

Work Disability in Newly Diagnosed Patients with Primary Sjögren Syndrome

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ABSTRACT. Objective. To study longterm work disability and possible predictors in newly diagnosed patients with primary Sjögren syndrome (pSS).

Methods. Because we wanted to include only patients with full work availability potential, eligible patients were aged 18-62 years. Fifty-one patients (mean age 46 yrs, range 18-61 yrs, 50 women) diagnosed with pSS between January 2001 and December 2012 were included in the study. For each patient we randomly selected 4 reference subjects from the general population and matched for age, sex, and area of residence. We linked data to the Swedish Social Insurance Agency and calculated the proportion as well as net days of work disability in 30-day intervals from 12 months before pSS diagnosis until 24 months after.

Results. Work disability was increased in patients with pSS in comparison to general population comparators. At diagnosis, 26% of patients were work-disabled, while 37% and 41% were disabled at 12 and 24 months after diagnosis, respectively ($p < 0.05$ and $p < 0.05$ vs baseline). Prior work disability status at diagnosis (OR 15.4, 95% CI 2.9–81.9; $p = 0.001$), concomitant fibromyalgia (OR 10.5, 95% CI 2.0–56.0; $p = 0.006$), and each additional year of age (OR 1.1, 95% CI 1.0–1.2; $p = 0.009$) were found to be associated with work disability 24 months after diagnosis.

Conclusion. Patients with pSS showed an increased work disability, in comparison with the general population, which increased significantly during the first 2 years after diagnosis. Work disability at diagnosis, concomitant fibromyalgia, and increasing age, but not anti-SSA/anti-SSB antibodies or disease activity, were associated with longterm work disability. (J Rheumatol First Release November 15 2016; doi:10.3899/jrheum.160932)

Key Indexing Terms:

PRIMARY SJÖGREN SYNDROME

WORK DISABILITY

Primary Sjögren syndrome (pSS) is a systemic autoimmune disease, characterized by lymphocytic infiltration of the exocrine glands resulting in exocrine hypofunction and sicca symptoms. Non-exocrine organs are also frequently affected, resulting in various extraglandular manifestations such as arthritis, pulmonary involvement, and neuropathy^{1,2}. Further, widespread pain^{3,4,5}, fatigue^{6,7}, and depression⁸ are all

commonly encountered in patients with pSS, are often more troublesome than the sicca symptoms^{9,10}, and have a substantial effect on health-related quality of life (HRQOL)^{8,10,11,12,13,14}. As previously shown, the disease burden in pSS results in increased direct healthcare costs, due to increased visits to various healthcare professionals and increased healthcare use¹⁵. It is poorly studied to what degree impairment of HRQOL contributes to reduced work ability and sick leave in pSS and thus indirect healthcare costs. Previous studies have reported an increased work disability in pSS^{9,16,17}, which was found to be associated to concomitant fatigue and depression⁹. However, the assessment of work disability in those studies relied on self-reported data and was assessed in prevalent patients with variable disease durations^{9,16}. The aim of this longitudinal population-based study was therefore to assess work disability, i.e., the extent of sick leave and receipt of a disability pension before and after having been diagnosed with pSS according to the American-European Classification Group (AECG) criteria¹⁸. Moreover, we wanted to study predictors of work disability in patients with pSS.

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MATERIALS AND METHODS

Patients. The Malmö Sjögren's Syndrome Register (MSSR) has been regis-

tering consecutive patients diagnosed with pSS at the Department of Rheumatology, Skåne University Hospital Malmö, Sweden, since 1984. Since 2002 only patients fulfilling the AECG criteria¹⁸ have been included. Patients included before 2002 have been assessed retrospectively and classified according to the AECG criteria. In the MSSR, data were recorded on objective ophthalmologic, oral, laboratory, and serological tests performed when diagnosing pSS. The European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI)¹ scores at diagnosis were retrospectively assessed and data on comorbidities including concomitant diagnosis of fibromyalgia (FM) evaluated by scrutinizing the patients' medical records. From the MSSR, eligible patients for this study were identified. Because we wanted to include only patients with full work availability potential during the observation period, eligible patients were aged 18-62 years. None of the included patients retired during the observation period. All patients were diagnosed with pSS according to the AECG criteria between January 2001 and December 2012, allowing for 3 years of followup, ranging from 12 months before to 24 months after pSS diagnosis. The pSS diagnosis date was defined as the date of first fulfillment of the AECG criteria¹⁸. Also, only patients with pSS living within the Skåne county in Southern Sweden were included. Seventy-seven consecutive patients with pSS were identified from the MSSR, of whom 9 were living outside the catchment area. Thus, 68 were asked by mail if they would like to participate in the study; if they agreed, a consent form was filled out and sent back to the corresponding author. Seventeen declined participation in the study, while 51 patients gave written informed consent and were included, resulting in a response rate of 75%. The 51 included patients did not significantly differ from the excluded patients with regard to age, presence of sicca symptoms, anti-SSA and anti-SSB antibody seropositivity, ESSDAI total score, or presence of concomitant FM (data not shown). Further characteristics of the patients with pSS are shown in Table 1.

