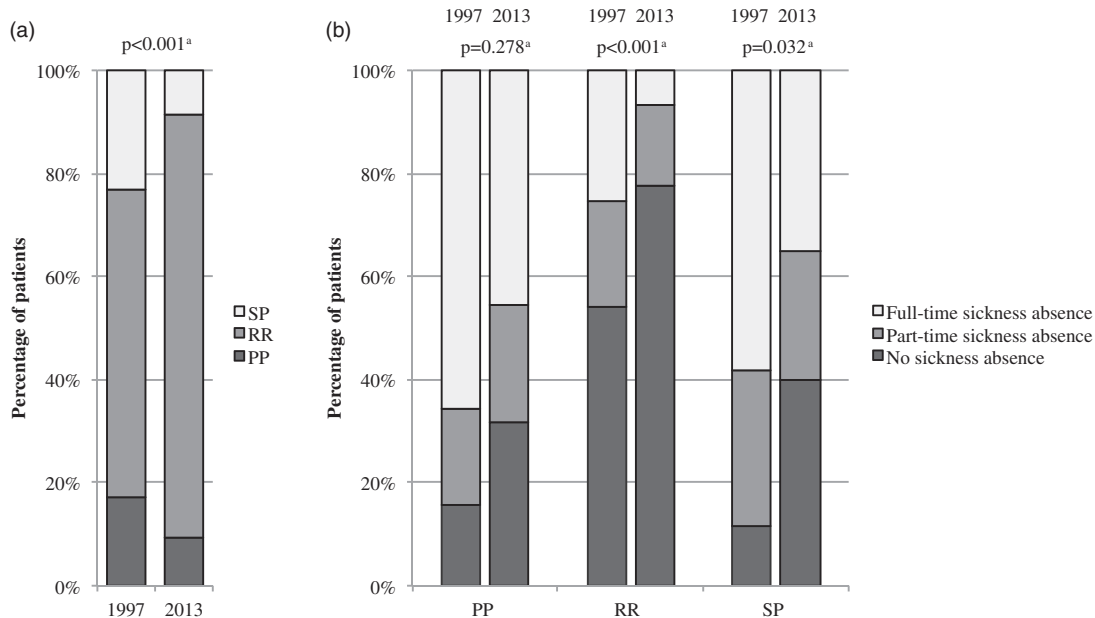
In this study, we have shown that sickness absence was significantly reduced for people with MS who lived in Västerbotten County in 2013 compared with 1997. In our investigated populations, 87% were able to study or work full or part time in 2013 compared with 61% in 1997. The study is of interest since it compares one untreated MS



