Understanding the Disease Burden of Unemployed Patients with Axial Spondyloarthritis. Results of the Spanish Atlas 2017

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Running head: Unemployed axSpA Patients' Burden

Authors:

Marco Garrido-Cumbrera, Prof. PhD. ORCID Id 0000-0001-9727-1189

Eduardo Collantes-Estevez, MD. ORCID Id 0000-0002-7647-6289

Victoria Navarro-Compán, MD. ORCID Id 0000-0002-4527-852X

Pedro Zarco-Montejo, MD. ORCID Id 0000-0002-3039-187X

Carlos Sastre, MSc. ORCID Id 0000-0002-1577-7838

José Correa-Fernández, MSc. ORCID Id 0000-0002-7788-5391

Sergio Sanz-Gómez, MSc. ORCID Id 0000-0001-6801-0836

Pedro Plazuelo-Ramos, Mr. ORCID Id N/A

Jordi Gratacos, MD. ORCID Id 0000-0002-7647-6289

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Corresponding author: Marco Garrido Cumbrera, Centro Internacional. Av de la Ciudad Jardín, 20, 22, 41005 Sevilla (Spain); phone number +34 955 420 796; mcumbrera@us.es

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ABSTRACT

Objective: To evaluate differences in sociodemographic factors and patient-reported outcomes (PROs) between unemployed and employed axSpA patients and to explore work-related issues.

Methods: Data through online survey from 680 unselected patients of the Spanish Atlas of Axial Spondyloarthritis were analysed in 2017. Active workforce participants were divided into employed and unemployed according to International Labour Organization standards. Sociodemographic characteristics, PROs [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and psychological distress through General Health Questionnaire GHQ-12 (0-12)] were assessed. Logistic regression analysis was used to evaluate the association with unemployment status.

Results: 415 (63.6%) patients were categorised in the active population, of which 325 (78.3%) were employed and 90 (21.7%) unemployed. 62.8% (N = 54) of unemployed declared that their joblessness was due to axSpA. Of the employed, 170 (54.3%) reported work-related issues in the year prior to the survey, being the most frequent "difficulty fulfilling working hours" (44.1%), "missing work for doctor appointments" (42.9%), and "taking sick leave" (37.1%). Being unemployed was associated with lower educational level (OR= 2.92), disease activity (OR= 1.37), spinal stiffness (OR= 1.21), functional limitation (OR= 1.05), worse mental health (OR= 1.15), anxiety (OR= 2.02) and depression (OR= 2.69) in the univariable models; and only with lower educational level (OR= 2.76) and worse mental health (OR= 1.15) in the multivariable.

Conclusions: Results show significant differences between employed and unemployed axSpA patients. Employed axSpA patients endure many problems at work related to

their condition, though unemployed patients present worse disease outcomes associated with greater psychological distress.

SIGNIFICANCE AND INNOVATIONS

- AxSpA is related to a high level of unemployment. A majority of participants report that the condition is the cause of their jobless status.

- More than half of employed patients reported work-related issues, with difficulty fulfilling working hours" (44.1%), "missing work for doctor appointments" (42.9%), and "taking sick leave" (37.1%) being the most frequent.

- Unemployed axSpA patients present worse disease outcomes to those employed, associated with greater psychological distress and lower educational level.

INTRODUCTION

Axial Spondyloarthirtis (axSpA) is a disease that has a significant impact on working life. The increase in disease activity is related to work productivity loss (1). As the age of disease onset is usually the third decade of life, at the peak of patients' productive capacity, the gradual and progressive loss of work productivity affects the work performance and employment possibilities of patients with axSpA (2). In any case, unemployment seems to be associated with even poorer disease outcomes in axSpA (3). For the case of Spain, this impact may be magnified by the fact that the country has one of the highest unemployment rates in the Eurozone (4).

The extensively demonstrated interactions between increased disease activity and disruption of patients' working lives stimulate the focus on the development of comprehensive and holistic treatments for axSpA (5). The ASAS/EULAR

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recommendations state that work productivity losses should be taken into account when assessing the cost-effectiveness of treatments (6). Consequently, it is important to evaluate the working life of people with axSpA in all its aspects: employment status, unemployment rates, work-related problems, in addition to the determinants of these problems in terms of the sociodemographic characteristics of patients and their disease outcomes.

The aim of this study is to compare employed and unemployed patients, and to assess the sociodemographic characteristics and patient- reported outcomes associated with unemployment status and define the work-related issues of employed axSpA patients.

METHODS

Working Group

Atlas 2017 is an initiative of the Spanish Coordinator of Patient Associations of Spondyloarthritis (CEADE), carried out by the research group Health & Territory Research (HTR) of the University of Seville and the Max Weber Institute, with the collaboration of the Spanish Society of Rheumatology (SER) and supported by Novartis Farmacéutica Spain. Further information on the methods of the Atlas 2017 study can be consulted in its seminal article (7).

Design and Survey Development

A patient questionnaire was designed for individuals suffering from axSpA based on expert opinion of a panel of rheumatologists and patients with axSpA and a broad literature review. The questionnaire was composed of 116 items and four open-ended qualitative questions. The dissemination of the patient questionnaire for the recruitment of a sufficient representative sample size was made through general and specific press releases to the medical community, emails to axSpA patient association

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members, websites, social networks, and patient meetings (7). A total of 838 patients with axSpA anonymously accessed the online questionnaire between May 1 and August 15, 2016. After the validation and normalization of the information, the sample consisted of a total of 680 patients who responded to the majority of the questionnaire (completion rate was higher than 75%). All participants signed an opt-in consent form prior to their participation in the survey. As it was a non-interventional study, no further approval by an ethics committee was required.