General population comparators. Using the Swedish population register, which includes data on date of birth, sex, and residential address of all

Table 1. Demographic and clinical characteristics of newly diagnosed patients with primary Sjögren syndrome included in the study. Results are presented as mean ± SD or percentage, with abnormal findings in tested subjects. Ocular variables are presented as the sum of both eyes.

Characteristics	Patients, n = 51
Age, yrs	45.6 ± 11.3
Sex, males/females	1/50
Duration of symptoms at diagnosis, yrs	3 ± 3
Schirmer-I test, mm/5 min	11 ± 15
van Bijsterveld's score	8 ± 5
Unstimulated whole sialometry, ml/15 min	0.8 ± 1.0
Anti-SSA antibody seropositives	80%
Anti-SSB antibody seropositives	53%
ANA seropositives	78%
RF seropositives	61%
IgG, g/l	18.0 ± 7.87
IgA, g/l	2.69 ± 1.28
IgM, g/l	1.38 ± 0.88
C3, g/l	1.13 ± 0.29
C4, g/l	0.22 ± 0.09
ESR, mm/h	26 ± 22
CRP, g/l	3.1 ± 2.5
Lip biopsy – focus score ≥ 1	93%
ESSDAI total score at diagnosis	5 ± 5
Concomitant fibromyalgia	22%

ANA: antinuclear antibody; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index.

Swedish residents, we randomly selected 4 subjects for each patient with pSS, matched for age, sex, area of residence, and months of study inclusion. The comparator subjects represent the general population in our study.

Data sources. The study was based on clinical data from the MSSR and the patients' medical records. Information on sick leave and disability pension was independently retrieved from the Swedish Social Insurance Agency (SSIA). The SSIA provides financial protection for subjects of working age affected by illness or injury and covers everyone who lives and works in Sweden, regardless of employment status. We defined sick leave as days with sick pay or sickness benefit of any degree paid by the SSIA. All sick leave exceeding 14 days is continuously and prospectively registered by the SSIA. Sick pay for shorter periods of work disability, i.e. up to 14 days, is paid by the employer and was therefore not included in this study. A disability pension is defined as a permanent social benefit paid by the SSIA. All kinds of work disability for both patients with pSS and the background population, irrespective of the cause, were included. After crosslinking data from the MSSR with data from SSIA, we calculated the proportions of sick leave, disability pension, and overall work disability in 30-day periods from 12 months before until 24 months after pSS diagnosis. The proportions of sick leave, disability pension, and overall work disability in the general population were also assessed. Work disability status was defined as the prevalence of any degree (binary) of sick leave and disability pension for periods of 30 days, i.e., for each month, for patients with pSS and the general population during the 12-month period before and the 24-month period after diagnosis. In Sweden people can work part-time (25%, 50%, or 75%) and receive sick pay or disability pension for the other part. Therefore, the net amount of time (no. days out of 30-day periods) the patients with pSS and the matched general population were work-disabled during the observed period was also calculated. The results with regard to sick leave and disability pension in patients with pSS were compared with corresponding data for the matched comparators drawn from the Swedish population registry. Predictors of work disability status at 24 months after pSS diagnosis (yes/no) were studied using univariate binary logistic regression modeling in which covariates entered were seropositivity for anti-SSA and anti-SSB antibodies, concomitant FM, work disability at the time of pSS diagnosis, as well as patients with low (≤ 4) vs moderate or high (> 4) disease activity as assessed by the ESSDAI total score¹⁹. The study was conducted in accordance with the STROBE statement and according to a prespecified protocol, available and published as open access at the Web site of the Parker Institute (www.parkerinst.dk).

