Sick Leave Before and After Diagnosis of Rheumatoid Arthritis — A Report from the Swedish TIRA Project

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ABSTRACT. ***Objective.*** Our study describes sick leave during 3 years before and 3 years after diagnosis of rheumatoid arthritis (RA) in relation to referents and identifies predictors for sick leave during the third year after diagnosis of RA.

Methods. One hundred twenty patients (76% women) from the Swedish early RA study TIRA were included. Disease activity and disability were registered regularly during 3 years in TIRA. Referents were matched for sex, age, and home town. Sick leave data were obtained for patients 3 years before and 3 years after diagnosis and for the referents for the corresponding 6 years.

Results. No differences were seen between patients and referents regarding sick leave during the first 2 years, whereas sick leave increased in patients 6 months before diagnosis, from 30% to 53%. During the 3 years after diagnosis, sick leave among patients was rather stable, varying between 50% and 60%, even though disability pension increased and sickness benefit decreased. Sick leave before diagnosis, disability 1 year after diagnosis, and type of work were identified as predictors for sick leave during the third year after diagnosis.

Conclusion. Not surprisingly, sick leave in patients increased the year before diagnosis. Although disease activity and disability diminished after diagnosis, the patients' sick leave remained essentially unchanged. Sick leave 3 years after diagnosis was foremost predicted by earlier sick leave, disability, and type of work. (J Rheumatol First Release May 1 2009; doi:10.3899/jrheum.080523)

Key Indexing Terms:
SICK LEAVE RHEUMATOID ARTHRITIS RISK FACTORS CASE-CONTROL STUDY

Rheumatoid arthritis (RA) is a chronic inflammatory disease often leading to disability[1]. In a Swedish adult population, the annual incidence of RA has been estimated to be 24/100,000[2] and the prevalence about 0.5%–0.7%[3,4]; women are affected about twice as often as men[5]. Sick leave caused by RA is high and the costs due to productivity loss are more than twice as expensive as medical costs[6-9].

Population-based studies[10,11] have indicated that patients with RA are significantly more on sick leave compared to the general population and the sick leave is high already early in the disease process[7,12-14]. Due to methodological differences in the studies and different social security systems, rate of sick leave due to RA varies between countries. About two-thirds are affected by sick leave during the 12 months after diagnosis of RA. After 7–10 years, between 20% and 70% of the patients did not work[12].

Sick leave due to RA is complex and depends on several factors[15-18] such as physically demanding work, activity limitations, and older age[19]. Several studies examined patients later in the disease course and used self-reported sick leave, approaches that could result in recall bias[12,20].

A high level of sick leave is a common socioeconomic problem in Western countries. Musculoskeletal conditions, including RA, are the largest group of diagnoses associated with high levels of sick leave. The improvements in activity limitations and impairments during the first months after diagnosis are well known[21], but knowledge about work disability early in the disease course is limited. More detailed knowledge about the pattern of sick leave during the years after diagnosis is needed, and also about its relation to disease activity, disability, education, work, and income. This is essential to identify subgroups of patients with special needs for early interventions, targeted at returning to work and clinically oriented interventions.

Our study describes sick leave during 3 years before and 3 years after diagnosis of RA in relation to sick leave in

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Swedish referents during the corresponding period. The study also identifies predictors of sick leave during the third year after diagnosis of RA.

MATERIALS AND METHODS

Patients. The Swedish TIRA project ("early intervention in RA") started in 1996 as a multiprofessional cooperation between 10 rheumatology units in southeast Sweden. The main purpose of TIRA was to establish efficient clinical routines for early diagnosis and early multiprofessional interventions[22]. In total, 320 patients, 215 women and 105 men, with recent-onset RA (onset of joint swelling ≤ 12 mo) were included in the TIRA cohort during 27 months (1996-98). Followup visits were performed at 3, 6, 12, 24, and 36 months (Month 0-Month 36) and multiprofessional interventions were offered when considered adequate.

Our study included the 178 patients still remaining in the TIRA project at Month 36 of age ≤ 62 years at inclusion. Of the 178 patients, 12 were not reachable since they had moved abroad, had an unknown address, or had died. Therefore, written information about the study and an inquiry about informed consent to participate were distributed to 166 of the patients. Of the 122 patients answering the query, 101 wanted to participate. The 43 nonresponding patients were contacted by telephone after 1 month and asked about participation. Nineteen patients wanted to participate, 7 declined, and 17 were not reachable. Hence, the final patient group consisted of 120 patients, 91 women and 29 men (Figure 1).

Referents. One referent was randomly matched to each patient by age, sex, and home town. The matching process was carried out by the Swedish social insurance agency and based on the Swedish population.

Ethics. All the patients included in the study gave written or verbal informed consent to participate. The study protocol for the TIRA project has been approved by the regional research ethics committee of Linköping University (Dnr 96035) and all patients in the cohort gave written informed consent to participate at time of inclusion in the TIRA project.

