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Work participation is unaffected in Belgian spondyloarthritis patients: data from the BelGian Inflammatory Arthritis and SpoNdylitis cohorT

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Key messages:

- Age- and sex-adjusted employment rate in Belgian SpA patients is similar to the general population.
- Belgian SpA patients do not encounter excess sick leave or restrictions while at work.

- Work outcomes depend on self-reported physical functioning and overall health status rather than clinical characteristics.

Abstract

Objectives

This study aimed to (1) investigate actual work participation in Belgian spondyloarthritis (SpA) patients compared to the general population, and (2) identify determinants of work-related outcomes.

Methods

Adult SpA patients from the Ghent University hospital based Be-GIANT cohort (fulfilling ASAS classification criteria) were cross-sectionally questioned on their socio-economic status and completed a Work Productivity and Activity Impairment questionnaire (May 2018 - May 2019). Results were compared to national and regional data on the general population using indirect standardization. Associations between clinical and job characteristics and work-related outcomes were analyzed with logistic regression (having a paid job) and negative binomial hurdle models (sick leave and presenteeism, i.e. restrictions while at work).

Results

215/262 (82%) patients of working-age (<65 y/o) had a paid job, corresponding to an age- and sex-adjusted employment ratio of 1.00 (95%CI 0.88;1.14). Patients worked 39.6±10.5h/week, and 49% (95%CI 42;56%) reported sick leave in the previous year, similar to the general population (39.7h/week, 42%). 56% reported presenteeism of median (IQR) 10% (0-20%). In multivariate analysis, functional impairment (BASFI) and health-related quality of life (HRQoL, EuroQoL-VAS) were associated with each work-related outcome, while contextual factors (education, physically demanding job) were positively associated with respectively having a paid job and presenteeism. Clinical characteristics showed no independent association with any of these outcomes.

Conclusion

Evidence from this academic cohort study does not support a work participation gap between SpA patients and the general population, but confirms the role of physical function, overall HRQoL, and education or job type as risk factors for adverse work outcomes.

Introduction

Spondyloarthritis (SpA) constitutes the prototype of a chronic inflammatory joint disease with a potential major individual and socio-economic burden [1]. Its impact results from an early age of onset, high proportion of co-morbidities, physical disability, psychological distress and reduced quality of life [2,3]. As a result, SpA patients often report work-related difficulties (e.g. productivity loss, sick leave, work disability) that contribute substantially to the disease-related costs, in particular indirect costs [4-6]. Nevertheless, the magnitude of the problem is partially country-dependent [7]. The international ASAS-COMOSPA study reported significant associations between being employed and indicators of socio-economic welfare on a country-level [8]. Even in countries with high healthcare expenditure, employment rates of SpA patients varied from 47% (South-Korea) to 83% (Canada); Belgium reported a crude rate of 68% (period 2013-2014, average disease duration of 13.7 years). Although biological DMARDs (bDMARDs) already made their appearance in SpA management at that time, several advances in diagnosis, management and treatment strategies have been made since. Altogether, patients are diagnosed and treated earlier nowadays, leading to better disease control and improved long-term clinical outcomes [9]. However, recent extended information about work participation of the Belgian SpA population, taking into account these advances, is currently lacking.

The paucity of up-to-date information has important consequences for SpA patients, who are usually diagnosed in a life phase that is characterized by decisions regarding family life, housing and career pathways [10]. Although every Belgian citizen is covered by a social security system provided by the government (e.g. income replacement in case of illness or disability), several private insurances are recommended to preserve living standards in case of income loss. Contrary to the social security system, which is based on solidarity, private insurance companies decide on acceptance and premiums according to the anticipated risk of a group of kindred insured persons. Applied to young people with SpA, this *segmentation* policy often implies an additional premium for or exclusion from a guaranteed income insurance because of a presumed higher risk of work disability [11]. In fact, risk assessment relies on historical data of AS patients, dating back to a pre-biologics era which cannot be considered to be applicable to the SpA population today [7,12]. A more up-to-date granular approach, tailored to the local

socio-economic situation in Belgium and considering the current disease management standards, is therefore warranted.

This has prompted us to investigate actual work participation of Belgian SpA patients, and to benchmark these data to the general population. Second, we aimed to identify determinants of work-related outcomes to facilitate an individualized risk assessment in the context of private insurances.

Patients and methods

Study population

This study was conducted in adult SpA patients who consulted a rheumatologist at Ghent University Hospital, a large regional hospital in Flanders (Dutch-speaking part of Belgium). All patients, who were diagnosed according to expert opinion and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial or peripheral SpA [13,14], were involved in a clinical care path (BelGian Inflammatory Arthritis and spoNdylitis cohorT, Be-GIANT), having started in 2010 and providing prospective standardized follow-up of newly diagnosed patients on a 6-months basis. Being an observational cohort of consecutive patients, Be-Giant mirrors daily clinical practice in an academic setting. Importantly, Belgian patients are free to consult a rheumatologist of their choice without the need for referral by a general practitioner, so access to tertiary care is not restricted.

Clinical data, including patient reported outcomes (PROs), pharmacological treatment, and laboratory markers, were collected as previously described [15]. PROs were used to assess disease activity (BASDAI, range 0-10, and AS Disease Activity Score (ASDAS)-CRP, high disease activity ≥2.1) [16,17], and impairment of activities and functions (BASFI, range 0-10, and HAQ-DI, range 0-3) [18,19]. Health-related quality of life (HRQoL) was quantified using the health utility index, according to the country-specific EuroQoL-5Determinants-5Levels (EQ-5D-5L) value set (range -0.53 to 1) [20,21] and the patient's self-reported global HRQoL through a visual analogue scale (EQ-VAS, range 0 = worst health to 100 = perfect health). Except for EQ-5D-5L and EQ-VAS, higher numbers on each scale indicate a worse status or outcome.

Work outcomes

Between May 2018 and May 2019, the treating rheumatologist cross-sectionally questioned patients' socio-economic status: educational level, current and past employment status, date of entry to the labor force, job status (manual worker, employee, civil servant, self-employed), job regimen (full-time, part-time), job type (predominant manual (blue collar) or non-manual (white collar) work, i.e. workplace physical demands as assessed by the patient), job sector, usual number of working hours per week, sick leave during the past year (number of episodes and days), reasons for not having a paid job, and duration and reason of work disability (if applicable). Patients completed a General Health Work Productivity and Activity Impairment (WPAI-GH) questionnaire, evaluating the impact of health problems on absenteeism (% of working hours lost due to absence from the work place) and presenteeism (% of productivity loss while at work) within a recall period of seven days [22]. A summary of the Belgian social security service is provided in Supplementary Data S1. Ethical approval was provided by the Ghent University Hospital (BC-07390). The study complies with the Helsinki Declaration; all patients provided written informed consent.