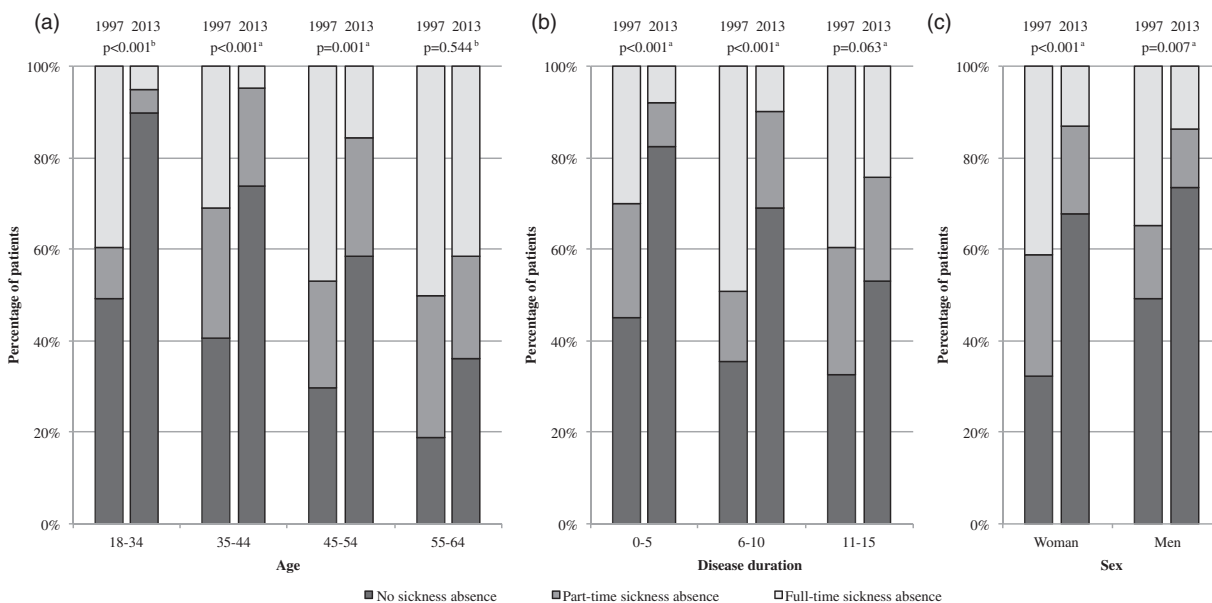
**Figure 1.** A comparison between people with multiple sclerosis (MS) in Västerbotten County in the years 1997 and 2013 with a disease onset 1982–1997 and 1998–2013, respectively. The proportions of different degree of sickness benefit and disability pension are presented in panel (a). The size of the various fields reflects the percentage distribution. In panel (b), the proportions of patients with no sickness absence, part-time sickness absence and full-time sickness absence in 1997 and 2013 are presented. <sup>a</sup>Fisher’s exact test for count data. <sup>b</sup>Pearson’s Chi-squared test with Yates’ continuity correction.

population with a population that underwent an active treatment strategy with systematic initiation of immunomodulatory treatment in the early stages of all patients with RRMS. Furthermore, both the

investigated populations have been surveyed in the same geographic area with similar demographic characteristics at both time points, which increase the validity of the results.