Disease activity and disability. At all followups in the TIRA project, assessments were performed using the erythrocyte sedimentation rate (ESR, mm) and serum level of C-reactive protein (CRP, mg/l). Anti-cyclic citrullinated peptide (anti-CCP) antibody was analyzed from serum samples at inclusion (cutoff value for positive anti-CCP reaction: 25 units/ml[23]). A 28-joint count of tender and swollen joints was registered[24] and the physician's global assessment of disease activity (PGA)[25] was estimated on a 5-point scale (0–4), where 0 corresponds to "no activity" and 4 to "high activity."

The patients were also asked to report their pain intensity on average during the last week. This was estimated on a 100-mm visual analog scale (VAS) ranging from 0 (no pain at all) to 100 (worst possible pain). Patient's global assessment of health (PaGA) was estimated in the same manner, 0 representing "best possible health" and 100 "worst possible health."

Grip force (newtons, N) was assessed using a Grippit^{TM} device (AB Detektor, Göteborg, Sweden)[26] and the average value of the right hand during 10 s was used. Range of motion was assessed by the Signals Of Functional Impairment (SOFI), which consists of 3 parts: hand function [SOFI-hand (scores 0–16)]; upper limb function (SOFI-upper; 0–12); and lower limb function (SOFI-lower; 0–16), where 0 corresponds to normal function[27]. The Grip Ability Test (GAT) tested grip ability and a high score corresponds to decreased hand function[28]. Activity limitations were reported by the Swedish version of the Health Assessment Questionnaire (HAQ). HAQ consists of 20 questions in 8 subcategories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities, and is self-reported by the patients. It generates a score ranging from no difficulties (0) to unable to perform (3)[29].

Demographic variables. At the time of diagnosis, patients completed a questionnaire about highest education level (compulsory school, public high school, upper secondary school or university, or other significant education), marital status (unmarried, married, divorced, or widow/widower), number of children living at home, and annual income. The data concerning the patients' type of work at time of diagnosis of early RA was collected in an epidemiological TIRA-associated study[30] during the years 1996 to 1998. The sample in our study was included from 1996 to 1998 and corresponded to 56% of the sample in the epidemiological TIRA-associated study. Using a standard classification system, one physician specializing in occupational medicine and one industrial hygiene engineer (IB) independently identified the patient's type of work at time of diagnosis. The categories of work type were "heavy material handling," "heavy repetitive," "medium heavy variable," "light repetitive," and "administration/computer work"[31]. There was an agreement in 80% of the cases. To determine the work type of the 20% of cases that were not agreed upon, the physician, the hygiene engineer, and the first author discussed the differences until they arrived at a consensus.

Sick leave variables. The purpose of the Swedish sickness benefit system is to compensate for loss of income due to disease or injury that reduces the work capacity by at least 25%. The benefit amounts to 80% of lost income with an upper limit, and can be paid for full- or part-time absence. In our study sick leave covers sickness benefit, rehabilitation benefit, and disability pension. Sickness benefit compensates for a major part of the lost income from temporary loss of work. There is no formal limit for the duration of sickness benefit. Rehabilitation benefit facilitates the vocational rehabilitation. Permanently reduced work capacity can be compensated by

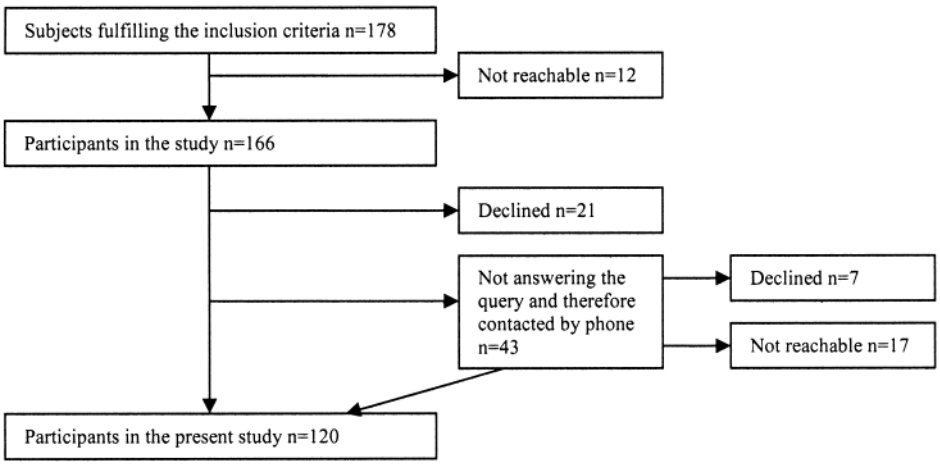

Figure 1. Procedure for selection of the study group.

part- or full-time disability pension until the age of 65, when old-age pension is granted. Disability pension, compensation for permanent work loss, was used until 2003 (including the time for our study); this benefit was replaced by sickness compensation and activity compensation[32].