Statistical analysis

Statistical analyses were performed using R (version 3.6.1). Descriptive statistics of clinical characteristics and employment status were limited to patients of working age (<65 y/o), while the description of job features and work-related outcomes was restricted to patients with a paid job. Working and work-disabled SpA patients were compared with Wilcoxon-rank-sum test (continuous outcomes), and Chi-squared or Fisher's exact test (categorical outcomes). 95% confidence intervals around proportions were based on exact confidence limits from a binomial distribution. Work disability in relation to SpA diagnosis and the median time spent on the labor market was investigated through survival analysis. Associations between three work-related outcomes and socio-demographic, clinical and job-related factors were explored with binary logistic regression (outcome 1: having a paid job) or negative binomial hurdle (NBH) models (outcome 2: days of sick leave in the past year, and outcome 3: presenteeism in the past week) because of overdispersion and excess sampling zeros. NBH models consist of two parts. The first part models whether the outcome occurred or not (i.e. positive count or not), using a binary logit model. The second part models the counts (number of days of sick leave

respectively the percentage of presenteeism) in patients reporting these outcomes (i.e. positive counts once the threshold ('hurdle') of zero counts is crossed), using a truncated negative binomial model. Supplementary Data S2 describes the rationale and interpretation of NBH models in further detail. For all outcomes, determinants with a p-value <0.10 in univariate analysis were subsequently analyzed within their variable block (i.e. demographics and lifestyle, disease characteristics, disease activity and function, and job characteristics) using a stepwise selection (sequential replacement), after verification of non-collinearity. Variables that remained significantly associated with the outcome within each block ($p<0.05$) were considered in a multivariate model to assess their potential independent effect.

Source information on the general population

Following substantial regional differences in Belgium, we used Flemish socio-economic information for comparison of employment rate (applying indirect standardization of age [5-year categories] and sex), and average number of working hours per week (Belgian statistical office – 2019) [23]. Data on sick leave in the past year were deduced from the 2018 Health Interview Survey, a cross-sectional population-based survey with a net sample of 10.000 participants. Among others, the survey enquired about sick leave and the number of absent days in those having a paid job within a recall period of one year, similar to our patient survey [24]. National data on long-term work disability in 2019 were from the National Institute for Health and Disability Insurance [25]. Data on the average duration of working life in Belgium in 2019 were deduced from the Labor Force Survey (coordinated by Eurostat), that includes 91.000 Belgian individuals from the active population [26]. No national or regional WPAI data are available in our country.

Results

The 262/275 (95%) participants who were at a working age (<65 y/o) were predominantly male (56%) with a mean±SD age of 40.7±11.0 and median (IQR) symptom duration of 7.8 (4.7-15.7) years (Table 1). The majority was classified as axSpA (73%); disease activity was generally low as indicated by ASDAS-CRP (1.9±1.0) and BASDAI (3.2±2.2). Nearly half of the patients (48%) were treated with bDMARDs.

Employment status

In the working-age population, 215/262 (82%) patients had a paid job, i.e. had an employment contract or were self-employed (Figure 1). The majority was highly educated (69% completed post-secondary education) and worked full-time as an employee or civil servant (Table 1). Part-time work was mainly related to social demands or part-time vacancies (32/46, 70%), while 14/46 (30%) patients disclosed a personal decision to work part-time because of disease. SpA patients were represented in the secondary (e.g. industry), tertiary (e.g. commercial services) and quaternary (e.g. non-commercial services) economic sectors.

Taking into account the different distribution of age and sex in the general Flemish population, we calculated an adjusted employment rate of 76% corresponding to a standardized employment ratio (SER) of 1.00 (95%CI 0.88-1.14). Patients worked 39.6±10.5 hours per week, compared to an average of 39.7h (full-time) and 25.7h (part-time) for Flemish employees. The median time spent on the labor market was 42.1 years (95%CI 40.1-43.7), whereas the average duration of working life in Belgium and Europe was respectively 33.6 and 35.9 years in 2019.

Sick leave and presenteeism

In the working SpA population, 102/208 patients (49%, 95%CI 42-56%) reported sick leave in the previous year (n=7 missing), with a mean±SD and median (IQR) number of 7±22 and 0 (0-5) working days absent in all patients, and 15±30 and 5 (3-14) working days in patients reporting at least one episode of sick leave. Patients attributed 37/141 (26%) episodes of sick leave to SpA. As a reference, 42% of the working Flemish population reported sick leave in 2018, with an average duration of 11.1 days in the total working population and 26.4 days in those reporting sick leave, with no significant differences for stratification by age, sex, or education.

Absenteeism in the past 7 days according to the WPAI-GH was reported by 17/197 (9%) patients (n=18 missing data for WPAI), while any presenteeism was reported in 105/188 (56%) (n=9 with 100% absenteeism were not considered for presenteeism), with a median (IQR) of 10% (0-20%) in all patients and 20% (10-40%) in the subgroup reporting any presenteeism (Figure 2).

Determinants of work-related outcomes

Supplementary Table S3 shows the potential determinants (univariate analysis) of three work-related outcomes: (1) being (self-)employed (i.e. having a paid job), (2) sick leave in the previous year, and (3) presenteeism in the previous week. In multivariate analysis (Table 2), lower BASFI, higher EQ-VAS and high educational level were significantly associated with having a paid job. The association between BASFI and employment status was not significantly different in higher versus lower educated patients (p-value interaction term 0.24). A similar finding was observed for EQ-VAS, that also showed no significant interaction with educational level (p=0.61).

Younger age, female sex and lower EQ-VAS were significantly associated with the chance to report sick leave in the past year, while the number of absent days was primarily associated with higher BASFI in patients reporting any sick leave. Regarding presenteeism, both its occurrence and severity were significantly determined by BASFI and EQ-VAS, while ASDAS-CRP and *white collar* work were only significantly associated with the latter. In all models, clinical characteristics (including SpA subtype and specific SpA features) were not significantly associated with any of the work-related outcomes in multivariate analysis, although we observed a positive univariate association between e.g. shorter diagnostic delay or less spinal mobility restriction and having a paid job (Supplementary Table S3).