Statistics. Results were presented as mean ± SD. When comparing groups, the Mann-Whitney U test was used for continuous and the chi-squared test or Fisher's exact test for discrete variables. When comparing paired continuous variables, the Wilcoxon rank sum test was used. McNemar's test was used to compare the average proportion of patients with pSS having work disability at diagnosis with the proportions 12 and 24 months after diagnosis. The relative risk of being on sick leave and disability pension compared with the general population including the 95% CI was calculated using crude proportions. Predictors of work disability status 24 months after diagnosis were studied using univariate binary logistic regression modeling. Owing to the limited size of the study, multivariate binary logistic regression modeling could not be performed. P values < 0.05 were considered significant.

Ethics. The study was approved by the local ethics board at Lund University (LU2015/310). All participants gave written informed consent according to the Declaration of Helsinki.

RESULTS

Figure 1 shows the prevalence of any degree of sick leave and disability pension for periods of 30 days for patients with pSS and the general population during the 12-month period before and the 24-month period after pSS diagnosis. At diagnosis, 26% of patients with pSS were work-disabled (10% on sick leave and 16% receiving a disability pension).

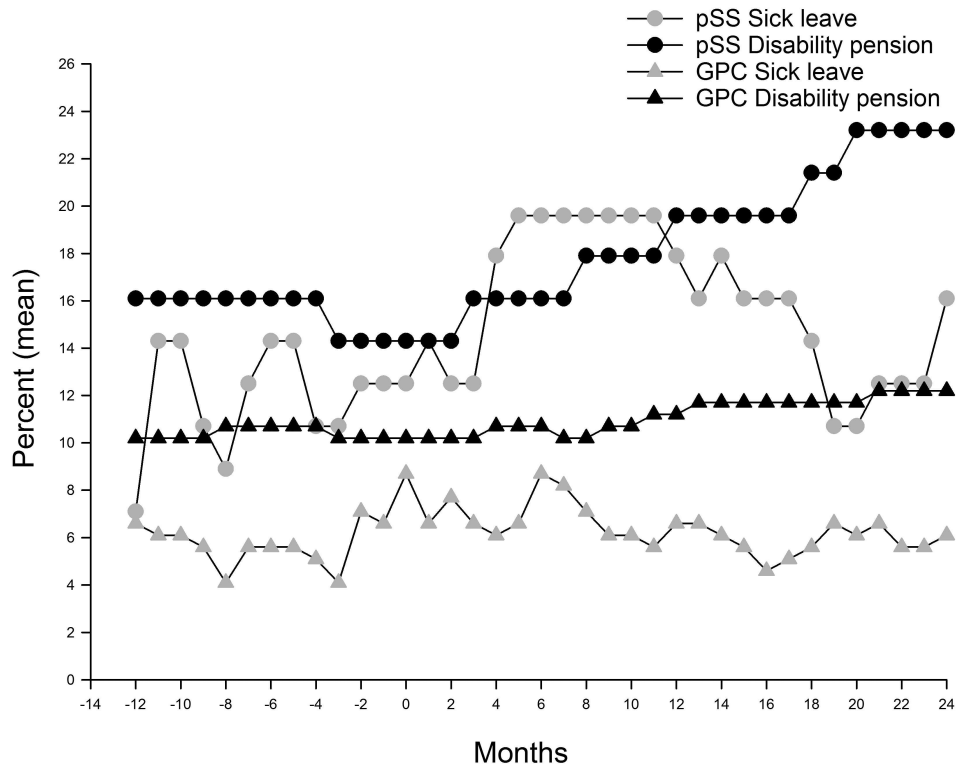


Figure 1. The prevalence of any degree of sick leave and disability pension, for periods of 30 days for patients with primary Sjögren syndrome (pSS) and the general population comparators (GPC) during the 1-year period before and 2 years after pSS diagnosis.

Work disability then significantly increased to 37% (16% on sick leave and 22% receiving a disability pension) at 12 months ($p < 0.05$) and 41% (16% on sick leave and 26% receiving a disability pension) at 24 months ($p < 0.05$) after diagnosis. The increase in work disability was initially due to an increase in sick leave and subsequently by an increase in disability pension. Work disability was significantly increased in patients with pSS with concomitant FM at pSS diagnosis, compared to patients without (73% vs 13%; $p < 0.001$). Work disability was also increased in patients with pSS with concomitant FM at 12 months (82% vs 25%; $p < 0.01$) and 24 months after diagnosis (82% vs 30%; $p < 0.01$). Comparing patients with pSS with the general population, the relative risks of being work disabled at pSS diagnosis as well as at 12 and 24 months after diagnosis were 1.30 (95% CI 0.74–2.28), 1.47 (95% CI 0.83–2.61), and 2.10 (95% CI 1.34–3.30), respectively (Table 2).