Data concerning sick leave due to any reason were obtained from the Swedish social insurance agency for the patients during the period 3 years before inclusion in TIRA to 3 years after inclusion. The same data for the corresponding period were obtained for referents. Since the employer is responsible for the economic compensation during the first 14 days (between January 1, 1997, and March 31, 1998, the first 28 days), these days are not included in the Swedish social insurance agency's data. Therefore, they are not included in our study. Data were grouped for each quarter during the 6-year period. Sick leave was divided into number of days with sickness benefits, rehabilitation benefits, and disability pension. The number of days was recalculated to equal full-time days.

Statistics. SPSS (version 15.0) and SIMCA-P+ (version 11.0) were used for the statistical analyses. To analyze patient characteristics and sick leave variables, Student's t-test and analysis of variance (ANOVA) were used. To identify predictors of sick leave, we used the multivariate partial least-squares method (PLS)[33] using SIMCA-P+. The basic assumption in projection methods like PLS is that data contain underlying latent variables that are fewer than the number of observed variables[33,34]. PLS has some advantages in comparison to more traditional multivariate methods, for example, multiple linear regression. PLS does not require interval-scaled data and it is not sensitive to violations of multivariate normality. Further, it has no assumptions about independence of observations and is therefore not so influenced by collinearity among the original variables. Last, it may be used with small samples and even with more original variables than participants[35].

PLS is based on the covariance between the X and Y matrix. In our study, PLS was used to predict sick leave during the third year after diagnosis (Y variable). The X variables were ESR, CRP, PGA, SOFI (all 3 parts), HAQ, GAT, Grippit result, pain, and general health at diagnosis and at the first-year followup. Also included were demographic data: sex, age, education level, marital status, number of children living at home, and type of work at Month 0 and the history of sick leave before diagnosis, expressed as total days with sick leave 1 year, 2 years, and 3 years before diagnosis. The categorical variables were used as dummy variables in the analyses.

In the PLS analysis, the relationships between the X variables and corresponding Y variable were calculated, and the importance of each X variable to the Y variable was expressed in the model. To interpret the PLS model, the R^2 value was used, which expresses the explained variation in the X matrix. The R^2 varies between 0 and 1, where 1 means a perfectly fitting model and 0 no fit at all. The predictive ability of the model was expressed in Q2, which varies between 0 and 1. The variable influence on projection (VIP) identifies the most contributing variables for the model. X variables with a VIP > 0.8[33,34] were considered to have a strong relationship to sick leave during the third year after diagnosis.

RESULTS

Dropouts. The dropouts were not significantly different from the study group according to sex, age, or the disease activity, disability, and demographic variables listed in Table 1. Type of work was not collected for the dropouts and therefore was not analyzed in relation to the study group.

Study group. Of the patients constituting the study group, 91 were women (76%) and 29 men (24%). The mean age in the study group at inclusion was 47 years [standard deviation (SD) 12]. All the disease activity and disability variables except number of swollen joints, PGA, PaGA, and GAT had improved significantly from inclusion to the 36-month followup (Table 1).

At the time of inclusion, 73% of the patients were taking nonsteroidal antiinflammatory drugs (NSAID), 18% oral corticosteroids, and 4% disease modifying antirheumatic drugs (DMARD). After one year (Month 12), 63% of the patients were taking NSAID, 34% oral corticosteroids, and 82% DMARD.

Total sick leave during the study period. Sick leave in the referents was stable during the 6 studied years, with no statistical differences between women and men. No differences between referents and patients were seen during the first 2 studied years; however, the total sick leave (disability pension, sickness benefits, and rehabilitation benefits summarized) increased significantly in the patients during the 6 months before diagnosis. In the first quarter after the diagnosis, the mean value of days with sick leave was 34 (SD 40) in the RA group and 4 (SD 15) days in the referents. Thereafter, the mean days with sick leave were rather stable in both groups, with significantly more sick leave days in the RA group (Figure 2). At time of diagnosis 53% of the patients with RA were on sick leave, after 1 and 2 years 58%, and after 3 years 55%. During this period the corresponding rate of sick leave in referents was significantly lower and varied between 7% and 12% (Figure 3).

Sick leave: sickness benefits, rehabilitation benefits, and disability pension rates. Three years before diagnosis, 3.3% of the TIRA patients had sickness benefits. Two years before diagnosis the number had increased to 8.3% and at 1 year before diagnosis to 12.5%. In the referents, 7.5%–10% had sickness benefits during the corresponding period, which is not significantly different from the patients. Six months before diagnosis sickness benefits started to increase for the TIRA patients, and at time of diagnosis significantly more TIRA patients had sickness benefits compared to the referents ($p < 0.001$) and during 3 months after diagnosis patients receiving sickness benefits increased from 38% to 43%. This rate declined to 33% at the beginning of the second year and to 25% at the end of the study period. The proportion of referents with sickness benefits was significantly smaller ($p < 0.001$) and varied between 3% and 5% during the corresponding period (Figure 3).