Work disability

Amongst the 47/262 (18%) SpA patients who were not engaged in paid work, 25 were work disabled (9.5% of the total population, 95%CI 6.5-13.7%). Other reasons for not having a paid job (i.e. no employment contract or not self-employed) are depicted in Figure 1. At the time of the survey, the duration of work disability was 5.8±4.2 years. As 50% of cumulative work disability was registered within 1.4 years after the diagnosis, and long-term disability per definition requires minimally one year of work incapacity, the onset often occurred prior or shortly after the diagnosis. As a reference, over 447.000 people (6.7% of the Belgian population aged 20-64 years) were work disabled in 2019.

Patients on long-term work disability because of SpA (n=20/25, 80%) were significantly older and had a longer symptom duration than those with a paid job, but age at diagnosis and diagnostic delay were

not significantly different (Table 3). They reported higher disease activity, more functional limitations and a lower HRQoL, reflected in different domains (Figure 3). Fewer patients were highly educated (25% vs. 69%) or previously performed *white collar* work (15% vs. 55%) compared to patients with a paid job, while they more often worked as a manual worker instead of employee/self-employed person.

Discussion

This real-world study is the first to investigate work participation amongst Belgian SpA patients in a biologics era. In patients receiving optimal care according to current diagnostic and therapeutic guidelines, we found similar employment rates, weekly working hours, and incidence of sick leave compared to the general population. Work outcomes universally depend on self-reported physical functioning and overall health status, thus advocating timely and tight disease control to support SpA patients in their working environment.

SpA often develops at a work-productive age. Although international and historical data suggest significant work impairment in this population [27], we hypothesized that early diagnosed and correctly treated SpA patients in Belgium currently have similar work outcomes compared to their healthy peers. Indeed, our data show an age- and sex-adjusted employment rate of 76% in SpA, corresponding to an SER of 1.00. Population-based studies in Belgium are lacking, but few studies previously investigated work participation alongside cost-of-illness analyses in SpA. In 1996, an age- and sex-adjusted employment rate of 72% was reported in Belgian AS patients taking part in the OASIS cohort [7]. The small sample size (n=26 of which 15 employed) with differences in patient characteristics (AS vs. SpA), different eras (pre- vs. post-biologics), and distinct definitions of the active population (i.e. exclusion of students, homemakers and early retirees) however preclude comparison to our results. In the same study, the adjusted employment rates in Belgium's neighboring countries were 55% (Netherlands) and 72% (France), while the more recent ASAS-COMOSPA study (2013-2014) reported crude employment rates of respectively 78% and 65% compared to 68% in Belgium [7,8]. These findings illustrate that not only clinical and methodological heterogeneity, but also socio-economic prosperity and differences in access

to medical care and social security have a significant impact on work participation, meanwhile emphasizing the importance of comparison to up-to-date national figures [28-30].

Working SpA patients reported a similar incidence of sick leave compared to the general population (49% vs. 42%), while they incurred fewer days of absence from work. Contrary to earlier studies, sick leave was not significantly associated with disease activity or physical functioning, which probably relates to the trivial (non-SpA-related) causes reported in this population [8,31-34]. The incidence of sick leave declined compared to 1996, as 73% of Belgian AS patients reported sick leave (all causes) at that time, with twice as many days of absence from work compared to the general population [7]. The decline in sick leave over time must have a major impact on indirect costs or productivity costs for society, also because sick leave generally predicts recurrent sick leave and increases the risk of permanently leaving the labor force [32,33]. In addition, the incidence and length of future sick leave is also known to be determined by presenteeism [34], which was reported by approximately half of our SpA cohort with a median of 10%. Our findings seem more optimistic than similar international studies (mean presenteeism 22-32%) [35,36], but again, country-specific socioeconomic and healthcare factors are known to influence these outcomes [29]. On a European level, 40-45% of the working population reports presenteeism on an annual basis, which is not negligible either [37]. Note that presenteeism refers to patients' perceived restrictions while being at work, which is not necessarily synonymous for objective productivity loss.

Having a paid job and presenteeism were primarily associated with disease activity (univariate) and functional limitations, which has consistently been observed in SpA [35,36]. The strong association with HRQoL also aligns with literature, although a cause-effect relationship cannot be deduced from our cross-sectional observations [33]. Furthermore, our data support the biopsychosocial model, with a prominent role of contextual factors in work participation and presenteeism. The importance of education for having a paid job probably reflects its multifactorial impact (e.g. job type, coping abilities and self-management skills), while a mismatch between functional capacities and job requirements may be accountable for more (severe) presenteeism in patients performing physically demanding jobs [33,38,39]. Finally, an interesting finding is the lack of association between biological/clinical

characteristics and work-related outcomes in the multivariate analysis. Although one could expect increased work impairment with increasing symptom duration and more extensive structural joint damage [30], this was not fully supported by our data. In fact, the univariate negative association between employment status and diagnostic delay or spinal mobility restriction was overruled by the comprehensive effect of functional limitations in multivariate analysis. In addition, we did not observe a positive impact of bDMARD treatment, although proven beneficial in clinical trials addressing presenteeism and sick leave [40,41], with however less convincing impact on employment status and work disability [42,43]. Potentially, in this real-world observational study, therapeutic choices act as a surrogate marker of disease severity, hence suggesting confounding by indication. It has been shown that a prompt reduction of disease activity, rather than the use of biologics in itself, is crucial to ensure a positive work outcome in SpA patients [44].

Musculoskeletal conditions are one of the leading causes of long-term work disability in Belgium, besides neuropsychiatric disorders [25]. In our SpA cohort, 9.5% of patients were work disabled (all causes), which equals the data in AS patients in 1996 [7,45]. This is remarkable considering the yearly increase of work disability (4-7%) in the Belgian population over the last 5 to 10 years [25]. Work disabled SpA patients were older, had longer symptom duration and more spinal mobility restriction compared to patients engaged in paid work, pointing towards a decisive role for cumulative impairment [45,46]. They also reported higher disease burden and lower HRQoL, even many years after labor force withdrawal, which should not be disregarded [45-47]. It is however unlikely that medical interventions alone will suffice to support return to work, as psychosocial factors are known to prevail over biomedical determinants when predicting long-term absence from work [48]. The onset of work disability was concentrated prior or shortly after diagnosis, which likely relates to high disease activity and sudden functional restrictions associated with the development of the disease, making this period crucial for preventing permanent withdrawal from the labor force. Finally, our data showed a role for job-related factors (e.g. physically demanding jobs as a manual worker), so prompt vocational rehabilitation may prove beneficial in these cases.