In absolute numbers, patients with pSS were work-disabled on average 6.2 days (2.1 days sick leave and 4.1 days disability pension) out of 30 days at diagnosis. During followup, the average number of days out of 30 days that the patients with pSS were work-disabled increased to 9.2 (3.3 days sick leave and 5.9 days disability pension) at 12 months after diagnosis ($p < 0.01$ at diagnosis) and to 10.2 (3.1 days sick leave and 7.1 days disability pension) at 24 months after diagnosis ($p < 0.05$ at diagnosis). Figure 2

Table 2. Relative risk of being on sick leave, receiving disability pension, and overall work disability, in patients with primary Sjögren syndrome (pSS) versus the background population at diagnosis of pSS, as well as 12 and 24 months after pSS diagnosis. Results are presented as crude proportions and 95% CI.

	Relative Risk	95% CI
Sick leave at pSS diagnosis	1.44	0.63–3.30
Sick leave at 12 mos	2.73	1.27–5.90
Sick leave at 24 mos	2.67	1.18–6.00
Disability pension at pSS diagnosis	1.40	0.65–3.00
Disability pension at 12 mos	1.75	0.90–3.39
Disability pension at 24 mos	1.90	1.03–3.48
Work disability at pSS diagnosis	1.30	0.74–2.28
Work disability at 12 mos	1.47	0.83–2.61
Work disability at 24 mos	2.10	1.34–3.30

shows the net amount of time (no. days out of 30-day periods) that the patients with pSS and the matched general population were on sick leave and receiving disability pension.

To search for predictors of longterm work disability, a univariate binary logistic regression model was computed based on any degree of work disability (sick leave or disability pension yes/no) 24 months after pSS diagnosis. Prior work disability status (yes/no) at pSS diagnosis (baseline) was found to be a strong predictor of work disability 24 months after pSS diagnosis, with an OR of 15.4

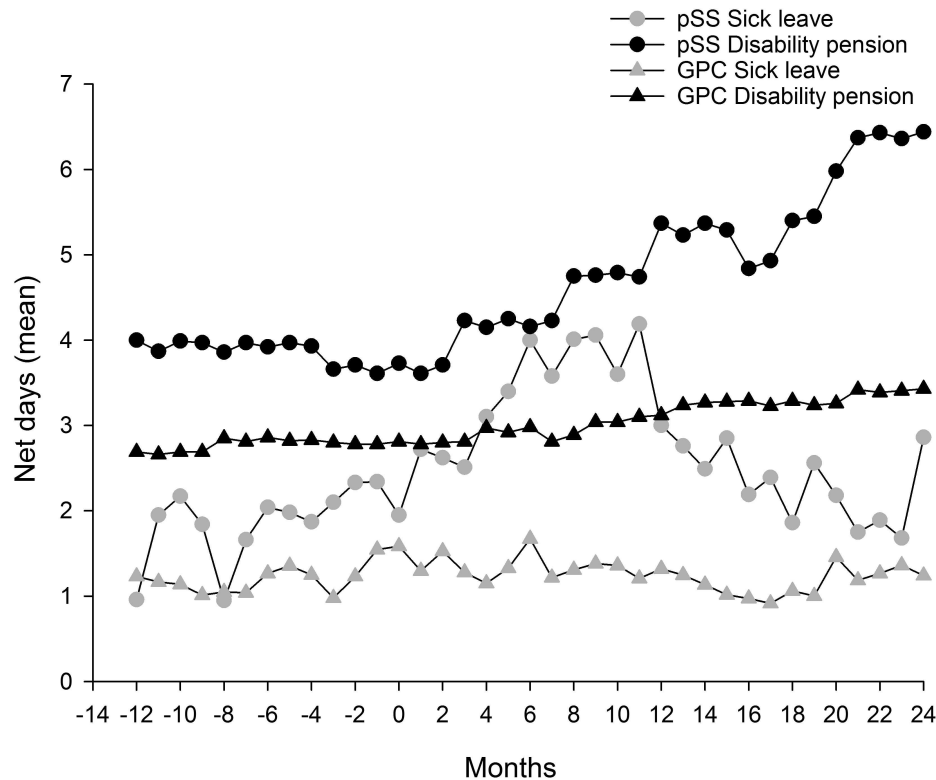


Figure 2. The net amount of time (no. days out of 30-day periods) that the patients with primary Sjögren syndrome (pSS) and the general population comparators (GPC) were on sick leave and receiving disability pensions during the 1-year period before and 2 years after pSS diagnosis.