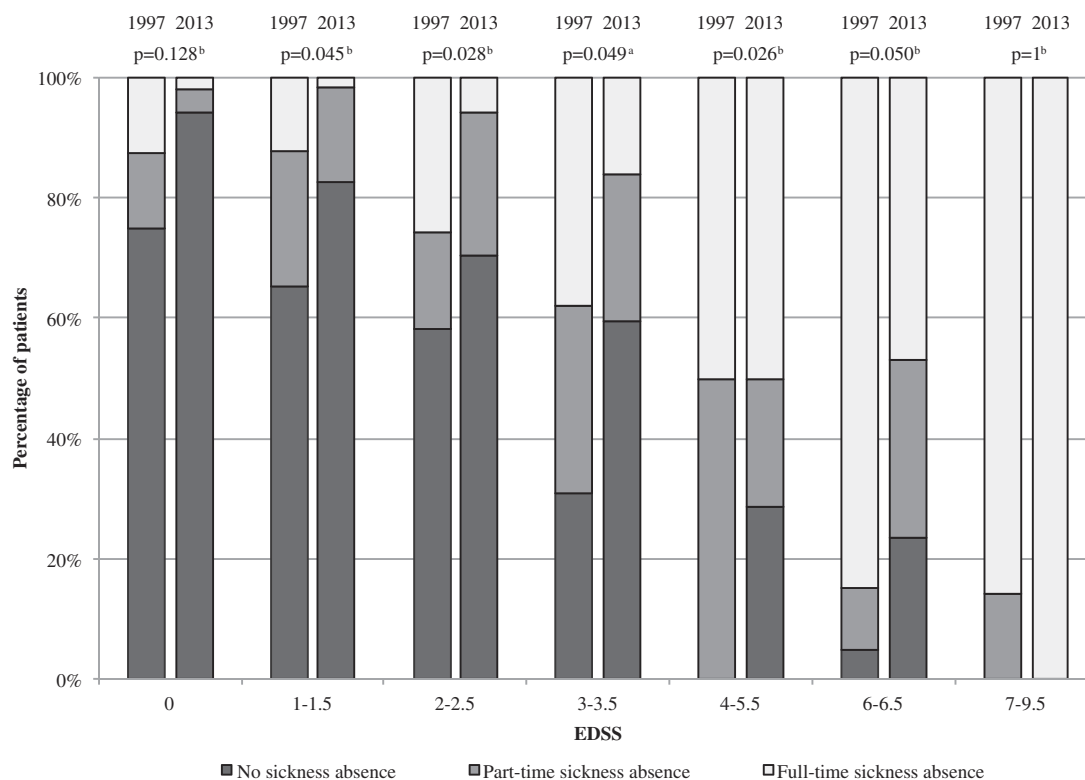


**Figure 2.** Both the disease course and the sickness absence in relation to disease course differed between 1997 and 2013. The distribution between the different clinical courses of MS, e.g. primary progressive (PP), relapsing–remitting (RR), and secondary progressive (SP), differed significantly between the two occasions (a). Most notably, patients remained in RR to a higher degree in 2013 compared with 1997. RR and SP patients could work to a higher extent in 2013 compared with 1997. <sup>a</sup>Pearson’s Chi-squared test with Yates’ continuity correction. In the 1997 population four patients were excluded because of missing data.



**Figure 3.** A comparison between people with multiple sclerosis (MS) in Västerbotten County in the years 1997 and 2013 regarding the degree of sickness absence within different groups of age (a), disease duration (b) and sex (c). Sickness absence decreased most in the age group 18–34 years and among those who had a disease duration 0–5 and 6–10 years. The degree of sickness absence improved for women and men and was equal between the genders in 2013. <sup>a</sup>Pearson’s Chi-squared test with Yates’ continuity correction. <sup>b</sup>Fisher’s exact test for count data.





**Figure 4.** A comparison regarding degree of sickness absence between people with multiple sclerosis (MS) in Västerbotten County in the year 1997 and 2013 in relation to different Expanded Disability Status Scale (EDSS) groups. Within the EDSS groups 1–6.5 the level of sickness absence decreased in 2013 compared with 1997. <sup>a</sup>Pearson’s Chi-squared test with Yates’ continuity correction. <sup>b</sup>Fisher’s exact test for count data.

Data on employment were collected through WAQ-MS questionnaires in the contemporary cohort and through follow-up interviews in the historical cohort. Even though these data were retrieved through different methods, they were for both cohorts self-reported and therefore judged comparable. It is important to note that our data do not describe the work ability among all MS patients at the indicated time points, such as in cross-sectional prevalence analyses, and are therefore it is not possible to compare with data from other studies. A direct comparison between the two 1997 and 2013 prevalence populations would have resulted in a large overlap of the two populations. We therefore created two incidence cohorts that were truncated at the prevalence days and not overlapping. In this way two independent populations were established that allowed statistical comparisons. By doing this, no patient had a disease duration more than 16 years and mean disease duration was approximately eight years in each population, which explains the apparently high work ability in the two groups. The advantage of this methodology is that we could perform

valid statistical comparisons between the groups, but the drawback is that our figures do not match the proportions that reflect the general MS population.

DMDs have been available from 1995 in Sweden but during the first 5–10 years the prescription of these drugs was quite restrictive, reserving treatment for patients with a high clinical disease activity of at least two exacerbations the previous two years. A more widespread use of DMDs in the early stage of the disease, e.g. after the first clinical episode, was not practiced regularly in Västerbotten until around 2002–2004. From clinical experience, however, it was not until natalizumab was introduced in 2006 that work ability appeared to improve more profoundly.<sup>7,8</sup> Apart from a more prominent effect on the inflammatory activity, fewer side effects and a positive effect on MS-related fatigue may have contributed to this observation.<sup>12,13</sup> The treatment strategy in Västerbotten has the goal of eradicating all inflammatory activity from the onset of the disease, which has led to a frequent use of the second-generation

immunomodulatory agents. The majority of RRMS patients in Västerbotten in 2013 were treated with the monoclonal antibody rituximab.