The findings of our study have implications for different stakeholders. First, *rheumatologists* should understand the important socio-economic consequences of timely and effective (non-)pharmacological interventions *('window of opportunity'* for continued work participation), (in)directly contributing to the maintenance of at-work productivity, sick leave prevention, and reduction of indirect costs. Potential work-related problems should thus be inquired at the initial diagnosis. Our observations also underscore the key importance of functional limitations, and call for additional non-pharmacological interventions by a multidisciplinary team of healthcare professionals to alleviate these constraints in the work context [49,50]. Although in Belgium it is yet uncommon that these professionals are involved in the follow-up of SpA patients, a recent act (12 Dec 2021) reinforced the role of a "return-to-work coordinator" who should facilitate work re-integration of people on long-term sick leave or work disability. Second, *private insurance companies* should shift their focus from disease characteristics to functional status and contextual factors when appraising patients' risk for adverse work outcomes, taking into account that SpA patients currently perform similar or even better than the general population. However, the timing of contracting insurances is crucial, as long-term work disability is mostly incurred prior or shortly after the diagnosis. Third, from a *societal perspective*, work disability may occur early in a patient's career, thus resulting in many potential work-years lost. Socio-economic interventions that aim to prolong individuals' careers should therefore also target this young patient population besides the older general working population. Fourth, *employers* may be re-assured that sick leave and at-work productivity loss in the SpA population is limited, provided that patients' functional capacities are being respected. Finally, *patients* should be reinforced to pursue a paid job or alternatively engage in unpaid work, following its positive association with HRQoL. Working contributes to autonomy and self-esteem, provides a social network, and mitigates the financial burden of a chronic disease, despite the challenging balance between work demands and energy levels.

The major strengths of this study consist of the comprehensive and updated description of work-related outcomes in SpA patients, the real-world setting reflecting current disease management in daily practice, and the comparison with national reference data. Several limitations should also be mentioned. First, the inclusion in an academic outpatient clinic may impact external validity, and care should be taken when

generalizing these observations to the Belgian SpA population. A university hospital attracts highly educated patients, possibly overestimating employment and at-work productivity. At the same time, it might select those with more severe disease, as was shown in a Swiss study of axial SpA patients who were eligible for treatment with biologics [51]. Nevertheless, the effect size of both potential sources of bias is unknown, and data comparing patient characteristics between academic and private centers in Belgium are lacking. Second, all work-related information was patient-reported and not verified by external sources. Third, the cross-sectional design did not allow to infer causal relationships. Fourth, the recall period for sick leave was one year, both in our study and in the reference population, which could have been too long for a reliable estimation. Finally, our cohort is relatively small compared to large population-based studies, making some subpopulations (e.g. patients with SpA-related work disability) too small for confounder-adjusted analysis.

In conclusion, our data from an academic cohort study do not support previous evidence that SpA patients, when diagnosed and treated according to current disease management standards, experience excess work impairment, sick leave and presenteeism compared to the general population. Although successful participation in paid work results from a complex interaction between personal and contextual factors, our study underscores the essential role of disease-related functional impact, meanwhile providing insights into potential strategies to support job-retention and productivity.

Tables & Figures

Table 1: Characteristics of SpA patients at a working age and the subgroup with a paid job.

	SpA population at a working age, <65y/o (n = 262)	SpA patients with a paid job (n = 215)
Male	148 (56%)	121 (56%)
Age (y)	40.7±11.0	40.5±10.3
Current smoker	41 (16%)	33 (16%)
Symptom duration (y) †	7.8 (4.7 – 15.7)	7.5 (4.5 – 15.1)
Age at diagnosis (y)	32.6±11.1	32.8±10.8
Diagnostic delay (y) †	1.1 (0.2 – 5.0)	1.0 (0.2 – 4.1)
HLA B27 positive	170 (70%)	143 (72%)
ASAS classification criteria		
• Axial SpA	192 (73%)	156 (73%)
• Peripheral SpA	70 (27%)	59 (27%)
Radiographic sacroiliitis [a]	63 (33%)	50 (32%)
History of extra-musculoskeletal manifestations	95 (36%)	78 (36%)
• Flare in previous 6 months	16 (6%)	14 (7%)
History of peripheral manifestations	120 (46%)	95 (44%)
• Flare in previous 6 months	18 (7%)	12 (6%)
78 TJC †	0 (0 – 0)	0 (0 – 0)
76 SJC †	0 (0 – 0)	0 (0 – 0)
BASMI	1.4±1.5	1.3±1.4
CRP (mg/L) †	1.7 (0.9 – 4.7)	1.5 (0.9 – 4.6)
ASDAS-CRP	1.9±1.0	1.8±0.9
BASDAI	3.2±2.2	2.8±2.0
BASFI	2.3±2.2	1.8±1.9
HAQ-DI	0.35±0.40	0.27±0.34
EQ-5D-5L	0.79±0.22	0.82±0.19
EQ-VAS	75±16	77±14
Medication use		
• NSAID	126 (49%)	105 (50%)
• csDMARD	47 (18%)	37 (17%)
• bDMARD	123 (48%)	97 (46%)
Educational level [b]		
• Low	100 (38%)	67 (31%)
• High	162 (62%)	148 (69%)
Job type		
• Blue collar (manual labor)	-	97 (45%)
• White collar (non-manual labor)	-	118 (55%)
Job regimen		
• Full-time	-	169 (79%)
• Part-time	-	46 (21%)
Job status		
• Employee/civil servant	-	154 (72%)
• Manual worker	-	32 (15%)
• Self-employed	-	29 (13%)
Top 3 job sectors	-	Technical
	-	Healthcare
	-	Administration

Categorical variables are presented as n (%), continuous variables as mean±SD except for symptom duration, diagnostic delay, 78 TJC, 76 SJC and CRP: presented as median (IQR) †.

[a] Radiographic sacroiliitis according to the modified New York criteria was only assessed in patients classified as axial SpA.

[b] Educational level: low = primary or secondary school, high = university or equivalent.

Data were missing for smoking status (n=5), HLA B27 (n=19), TJC/SJC (n=1), BASMI (n=17), CRP (n=48), ASDAS-CRP (n=57), BASDAI/BASFI (n=4), HAQ-DI (n=5), EQ-5D-5L/EQ-VAS (n=7), medication use (n=4).