(95% CI 2.9–81.9; $p = 0.001$). Also, concomitant FM (OR 10.5, 95% CI 2.0–56.0; $p = 0.006$) and each additional year of age at diagnosis (OR 1.1, 95% CI 1.0–1.2; $p = 0.009$) were associated with work disability 24 months after pSS diagnosis. In contrast, seropositivity for anti-SSA and anti-SSB antibodies, and disease activity as assessed by the ESSDAI total score¹⁹, were not associated with work disability 24 months after diagnosis (Table 3).

DISCUSSION

In our present study, patients with pSS showed increased work disability in comparison with the general population. Work disability in patients with pSS increased significantly from baseline during 2 years of followup after diagnosis, initially by an increase in sick leave and subsequently by an increase in disability pension. Work disability at diagnosis, concomitant FM, and increasing age were found to be predictors of longterm work disability, while disease activity and serological markers of the disease were not.

Sicca symptoms, classically affecting eyes and mouth, characterize pSS. Also, extraglandular disease, affecting joints, lungs, and peripheral nerves, is found in a substantial fraction of patients². In addition to the classic sicca and extraglandular symptoms of the disease, fatigue^{6,7}, depression⁸, anxiety⁶, and widespread pain^{3,4,5} are all common in

Table 3. Predictors of work disability at 24 months after diagnosis of primary Sjögren syndrome (pSS). Results are presented as OR and 95% CI based on univariate logistic regression modeling.

Predictors	OR	95% CI
Work disability at baseline (yes/no)	15.4	2.9–81.9
Fibromyalgia	10.5	2.0–56.0
Age at pSS diagnosis	1.1	1.0–1.2
Anti-SSA or anti-SSB antibody seropositivity	2.6	0.6–10.7
ESSDAI (low activity/moderate-high activity)	1.1	0.4–3.5

ESSDAI: European League Against Rheumatism Sjögren's Syndrome Disease Activity Index.

pSS and often have a more pronounced effect on HRQOL than the sicca symptoms^{9,10}. Several studies have reported an impaired HRQOL in pSS that has been attributed to an increased experience of fatigue^{7,8,16}, concomitant depression^{8,13,14,20}, and pain^{8,11,12,20}. Accordingly, factors measured by the EULAR Sjögren Syndrome Patient Reported Index (ESSPRI)²¹, not only the severity of subjective sicca symptoms but also pain and fatigue, have been reported to be associated with decreased HRQOL in patients with pSS^{12,13,22,23}. The impaired HRQOL in patients with pSS is indeed a burden for the individual patient but does also result in consequences for society from increasing direct healthcare

costs^{8,15}, with an increase in both physician visits and healthcare use^{8,9,15}, as well as indirect healthcare costs related to work disability^{9,16,17}. Work disability in pSS has previously, to the best of our knowledge, been studied only 4 times^{8,9,16,17} and never in a population-based longitudinal setting with matched comparator subjects. In our present study, work disability in patients with pSS was assessed from an independent and complete source (SSIA), and 26%, 37%, and 41% of patients with pSS were found to be work-disabled at the time of pSS diagnosis, 12, and 24 months after diagnosis, respectively. Work disability was thus 2-fold higher in comparison with the general population 24 months after pSS diagnosis. Because none of the patients retired during the observation period, the work disability numbers in the current study are considered representative for patients with pSS of working potential. In previous studies on work disability, Westhoff, *et al* reported a 10.4% sick leave and 28.3% early retirement among patients in their cohort⁹, while Meijer, *et al* reported that 45.0% of patients with pSS in their study were receiving disability compensation¹⁶. Both results compare to the numbers in our cohort at followup. Bowman, *et al* reported an increased loss of work productivity among patients with pSS in comparison with controls, resulting in increased indirect healthcare costs¹⁷. On the other hand, in the study by Segal, *et al*⁸, performed in the United States, only 12% of patients with pSS reported being unemployed because of disability. However, those studies were all performed in prevalent pSS patients with variable disease duration and age; the studies relied on self-reported data and defined work disability differently. Differences in the results must also take into account that the studies were performed in different countries with different social security systems. Our current study also showed that work disability increased significantly during the first 2 years after diagnosis, initially driven by an increase in sick leave and subsequently by an increase in patients receiving a disability pension. Although comparisons between studies from different countries with different social security systems should be performed with care, the similarities between our present study and 2 European studies^{9,16} underline that a substantial fraction of patients with pSS end up with a permanent work disability after a couple of years of disease. Similar findings, with an increased baseline work disability that further increased during 3 years of followup, have also been reported in newly diagnosed patients with rheumatoid arthritis (RA)²⁴ and systemic sclerosis (SSc)²⁵.