No patient had rehabilitation benefits during the third year before diagnosis. At the end of the second year before diagnosis, about 2% of the patients received rehabilitation benefits, and this varied between 4% and 1% until time of diagnosis. In the referents, about 2% received rehabilitation benefits during the same period. The frequency of patients and referents with rehabilitation benefits was still low after the time of diagnosis. Among the patients it varied between 1% and 5% and it was zero among the referents (Figure 3).

At the start of the study (3 yrs before diagnosis), almost 7% of the patients and no referents ($p < 0.001$) received disability pension. During the 3 years before diagnosis, the proportion of the TIRA patients with disability pension did not change considerably, but disability pension among the refer-

Table 1. Disease activity, disability, and demographic variables in the study group (n = 120) at inclusion (M0) and 36 mos followup (M36).

Variables		Month 0	Month 36	Month 0 vs Month 36 p
Disease activity				
Anti-CCP (> 25 units mg/l), missing 25%	% pos	51		
ESR, mm	Mean (SD) Md	31 (20) 26	21 (21) 14	< 0.001
CRP. mg/l	Mean (SD) Md	24 (23) 13	13 (15) 5	0.003
Swollen joints, 0–28	Mean (SD) Md	8 (6) 7	4 (0) 2	NS
Tender joints, 0–28	Mean (SD) Md	9 (7) 7	4 (6) 2	0.018
PGA, 0–4	Mean (SD) Md	2 (1) 2	1 (1) 1	NS
Disability				
Pain intensity, VAS 0–100 mm	Mean (SD) Md	48 (25) 45	36 (26) 32	0.05
PaGA, VAS 0–100 mm	Mean (SD) Md	43 (25) 40	35 (25) 30	NS
GAT, 10–276	Mean (SD) Md	23 (8) 21	21 (20) 17	NS
Grip force, newtons	Mean (SD) Md	118 (91) 101	150 (88) 143	< 0.001
SOFI-hand, 0-16	Mean (SD) Md	2 (2.6) 2	2 (2) 1	0.015
SOFI-upper limb, 0–12	Mean (SD) Md	1 (2) 0	1 (1) 0	0.003
SOFI-lower limb, 0–16	Mean (SD) Md	2 (2) 2	2 (2) 1	< 0.001
HAQ, 0–3	Mean (SD) Md	0.9 (0.8) 0.8	0.6 (0.5) 0.5	< 0.001
Demographic variables				
Marital status (missing 2%)				
Unmarried	%	28		
Married	%	53		
Divorced	%	14		
Widow/widower	%	3		
Number of children living in the household	Mean (SD) Md	0.8 (1) 0		
Highest education level (missing 2%)				
Compulsory school	%	47		
Folk high school	%	7		
Upper secondary school or university	%	26		
Other significant education	%	6		
Annual income, SEK	Mean (SD) Md	163,400 (53,665) 163,959		
Type of work (missing 44%)				
Heavy material handling	%	7		
Heavy repetitive	%	5		
Medium heavy variable	%	12		
Light repetitive	%	7		
Administration/computer work	%	25		

Data are presented as mean and standard deviation (SD) and median (Md). Missing data are presented as percentage. ESR: erythrocyte sedimentation rate (mm); CRP: C-reactive protein (mg/l); PGA: physician's global assessment of disease activity; VAS: visual analog scale; PaGA: patient's global assessment of health; GAT: Grip Ability Test; SOFI: Signals of Functional Impairment; HAQ: Health Assessment Questionnaire; NS: not significant; SEK: Swedish krona.

ents increased to 2.5% at time of diagnosis. After diagnosis, disability pension in the TIRA cohort started to increase, in contrast to the decreasing sickness benefit. At the start of the first quarter of the second year, 19% of the patients received disability pension. At the start of the third year this increased to 27%. During the corresponding time, 3%–4% of the referents received disability pension, which is a significantly ($p < 0.001$) smaller part (Figure 3).

Predictors of sick leave during the third year after diagnosis of RA. All patients: The model explained 44% of the total sick leave during the third year after diagnosis (second quarter 33%). The PLS-model identified a high number of days with sick leave during the first year before diagnosis as an important predictor. Other important predictors were impairment in the lower extremities (due to SOFI-lower), disability according to HAQ, and high pain intensity at Month 12. High numbers of days with sick leave during the second and third year before diagnosis were also important predictive variables to the outcome. PaGA at Month 12, GAT at Month 0 and Month 12, SOFI-lower and HAQ at Month 0, and ESR at Month 12 were predictive variables (Table 2).