Abbreviations: ASAS, Assessment of SpondyloArthritis international Society; TJC, tender joint count; SJC, swollen joint count; ASDAS, Ankylosing Spondylitis Disease Activity Score; HAQ-DI, health assessment questionnaire - disability index; EQ-5D-5L, EuroQoL-5dimensions-5levels; EQ-VAS, EuroQoL visual analogue scale; NSAID, non-steroidal anti-inflammatory drug; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; bDMARD, biological DMARD.

Table 2: Multivariate associations of sociodemographic, clinical and job-related features with work-related outcomes.

	Outcome 1: Employed (n = 262)		Outcome 2: Sick leave (n = 208) [a]				Outcome 3: Presenteeism (n = 188) [a]			
			Zero-hurdle model		Count model		Zero-hurdle model		Count model	
	OR (95% CI)	p-value	OR (95% CI)	p-value	IRR (95% CI)	p-value	OR (95% CI)	p-value	IRR (95% CI)	p-value
1) **Demographics and lifestyle**										
Male sex	-		0.5 (0.3 – 0.9)	**0.03**	-		-		-	
Age, y	-		1.0 (0.9 – 1.0)	**0.04**	1.0 (1.0 – 1.1)	0.06	-		-	
Current smoker	-		-		-		-		1.0 (0.7 – 1.3)	0.80
2) Disease characteristics										
Symptom duration, short [b]	-		†		-		-		-	
Age at diagnosis, y	-		-		1.0 (1.0 – 1.0)	0.80	-		-	
Diagnostic delay, y	†		-		-		-		-	
HLA B27 positive	-		-		-		-		1.0 (0.8 – 1.3)	0.97
ASAS axial SpA classification	-		-		†		-		-	
Radiographic sacroiliitis [c]	-		-		-		-		-	
Peripheral manifestations	-		-		†		-		-	
Extra-musculoskeletal manifestations	-		-		†		-		-	
BASMI	0.9 (0.7 – 1.1)	0.32	-		-		-		-	
bDMARD treatment	-		-		-		-		-	
3) Disease activity, function, HRQoL										
ASDAS-CRP	†		†		†		†		1.2 (1.1 – 1.4)	**0.005**
BASDAI	*		*		*		*		*	
BASFI	0.8 (0.6 – 1.0)	**0.03**	-		1.4 (1.2 – 1.7)	**<0.001**	2.1 (1.4 – 3.2)	**<0.001**	1.1 (1.1 – 1.2)	**<0.001**
HAQ-DI	*		†		*		*		*	
EQ-VAS [d]	1.5 (1.1 – 1.9)	**0.005**	0.8 (0.6 – 0.9)	**0.02**	-		0.6 (0.4 – 0.9)	**0.01**	0.9 (0.8 – 1.0)	**0.01**
4) Education & job characteristics										
Educational level, high	3.3 (1.4 – 7.5)	**0.005**	-		-		-		†	
Job type, white collar	†		-		-		0.5 (0.2 – 1.1)	0.08	0.8 (0.6 – 0.9)	**0.01**
Job regimen, full time	-		-		-		†		†	
Job status, employee/self-employed	†		-		-		-		†	

[a] Negative binomial hurdle models (outcome 2 and 3) are presented as 2 parts: the zero-hurdle model should be interpreted as the odds of showing the outcome of interest (i.e. sick leave or presenteeism); the count model is only applied if the hurdle for zero counts is exceeded and should be interpreted as an incidence rate ratio (IRR).

[b] Symptom duration was dichotomized (long versus short) as > or ≤7.8 years, the median symptom duration in patients <65 y/o.

[c] Radiographic sacroiliitis according to the Modified New York criteria was only assessed in patients classified as axial SpA.

[d] EQ-VAS was analyzed on a scale 0-10.

– Not retained after univariate analysis ($p \geq 0.10$). *$p<0.10$ in univariate analysis but not retained for stepwise selection because of collinearity between ASDAS-CRP and BASDAI, and between BASFI and HAQ-DI.

†Not retained within the variable block after stepwise selection ($p \geq 0.05$).

Abbreviations: see Table 1. Significant p-values ($p<0.05$) are in bold.

Table 3: Clinical characteristics of SpA patients with a paid job and those reporting SpA-related work disability.

	Have a paid job (n = 215)	Work disabled because of SpA (n = 20)	p-value
Male	121 (56%)	11 (55%)	1
Age (y)	40.5±10.3	46.6±10.5	**0.02**
Current smoker	33 (16%)	5 (25%)	0.34
Symptom duration (y) †	7.5 (4.5 – 15.1)	12.4 (7.6 – 27.5)	**0.01**
Age at diagnosis (y)	32.8±10.8	35.5±12.6	0.32
Diagnostic delay (y) †	1.0 (0.2 – 4.1)	1.3 (0.5 – 7.9)	0.16
HLA B27 positive	143 (72%)	11 (55%)	0.19
ASAS axSpA classification	156 (73%)	14 (70%)	1
Radiographic sacroiliitis [a]	50 (32%)	7 (50%)	0.24
History of extra-musculoskeletal manifestations	78 (36%)	7 (35%)	1
History of peripheral manifestations	95 (44%)	10 (50%)	0.79
BASMI	1.3±1.4	2.7±2.0	**<0.001**
ASDAS-CRP	1.8±0.9	2.6±0.9	**0.002**
BASDAI	2.8±2.0	5.1±1.6	**<0.001**
BASFI	1.8±1.9	5.0±1.4	**<0.001**
HAQ-DI	0.27±0.34	0.91±0.37	**<0.001**
EQ-5D-5L	0.82±0.19	0.55±0.31	**<0.001**
EQ-VAS	77±14	56±19	**<0.001**
bDMARD use	97 (46%)	13 (65%)	0.16
Educational level, high [b]	148 (69%)	5 (25%)	**<0.001**
Job type, white collar	118 (55%)	3 (15%)	**0.001**
Job regimen, full time	169 (79%)	12 (60%)	0.09
Job status, employee/self-employed	183 (85%)	12 (60%)	**0.01**

Categorical variables are presented as n (%), continuous variables as mean±SD except for symptom duration and diagnostic delay: presented as median (IQR) †. Significant p-values ($p<0.05$) are in bold.

[a] Radiographic sacroiliitis according to the modified New York criteria was only assessed in patients classified as axial SpA.

[b] Educational level: low = primary or secondary school, high = university or equivalent.

Data were missing for smoking status (n=5), HLA B27 (n=16), BASMI (n=15), ASDAS-CRP (n=51), BASDAI/BASFI (n=4), HAQ-DI (n=5), EQ-5D-5L (n=6), EQ-VAS (n=6), bDMARD treatment use (n=3).