From the subgroup analyses we could see that the most prominent reduction of sickness absence was seen among younger individuals with short disease duration. In fact, as much as 88% in the youngest age group (18–34 years) had no sickness absence at all in the 2013 population compared with 54% in the 1997 population. However, for the other older age groups a similar reduction of sickness absence was seen although it subsided when reaching the oldest age groups.

The proportion of patients with RRMS disease course increased and overall sickness absence decreased within the RRMS group from 1997 to 2013. This points toward a positive effect from early effective treatment combined with early work-promoting interventions on work ability in MS. Besides being an effect of early treatment, the results may also be influenced by the change of diagnostic criteria. In the study population from 1997 the Poser criteria was used but in the study population from 2013 the use of McDonald criteria made an earlier diagnosis possible. The new diagnostic criteria may have contributed to lower EDSS scores in the contemporary cohort since they allow a shorter time to MS diagnosis and facilitate diagnosis in cases with minor symptoms and presumed benign disease course. The disease duration was, however, the same in both cohorts. Importantly, working ability was increased in all EDSS categories in the contemporary cohort, thus pointing toward other explanatory factors such as early DMD treatment and work-promoting rehabilitation measures.

EDSS was once again shown to be one of the main predictors for reduced work ability: The higher the EDSS score, the less likelihood for retained work ability.<sup>4</sup> There was an obvious impact of decreased EDSS scores in the contemporary population on the reduction of sickness absence in the groups of younger patients (18–34 years) and patients with short disease duration (0–5 years). However, there were still differences in work ability within several EDSS groups when comparing the 2013 and 1997 populations. At an EDSS score of 0 a low level of sickness absence was seen both in the 1997 and 2013 populations without a significant difference. At EDSS score levels 2–6.5 an increased proportion of patients with no sickness absence and sickness absence at part-time were seen in the 2013 population, indicating that it is possible to adapt the work

situation for people at median EDSS score levels so they can study or work to a higher degree. This emphasizes that, besides slowing the underlying disease process to maintain as low an EDSS score as possible, systematic work-promoting interventions may further improve work ability. Even for patients with lower EDSS scores, work ability may not be sufficient in relation to requirements, and different vocational rehabilitation interventions then probably play an important role in preserving work ability.

Specific rehabilitation measures most likely play a role in work ability. In the mid-1990s a comprehensive rehabilitation course for people with early MS was established in Västerbotten County. The course aims to equip patients with tools to influence their own work and study situation. In a recently published qualitative study, MS patients' understanding of their own symptoms in relation to the requirements of their employment were important for their rehabilitation back to work,<sup>14</sup> which is in line with our observations.

In conclusion, we found that more people with MS are at work today compared to the era when DMDs were not available. Our results indicate that patients in the early inflammatory phase of the disease may retain their work ability several years after disease onset if they are subjected to effective anti-inflammatory treatment regimens from disease onset. Furthermore, work ability may be additionally improved by systematic work-promoting interventions aiming at retaining work ability at the highest possible level. It is obvious that these results have implications for society both in terms of positive economic effects and improved quality of life from increased work-life participation. Long-term follow-up of our data is required to determine whether these positive effects are durable over longer time periods.

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### **Conflicts of interest**

Anne Wickström has received research support and travel grants from Biogen Idec AB.



Peter Sundström has served on a scientific advisory board for Novartis and has received travel support from Novartis and Biogen Idec.

Lucas Wickström has nothing to declare.

Charlotte Dahle has received an unrestricted research grant from Biogen Idec AB and Novartis and lecture honoraria from Biogen Idec and Merck Serono.

Magnus Vrethem has received an unrestricted research grant from Biogen Idec AB and Novartis and lecture honoraria from Biogen Idec and Merck Serono.

Anders Svenningsson has served on advisory board for Sanofi-Genzyme and has received travel funding and/or speaker honoraria from Biogen Idec, Sanofi-Genzyme, Novartis and Baxter Medical.

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