Type of work at diagnosis was also an important predictor for sick leave; working in administration or with computers was negatively correlated to high sick leave. A medium to heavy type of work was an important predictor of sick leave during the third year after diagnosis, as was education: upper secondary school was negatively correlated to high sick leave and compulsory school was positively correlated (Table 2).

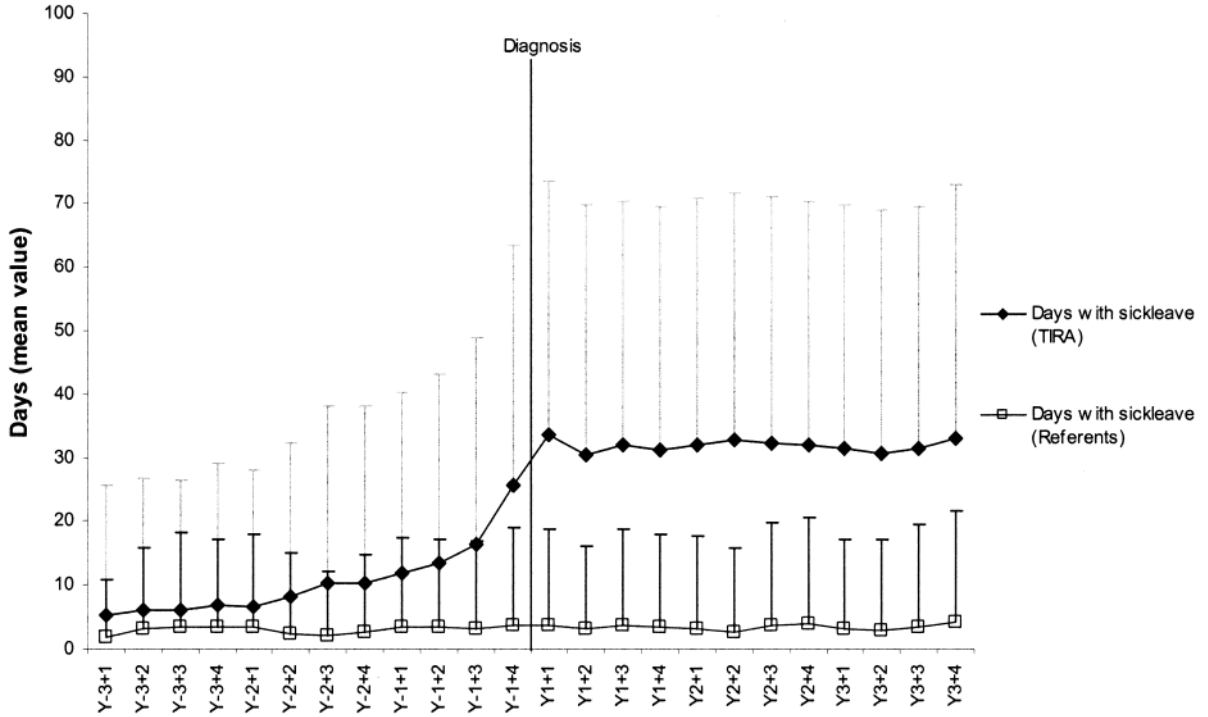

Figure 2. Days (mean + SD) with sick leave (sickness benefits, rehabilitation benefits, and disability pension summarized) in the TIRA cohort and among the referents. "Y" indicates year in relation to diagnosis and quarter that year (e.g., Y-3+1 = third year before diagnosis, months 1–3). Data include sick leave periods longer than 14 days. Data of shorter periods not included.