Abbreviations: see Table 1.

Figure 1: Overview of different socio-economics states in the SpA population of working age.

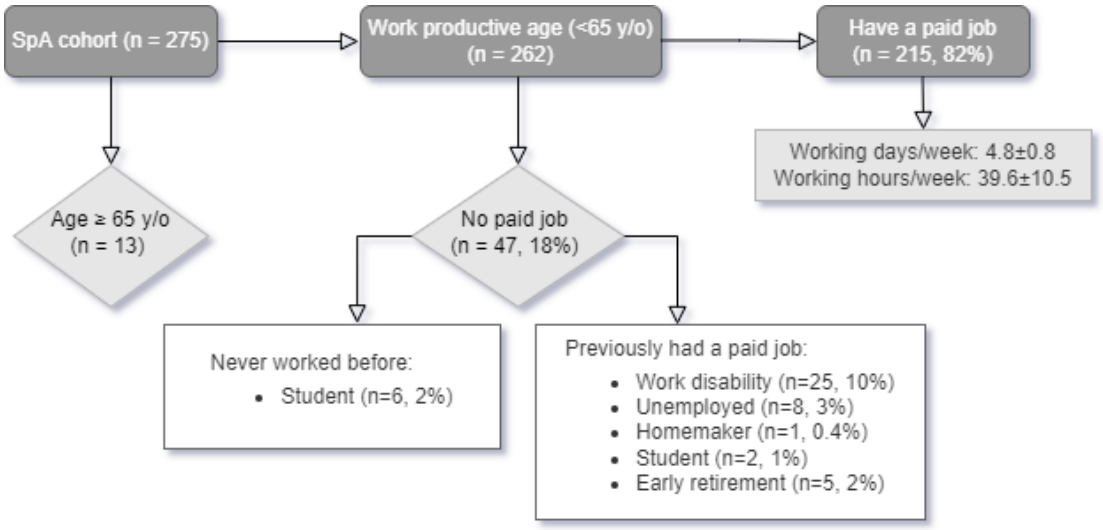


Figure 2: Proportion of working SpA patients reporting absenteeism (%) and presenteeism (%) in the previous week.

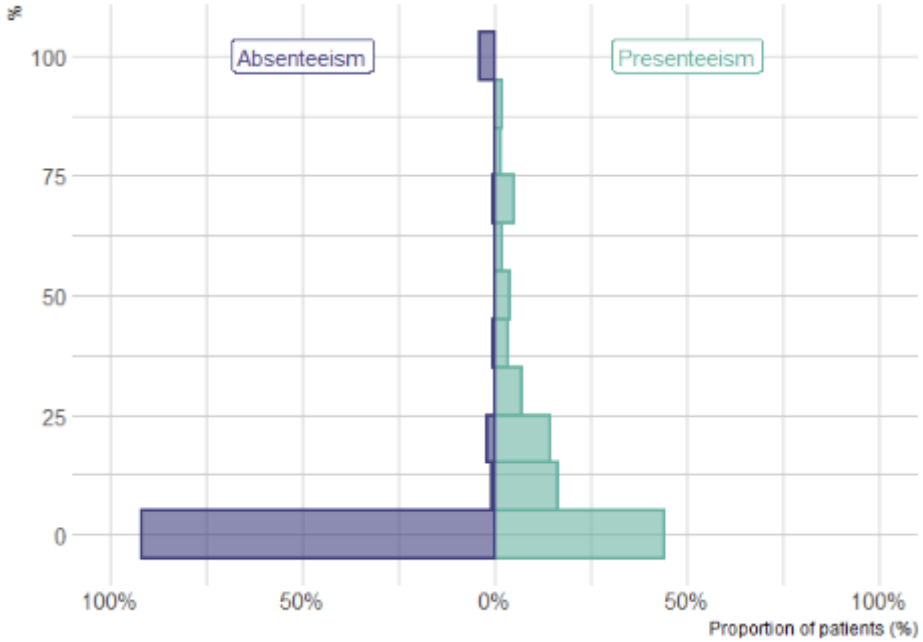
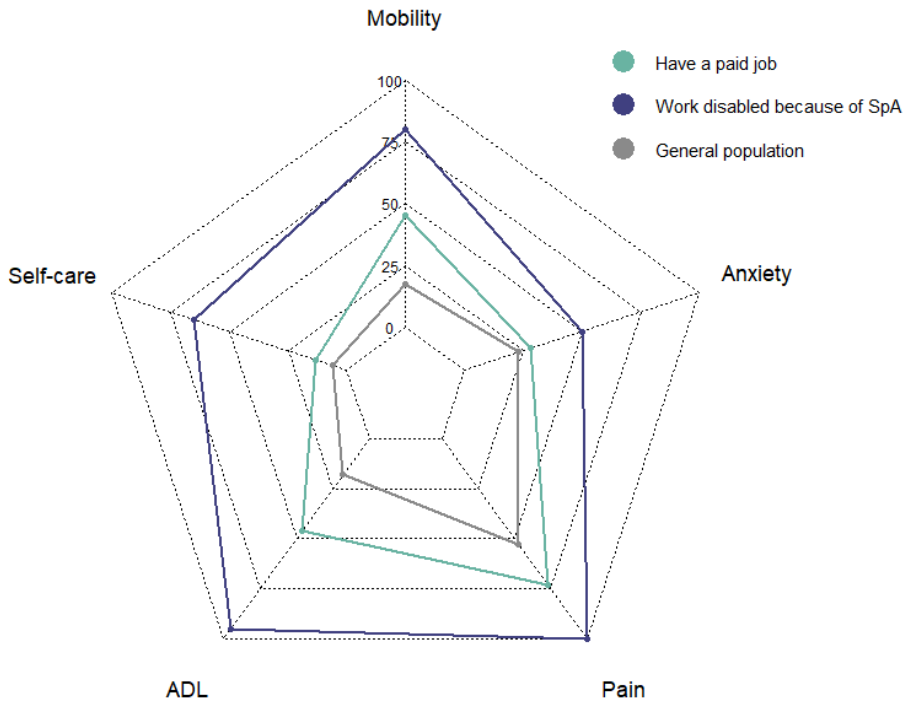


Figure 3: Proportion of patients (%) indicating any difficulty in the five domains of the EQ-5D-5L.

Comparison between patients with a paid job and those work disabled because of SpA versus the general Flemish population. EQ-5D-5L, EuroQoL-5dimensions-5levels; ADL, activities of daily living.