The Work Productivity and Activity Impairment (WPAI) questionnaire is gaining more influence and importance in the field of rheumatology because it is a self-administered instrument, used to assess the effect of disease on productivity in the previous 7 days. It is especially suitable for randomized controlled trials, because it captures both presenteeism and absenteeism. Our current study, on the other hand, only focused on absenteeism. However, the WPAI relies on

self-reported data and a cross-sectional approach, resulting in obvious shortcomings compared to the method we used.

When studying predictors of longterm work disability, work disability already at diagnosis was the strongest predictor, although concomitant FM and increasing age were also significant predictors. Disease activity, as evaluated by the ESSDAI total score and anti-SSA and anti-SSB seropositivity, was not. These findings are in line with previous studies reporting dryness, pain, and fatigue, assessed by the ESSPRI, as stronger predictors of HRQOL in patients with pSS than systemic involvement, assessed by the ESSDAI^{22,23}. Although prior work disability has not previously been reported as a predictor of longterm work disability in pSS, it has been shown in several other groups of patients with various rheumatologic diseases, such as RA²⁴, psoriatic arthritis²⁶, and SSc²⁵. Westhoff, *et al* also reported age as predictive of working status as well as disease duration, functional capacity, and lack of stamina, but of note, not pain or sicca⁹. On the other hand, Meijer, *et al* reported that the number of extraglandular manifestations, use of artificial saliva and antimalarials, comorbidities, high level of education, and male sex were associated with receiving disability compensation¹⁶. The lack of association between pain and work disability in those 2 studies is thus in contrast with the findings in our present study, in which FM was associated with subsequent work disability. Differences in the assessment of pain between the studies could possibly explain the discordant results. We could not find an association of extraglandular disease with work disability¹⁶, possibly also due to different assessments of extraglandular disease as well as differences in disease duration and thus differences in the prevalence of extraglandular disease. Although it would be interesting to study whether fatigue, depression, and/or anxiety were predictors of work disability, because these have previously been shown to significantly correlate with HRQOL in pSS²⁰, no evaluation of these variables was performed at the time of pSS diagnosis in our present study.

Considering new emerging therapies in pSS, the results of our study underline the importance of not only treating symptoms of systemic disease but also addressing symptoms that result in reduced HRQOL and thus increased work disability, because the cost of such therapies may be justified if they affect work disability and thus indirect costs of the disease.

A strength of our study was the use of an external and independent source such as the SSIA for retrieval of data on work disability. The data are considered high-quality because they are linked to the payment system. Further, because the MSSR includes all consecutive and newly diagnosed patients with pSS since 1984 followed at the Department of Rheumatology, Skåne University Malmö, Sweden, and our unit is the only one treating patients with pSS in the area, we consider this cohort population-based and representative of

incident patients with pSS in general. However, there are also several limitations, including the small sample size and the lack of quantitative data on other factors influencing work disability such as fatigue, pain, anxiety, and depression. Although data on fatigue and pain are now collected by assessment of the ESSPRI, the cohort was collected prior to the development of that instrument and thus such data were lacking. In addition, data were lacking on other factors potentially influencing work disability, such as level of formal education and socioeconomic status. Another limitation is the lack of information on the cause for work disability, which may be due not only to pSS but also to comorbidities and unrelated diseases. In addition, the study did not yield data on potential productivity of patients available for the work force, and thus presenteeism, as a possible confounder of the results, cannot be estimated. Finally, periods of sickness shorter than 15 days were not registered by the SSIA and were not included in our study. Because short periods of sick leave are often due to episodes of mild infection or minor injuries, it is reasonable to assume that such sick leave is more evenly distributed between patients with pSS and the general population. However, no conclusions can be drawn with regard to differences in short-term work disability between patients with pSS and the general population from our study.

Patients with pSS were found to have an increase in work disability in comparison with the general population as well as an increase in work disability during the first 2 years after diagnosis. Work disability at diagnosis, concomitant FM, and increasing age were predictors of longterm work disability, while disease activity and serological markers of the disease were not.

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