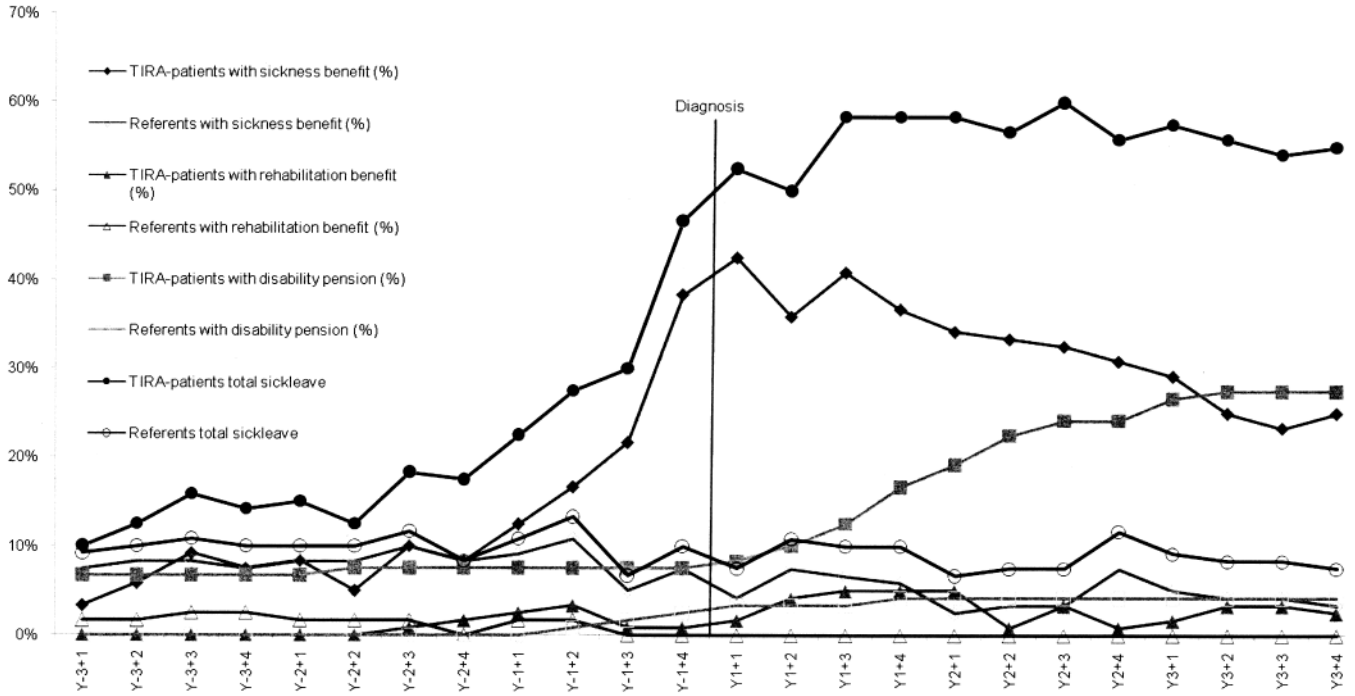

Figure 3. Rate of total sick leave, sickness benefits, rehabilitation benefits, and disability pension during 3 years before and 3 years after diagnosis in the TIRA cohort and in corresponding period for referents. "Y" indicates year in relation to diagnosis and quarter that year (e.g., Y-3+1 = third year before diagnosis, months 1–3).

Table 2. The variables important to sick leave during the third year after diagnosis. Variables with VIP value > 0.8 were defined as significant predictors. The sign "+" indicates a positive correlation to high sick leave and "–" a negative correlation to high sick leave. Month 0 indicates diagnosis/inclusion in TIRA and Month 12 the 12-month followup.

Variable	Correlation	VIP
Sick leave during the first year before diagnosis	+	2.8
SOFI-lower Month 12	+	2.1
HAQ Month12	+	2.0
Pain intensity Month 12	+	1.9
Sick leave during the second year before diagnosis	+	1.9
Sick leave during the third year before diagnosis	+	1.7
Administration/computer work	–	1.4
PaGA	+	1.4
GAT Month 0	+	1.4
Age	+	1.3
GAT Month 12	+	1.2
Medium heavy variable type of work	+	1.0
Upper secondary school as highest education	–	1.0
SOFI-lower Month 0	+	1.0
ESR Month 12	+	0.9
HAQ Month 12	+	0.9
Compulsory school as highest education	+	0.8
R^2/Q^2		0.44/0.33

SOFI: Signals of Functional Impairment; HAQ: Health Assessment Questionnaire; PaGA: patient's global assessment of health; GAT: Grip Ability Test; ESR: erythrocyte sedimentation rate; VIP: variable influence on projection.

Variables indicating disease activity (PGA, ESR, CRP, anti-CCP, and swollen or tender joints) were not identified as important in the prediction of sick leave, with the exception of ESR at Month 12 (Table 2).

Men and women separately: In the next step of the analysis, 2 more PLS-models were created, one for women and one for men (Table 3). The model based on the women's data explained 43% of sick leave during the third year after diagnosis of RA (second quarter 31%). In the model based on men, the corresponding values were 56% and 23%. The important predictors (VIP > 0.8) in the model based on women were almost identical to the model comprising the total study group, but the model identified some additional predictors; Grippit score at Month 12 and excluding ESR at Month 12 and type of work were important predictors (Table 3).

In the model based on men, type of work was important. Working in administration or computer work was identified as an important indicator, negatively correlated to sick leave after 3 years. In men, more variables concerning disease activity were identified as significant predictors (ESR at Month 12, PGA at Month 12, and number of swollen joints at Month 0; Table 3).