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Author contributions

Study conception and design: AB, PC, FVdB. Acquisition of data: ADC, LiD, TR, ID, LaD. Analysis: ADC, ID, LaD. All authors were involved in interpretation of the data, drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. ADC had full access to all data in the study and takes responsibility for its integrity and the accuracy of the data analysis.

Conflicts of interest

ADC, LiD, TR, ID, LaD, SD, XJ, and PC declare no conflicts of interest. AB reports grants from AbbVie (paid to institution), speakers fees from Novartis (paid to institution), and participation on advisory board from Lilly and AbbVie (paid to institution). DE reports speakers fees and/or consultancy fees from AbbVie, Eli Lilly, Galapagos, Janssen, Novartis, Pfizer and UCB. FVdB reports consulting fees from AbbVie, Amgen, Eli Lilly, Galapagos, Janssen, Moonlake, Novartis, Pfizer, and UCB.

Data sharing statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Patient involvement

Patients were not involved in the design or the conduct of this study.

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Supplementary material

Supplementary Data S1: Summary of social security service in Belgium

In Belgium, employees benefit from a guaranteed income (100% gross wage) covered by their employer during the first month of sick leave, provided that their incapacity to work has been certified by a physician. For manual workers, this period is limited to two weeks (respectively 100% and 85% of the gross wage during the first and second week), after which he/she receives a sickness benefit that is co-payed by the employer and the health insurance fund. When sick leave lasts longer than one month (in Belgium referred to as *primary incapacity to work*), one receives an income replacement from the health insurance fund (60% of a capped wage). From the second year onwards, the medical council of the national social security organization can grant work disability (*invalidity*), with disability benefits ranging from 40% to 65%. During this period, part-time work can be allowed by the consulting physician of the health insurance fund. In that way, people combine their salary with a benefit but remain on sick leave. The social security system for self-employed and civil servants differs slightly from employees.

Supplementary Data S2: Negative binomial hurdle models

Outcomes such as the number of days of sick leave, absenteeism and presenteeism are count data (i.e. non-negative integer values) and are generally not normally distributed. Their distribution often shows zero-inflation (i.e. it contains a large amount of zeros) and overdispersion (i.e. the variance is greater than the mean, so the histogram is severely right-skewed as illustrated in Figure 2 of the manuscript).

One solution to model these outcomes is to transform the outcome into two or more categories, and to use binary or ordinal logistic regression models. However, some pieces of information are inevitably lost using such an approach.

Poisson regression models are commonly used to model count data. Although they are flexible to some extent, overdispersion of the data will lead to unreliable results. Negative binomial regression models are useful is such situation, as they do not assume that the conditional variance is equal to the conditional mean. The interpretation of the coefficients is the same in a Poisson or negative binomial model: the outcome variable is conceptualized as a rate. The exponentiated coefficients are called Incidence Rate Ratios (IRR), which should be interprered similar to an odds ratio (OR). Each unit change in the predictor causes $(e^{\beta}) * 100\%$ increase or decrease in the outcome rate (with β the predictor's coefficient).

Zero-inflated or hurdle models can provide a solution for zero-inflated distributions. They differ in the way they conceptualize the zeros. In zero-inflated distributions, zeros theoretically stem from two different sources: "sampling zeros" and "structural zeros". Sampling zeros are zeros that occur because of individuals who were potentially exposed to the outcome but did not experience it (e.g. patients with a paid job who are at risk for sick leave but explicitly reported that they had 0 days of sick leave).

Structural zeros arise from subjects that will always produce zero counts because they are not at risk for the outcome of interest (e.g. students that do not actively engage in paid work will also report 0 days of sick leave, because they are not at risk for the outcome). In our study, all zeros were sampling zeros; therefore a hurdle model was preferred over a zero-inflated model.

The distribution of the outcomes in our study (resp. number of days of sick leave and presenteeism) show zero-inflation (due to sampling zeros) and overdispersion. Therefore, a negative binomial hurdle model (NBH) was preferred. NBH models are two-component models: the probability of occurrence is modeled separately from the frequency of occurrence. The first component models the probability of occurrence of zero versus positive counts (called "zero-hurdle model"), and is in fact a binomial regression model, that investigates the relationship between a certain predictor (e.g. male sex) and the probability of the outcome (e.g. reporting sick leave in the past year no/yes, which is identical to the number of days of absence from work 0 or >0). The exponentiated coefficients are interpreted as an odds ratio (OR). The second component (called the "count model") models the positive counts (e.g. the number of days of sick leave) once the threshold ('hurdle') of zero counts is crossed. The exponentiated coefficients are called Incidence Rate Ratios (IRR).

Reference: Feng CX. A comparison of zero-inflated and hurdle models for modeling zero-inflated count data. Journal of Statistical Distributions and Applications 2021;8(1):8.

Supplementary Table S3: Univariate associations of sociodemographic, clinical and job-related features with work-related outcomes. Negative binomial hurdle models (outcome 2 and 3) are presented as 2 parts: the zero-hurdle model should be interpreted as the odds of showing the outcome of interest (i.e. sick leave or presenteeism); the count model is only applied if the hurdle for zero counts is exceeded and should be interpreted as an incidence rate ratio (IRR).

	Outcome 1: Employed (n=262)		**Outcome 2: sick leave (n=208) [a]**				**Outcome 3: presenteeism (n=188) [a]**			
			Zero-hurdle model		**Count model**		**Zero-hurdle model**		**Count model**	
	OR (95% CI)	p-value	OR (95% CI)	p-value	IRR (95% CI)	p-value	OR (95% CI)	p-value	IRR (95% CI)	p-value
1) **Demographics and lifestyle**										
Male sex	1.0 (0.5 – 1.8)	0.88	0.6 (0.3 – 1.0)	**0.04**	1.2 (0.6 – 2.5)	0.58	1.1 (0.6 – 2.0)	0.69	0.8 (0.6 – 1.1)	0.11
Age, y	1.0 (1.0 – 1.0)	0.58	1.0 (0.9 – 1.0)	**0.02**	1.0 (1.0 – 1.1)	**0.02**	1.0 (1.0 – 1.0)	0.98	1.0 (1.0 – 1.0)	0.62
Current smoker	0.9 (0.4 – 2.0)	0.78	1.6 (0.8 – 3.5)	0.21	1.5 (0.6 – 3.7)	0.37	0.6 (0.3 – 1.4)	0.29	1.5 (1.0 – 2.3)	**0.04**
2) Disease characteristics										
Symptom duration, short [b]	1.4 (0.8 – 2.7)	0.26	1.7 (1.0 – 2.9)	**0.07**	1.4 (0.7 – 2.8)	0.38	0.6 (0.3 – 1.1)	0.10	0.9 (0.7 – 1.2)	0.48
Age at diagnosis, y	1.0 (1.0 – 1.0)	0.60	1.0 (1.0 – 1.0)	0.11	1.0 (1.0 – 1.1)	**0.02**	1.0 (1.0 – 1.0)	0.77	1.0 (1.0 – 1.0)	0.96
Diagnostic delay, y	0.9 (0.9 – 1.0)	**0.02**	1.0 (0.9 – 1.0)	0.61	0.9 (0.9 – 1.0)	0.10	1.0 (1.0 – 1.1)	0.44	1.0 (1.0 – 1.0)	0.98
HLA B27 positive	1.6 (0.8 – 3.2)	0.17	1.2 (0.7 – 2.3)	0.49	0.7 (0.3 – 1.5)	0.40	1.0 (0.5 – 2.0)	0.98	0.8 (0.6 – 1.0)	**0.07**
ASAS axial SpA classification	0.8 (0.4 – 1.7)	0.58	0.8 (0.4 – 1.4)	0.40	0.5 (0.2 – 1.1)	**0.09**	1.6 (0.9 – 3.1)	0.14	1.2 (0.9 – 1.6)	0.33
Radiographic sacroiliitis [c]	0.8 (0.4 – 1.8)	0.64	0.7 (0.3 – 1.3)	0.25	0.9 (0.4 – 2.1)	0.80	1.0 (0.5 – 2.1)	0.99	0.9 (0.7 – 1.2)	0.50
Peripheral manifestations	0.7 (0.4 – 1.3)	0.26	1.4 (0.8 – 2.3)	0.28	1.9 (0.9 – 3.7)	**0.07**	0.8 (0.4 – 1.4)	0.32	1.0 (0.8 – 1.3)	0.96
Extra-musculoskeletal manifestations	1.0 (0.5 – 1.9)	0.99	0.8 (0.5 – 1.5)	0.51	2.1 (1.0 – 4.3)	**0.05**	1.4 (0.8 – 2.6)	0.27	1.0 (0.8 – 1.4)	0.80
BASMI	0.8 (0.6 – 0.9)	**0.003**	0.9 (0.7 – 1.1)	0.38	1.4 (0.9 – 2.4)	0.16	1.0 (0.8 – 1.3)	0.77	1.1 (1.0 – 1.2)	0.15
bDMARD treatment	0.7 (0.4 – 1.3)	0.24	0.8 (0.5 – 1.4)	0.42	1.4 (0.7 – 2.8)	0.34	1.3 (0.7 – 2.3)	0.41	1.1 (0.9 – 1.5)	0.37
3) Disease activity, function, HRQoL										
ASDAS-CRP	0.5 (0.3 – 0.7)	**<0.001**	1.5 (1.0 – 2.1)	**0.03**	1.5 (1.0 – 2.3)	**0.04**	3.2 (1.9 – 5.4)	**<0.001**	1.7 (1.5 – 1.9)	**<0.001**
BASDAI	0.7 (0.6 – 0.8)	**<0.001**	1.2 (1.0 – 1.3)	**0.04**	1.2 (1.0 – 1.5)	**0.03**	2.0 (1.6 – 2.6)	**<0.001**	1.3 (1.2 – 1.3)	**<0.001**
BASFI	0.6 (0.5 – 0.7)	**<0.001**	1.1 (1.0 – 1.3)	0.10	1.5 (1.2 – 1.8)	**<0.001**	2.1 (1.6 – 2.8)	**<0.001**	1.3 (1.2 – 1.3)	**<0.001**
HAQ-DI	0.1 (0.0 – 0.2)	**<0.001**	2.2 (1.0 – 4.9)	**0.07**	6.3 (2.0 – 19.4)	**<0.001**	39.1 (9.1 – 167.1)	**<0.001**	2.6 (1.9 – 3.6)	**<0.001**
EQ-VAS [d]	1.7 (1.4 – 2.1)	**<0.001**	0.8 (0.6 – 0.9)	**0.009**	0.9 (0.6 – 1.2)	0.42	0.4 (0.3 – 0.6)	**<0.001**	0.8 (0.7 – 0.8)	**<0.001**
4) Education & job characteristics										
Educational level, high	5.2 (2.6 – 10.4)	**<0.001**	1.3 (0.7 – 2.4)	0.38	0.7 (0.3 – 1.4)	0.28	0.7 (0.4 – 1.4)	0.36	0.7 (0.6 – 1.0)	**0.02**
Job type, white collar	3.8 (1.8 – 8.1)	**<0.001**	0.9 (0.5 – 1.6)	0.80	0.6 (0.3 – 1.2)	0.18	0.4 (0.2 – 0.8)	**0.008**	0.7 (0.5 – 0.9)	**0.002**
Job regimen, full time	1.5 (0.7 – 3.2)	0.27	0.7 (0.4 – 1.3)	0.25	0.6 (0.3 – 1.4)	0.28	0.5 (0.2 – 1.0)	**0.06**	0.7 (0.5 – 1.0)	**0.03**
Job status, employee/self-employed	4.0 (1.9 – 8.2)	**<0.001**	0.5 (0.2 – 1.2)	0.13	0.5 (0.2 – 1.3)	0.15	0.5 (0.2 – 1.3)	0.19	0.6 (0.4 – 0.9)	**0.009**

[a] Negative binomial hurdle models (outcome 2 and 3) are presented as 2 parts: the zero-hurdle model should be interpreted as the odds of showing the outcome of interest (i.e. sick leave or presenteeism); the count model is only applied if the hurdle for zero counts is exceeded and should be interpreted as an incidence rate ratio (IRR).

[b] Symptom duration was dichotomized (long versus short) as > or ≤7.8 years, the median symptom duration in patients <65 y/o.

[c] Radiographic sacroiliitis according to the Modified New York criteria was only assessed in patients classified as axial SpA.

[d] EQ-VAS was analyzed on a scale 0-10.

Abbreviations: ASAS, Assessment of SpondyloArthritis international Society; bDMARD, biological disease-modifying anti-rheumatic drugs; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein; HAQ-DI, health assessment questionnaire - disability index; EQ-VAS, EuroQoL visual analogue scale.

Significant p-values in univariate analysis (p<0.10) are in bold.