DISCUSSION

Sick leave during the study period. Our study describes sick leave before and after diagnosis of RA in relation to referents, and investigates predictors of sick leave the third year after diagnosis. In a systematic review, Burton, *et al*[12] found that 22%–76% of patients with RA were on sick leave 6 months after diagnosis and 36%–84% after 1 year. In our study, the corresponding values were 50% and 58%. Sick leave increased most rapidly early in the disease course. In an earlier report from the Swedish TIRA project based on self-reported sick leave data, 28% of the total study group were on sick leave at time of diagnosis. The rate remained mainly unchanged during the following 3 years[7]. In our study, the rate of sick leave at time of diagnosis was 53% and also remained stable after. The differences in sick leave rates in the 2 studies may reflect the difficulty of comparing self-reported and register-based sick leave data. Research focusing on sick leave and RA has presented several methodological issues, making comparisons of sick leave between different studies difficult. For example, studies use different methods to collect data. Several studies are based on self-reported data collected by questionnaire or by telephone[12], with the associated risk for recall bias[20]. We had the possibility of using data from the Swedish social insurance agency. This increases the reliability, but has the limitation that sick leave during the first 2 weeks is not reported to the social insurance agency. For instance, this makes comparisons between referents and patients regarding number of short sick leave spells impossible. Another limitation of our study is that the dropout rate is rather high and may also have influenced the reliability of our study. The findings should therefore be confirmed in a larger sample. However, our results are similar to previous studies of early RA in the UK[36], Finland[14], Germany[13], and in The Netherlands[37].

The frequency of sick leave had already started to increase during the year before diagnosis. One of the inclusion criteria in the TIRA project was that the patients should have had joint swelling for not more than 12 months. Since the disease process may have started during the 12 months before diagnosis, this may explain a part of the increased sick leave in relation to referents during this period. The improvements in disability and disease activity during the first months after diagnosis are well known[21,38,39]. However, even though some studies have found a relation between effective drug treatment and reduced sick leave[40-42], it is not obvious that sick leave, disability, and disease activity follow the same pattern. The relation between RA and sick leave is, however, complex. Sick leave is often used as an outcome measure of social consequences of a person with a disease[43]. Even though the degree of overlap between illness (the ill health the person identifies themselves with) and disease (a condition that is diagnosed by a physician) in relation to sick leave has been identified as rather low[44]. This may explain the different trends over time in sick leave and other aspects of disability in TIRA patients, and indicate the importance of explaining sick leave with a wide range of aspects.

Table 3. Order of the variables important to sick leave during the third year after diagnosis in men and women. Variables with variable influence on projection (VIP) value > 0.8 were defined as significant predictors. The sign "+" indicates a positive correlation to high sick leave and "–" a negative correlation to high sick leave. Month 0 indicates diagnosis/inclusion in TIRA and Month 12 the 12-month followup.

Order of Predictors	Women			Men		
	Variable	Correlation	VIP	Variable	Correlation	VIP
1	Sick leave during the first year of diagnosis	+	2.8	Sick leave during the first year before diagnosis	+	2.2
2	SOFI-lower Month 12	+	2.2	Administration/computer work	–	2.1
3	HAQ Month 12	+	2.2	Pain intensity Month 12	+	2.1
4	Pain intensity Month 12	+	1.8	ESR Month 12	+	1.9
5	Sick leave during the second year before diagnosis	+	1.7	Sick leave during the second year before diagnosis	+	1.9
6	GAT Month 0	+	1.6	HAQ Month 12	+	1.9
7	Sick leave during the third year before diagnosis	+	1.4	PaGA Month 12	+	1.8
8	HAQ Month 0	+	1.3	Sick leave during the third year before diagnosis	+	1.7
9	Age	+	1.2	SOFI-lower Month 12	+	1.5
10	Medium heavy variable type of work	+	1.2	Grippit Month 12	+	1.4
11	Grippit Month 12	+	1.2	GAT Month 12	+	1.3
12	PaGA Month 12	+	1.1	Heavy material handling as type of work	+	1.3
13	GAT Month 12	+	1.1	Light repetitive type of work	+	1.2
14	Upper secondary school as highest education	+	1.1	SOFI-hand Month 0	+	1.0
15	SOFI-lower Month 0	+	1.0	Grippit Month 0	+	0.9
16	Administration/computer work	–	1.0	PGA Month 12	+	0.9
17	Compulsory school as highest education	–	0.9	Age	+	0.9
18	SOFI-upper Month 0	+	0.8	Other significant education	+	0.9
19				Number of swollen joints Month 0	=	0.8
20				CRP Month 12	+	0.8
R^2/Q^2			0.43/0.31			0.56/0.36

SOFI: Signals of Functional Impairment; HAQ: Health Assessment Questionnaire; GAT: Grip Ability Test; PaGA: patient's global assessment of health; ESR: erythrocyte sedimentation rate; PGA: physician's global assessment of disease activity; CRP: serum C-reactive protein.

Sick leave is also a variable that is affected by society due to, for example, economic services, systems, and policies. During the study period some changes were made in the work related systems, possibly affecting the rates of sick leave in the study group. For instance, the number of days compensated by the employer in the beginning of a sick leave spell was changed from 14 to 28 during a period in 1997-1998. The regulations for disability pension have also been changed, and from 1997 it is based on assessment strictly in relation to the medical conditions of the individual[45].

One purpose of including referents in the study was to control for these changes in sick leave due to changes in the Swedish social insurance system and in employment rates. The referents were randomly selected from the Swedish population and matched to a TIRA patient on an individual basis with respect to home town, sex, and age. At the time of the patients' diagnosis, 7% in the referent group were on sick leave. This is a higher proportion compared to sick leave in the total Swedish population at that time (3.7%)[46] and may be explained by the higher average age among the referents compared to the working Swedish population and a higher proportion of women. Age and sex are 2 factors affecting sick leave[47,48].

Predictors of sick leave during the third year after diagnosis of RA. In the multivariate analysis, we found that the strongest predictor of sick leave during the third year after diagnosis was sick leave before diagnosis. History of sick leave had also been identified as an important predictor in earlier studies[49-51]. Age also has a well known relation to sick leave in the general population[52] as well as in patients with RA[47,53], and our study confirmed the importance of this factor.

The relation between disease activity in RA and sick leave seems to vary. In our study, ESR at Month 12 was the only predictive disease activity variable, and this is in accord with results described by Young, *et al*[36]. Anti-CCP has been identified as a predictor of disease course[23] and was therefore of interest as a predictor in our study, but it was not associated with sick leave. Our results generally agreed with other studies' results implying that disease activity is not strongly related to sick leave[54].

SOFI-lower and HAQ were also important predictors of sick leave. In an earlier study focusing on pain intensity in patients with RA, we found HAQ and SOFI-lower to be intercorrelated, which might explain their appearance together (Björk, *et al*, unpublished data). HAQ has been identified as a predictor of sick leave[14,36,47,53,55], indicating the close relation between activity limitation and participation restrictions in the context of the International Classification of Functioning, Disability and Health (ICF)[56]. In our study, pain intensity and PaGA are 2 self-reported measures that also were identified as important for sick leave. Self-reported health measures like pain intensity

(Merkesdal, *et al*[13]) have been identified to predict sick leave[57], and further self-reported assessment could have been useful in our study. For example, coping strategies are known to be associated with sick leave[58].

Even though the rate of missing data was high (44%) in the type of work variable, type of work was identified as an important predictor. A physically demanding type of work and low education level are closely associated[48,59] and were identified as predictors in our study. Manual work[16], nonprofessional or nonadministrative work, and physically demanding work[53] have been found as important factors for sick leave due to RA. In contrast to several other studies[14,36,59], we did not find sex to be an important predictor. Since the 1970s, Swedish women are in general on sick leave more than men[45]. We did not find this difference among the patients with RA. One explanation may be that there were more men than women ($p = 0.036$, calculated with Mann-Whitney U-test) in the sample that worked in the category "heavy material handling" (32% men and 4% women). It has been shown that high physical demands at work are a risk factor for sick leave in patients with RA[19]. Although men in general are employed in jobs with a higher physical loading than women[60], being diagnosed with RA may affect functioning at work. Also, even if a diagnosis such as RA will affect functioning at work, being on sick leave or not is also determined by contextual factors including, for example, the possibility of adjustments of work tasks and working time or pace. A low possibility of adjustments at work has been identified to be associated with an increased risk of sick leave[61]. Possibility of adjustments varies from workplace to workplace, and women and men have different types of jobs implying different opportunities to adjust[62]. A question that can be raised in this context is whether the possibility to make adjustments at work is higher at workplaces or sectors with lower physical workload and also dominated by women. Among the patients with RA, significantly more women ($p = 0.036$; 65% women and 36% men) were employed in jobs categorized either as "light repetitive" or "administration/computer work" including, for example, child care, assistants, secretaries, or teachers. From this perspective, women with RA may have greater possibilities to adjust their workplace with the aim to continue work even after diagnosis of RA.

Further, the separate models for women and men with RA mainly showed similarities in predictors, but they also showed interesting differences. For example, in men, disease activity seems to be more important. We found this earlier when we analyzed pain intensity as the outcome variable (Björk, *et al*, unpublished data). Our results with respect to sex should be confirmed in larger studies.

The recommendation that the differences between R^2 and Q^2 should not be less than 20%–30%[33] was fulfilled, indicating stability in the model. Anyhow, due to the R^2 value, 56% is still unexplained, partly due to variables not included. Additional variables of interest are, for example, the degree of psychosocial demand and sense of control at work, since these factors are related to sick leave[45,63]. Also in RA, the possibility to adjust the physical environment[64], the work tasks, and working hours[36,64] are important, although these were not considered in our study. The effectiveness of medication in reducing sick leave should also be a focus of future research.

Sick leave increased 6 months before diagnosis in relation to referents. Although disease activity and disability diminished significantly after diagnosis and intervention, sick leave remained essentially unchanged during the 3 years after diagnosis. This indicates that participation, represented by sick leave in our study, needs to be a focus of clinical assessments and intervention planning, since it does not follow the same pattern of early improvement. History of sick leave before RA diagnosis, disability 1 year after diagnosis, and type of work were important predictors related to sick leave.

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