Sample selection and recruitment

The inclusion criteria required participants to: be aged ≥18 years, resident in Spain, having received a self-reported clinician-provided diagnosis of axSpA, including Ankylosing Spondylitis or non-radiographic axSpA, and having visited a healthcare professional for axSpA in the 12 months prior to participation. Further selection for specific analysis are depicted in Figure 1.

Working life variables in the Atlas 2017

In relation to the working life variables, participants were asked about their employment status through a multiple-choice question in which they could choose one option between employed, unemployed, on temporary sick leave, on permanent sick leave, retired, early retired, student and homemaker.

A section of the Atlas 2017 questionnaire was only available for those reporting "employed" as their employment status for the assessment of work-related issues in the year prior to the survey. Survey respondents could state if they had experienced work-related issues in the past 12 months via a yes/no question. Those reporting yes could choose all work-related issues applicable to them in the year prior to the survey from the following list: 'I asked for some days off/leave of absence'; 'I took sick leave'; 'I

reduced my working hours'; 'I missed work only for the time my doctor's appointment took'; 'It has been difficult for me to fulfil working hours'; 'I have occasionally changed my work shift'; 'My professional life has suffered (e.g. missed promotion)'; 'I had to give up my previous job'. This list was developed with patient research partners in order to best reflect the actual impact of the condition in the workplace.

Finally, two yes/no questions were open to all participants: 'Do you think it is or it would be difficult for you to find a job because of your Spondylitis/Spondyloarthritis?' and 'Do you think your current or past work choice was in any way determined by your Spondylitis/Spondyloarthritis?'

Labor force and employment rates

The unemployment of people with axSpA has been the focus of much research. However, methodological differences when defining the employment ratio of different countries has led to inconsistent conclusions, often within the same population (8). In order to provide reliable indicators that allow comparison between countries, we calculate the unemployment rate following the indications of the International Labour Organization (ILO), endorsed by other institutions such as EUROSTAT.

Therefore, participants were classified according to whether they were part of the labor force (active population) or the economically inactive population. The labor force was composed of those who are employed or unemployed of working age (15-64years old). Respondents who indicated that they are on temporary sick leave, permanent sick leave, retired, early retirement, students or homemakers were

considered inactive. Employment and unemployment rates were calculated by comparing employed and unemployed participants within the labor force.

Supplementary indices

In addition, a range of supplementary measures were collected in the questionnaire to

assess the specific domains of the disease:

1. BASDAI (Bath Ankylosing Spondylitis Disease Activity Index): A validated self-administered questionnaire assessing disease activity in patients with axSpA. Possible scores range from 0 (no activity) to 10 (maximum activity). The Cronbach's alpha score for the BASDAI was 0.879 for this study (7).

2. Spinal Stiffness Index: This index, developed specifically for this study, assesses the degree of stiffness experienced by patients in the spinal column, distinguishing between the cervical, dorsal, and lumbar areas. Possible responses range from least to most affected (1: without stiffness, 2: mild stiffness, 3: moderate stiffness, and 4: severe stiffness), total scores are obtained by adding together the responses for each area of the spine without weighting, resulting in a scale ranging from 3 to 12. This index showed an acceptable internal reliability (Cronbach Alpha =0.79) (7).

3. Functional Limitation Index: This index, developed specifically for this study, assesses the degree of functional limitation in 18 activities of daily life (dressing, bathing, showering, tying shoelaces, moving about the house, climbing stairs, getting out of bed, using the bathroom, shopping, preparing meals, eating, household cleaning, walking down the street, using public transportation, driving, going to the doctor, doing physical exercise, having sex). Each of these 18 activities was assigned as 0 for no limitation, 1 low limitation, 2 medium limitation, and 3 high limitation, resulting in values between 0 and 54. A total score between 0 and 18 was considered low limitation, between 18 and 36 medium limitation and between 36 and 54 high limitation. Cronbach Alpha of 0.97 demonstrated excellent internal reliability (7).

4. GHQ-12 (The 12-item General Health Questionnaire): This questionnaire evaluates psychological distress using 12 questions. For the present study, these were

transformed into a dichotomous score (0-0-1-1), called the GHQ score, to eliminate any bias resulting from the tendency of respondents to choose answers 1 and 4 or 2 and 3. The cut-off point of 3 implied those with a score of 3 or more may be experiencing psychological distress (9).

Statistical analysis

Sociodemographic characteristics, and Patient-reported Outcomes (PROs) [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and psychological distress (0-12, General Health Questionnaire GHQ-12)] were compared between employed and unemployed participants through bivariate analysis. The X^2 test was used for qualitative variables and the Mann-Whitney test for quantitative variables. Signification level was set at 0.05.

Univariable logistic regression analysis was used to evaluate the association between the independent variables and the dependent variable (0 = employed; 1 = unemployed). The variables introduced in the models as independent were those that showed a statistically significant association in the bivariate analysis: educational level, BASDAI (0-10), Spinal Stiffness (3-12), Functional Limitation Index (0-54), GHQ-12, anxiety and depression. A hierarchical logistic regression was carried out in two blocks using the "enter" method. In the first block, patient reported-outcomes [BASDAI (0-10), Spinal Stiffness (3-12), Functional Limitation Index (0-54), GHQ-12, self-reported diagnosis of anxiety and depression] were included. In the second block, educational level (reference category: no universitylevel) was entered in the model.

RESULTS

Labor force distribution

680 people participated in the Atlas 2017 survey. Of those, 653 reported their employment status. All 653 met the conditions to be considered in either the active or inactive population following ILO classification. 415 (63.5%) were part of the labor force while the rest 238 (36.5%) were economically inactive population.

Of the labor force, 325 (78.3%) were employed and 90 (21.7%) unemployed. Of the 90 unemployed participants, 86 reported whether axSpA was the cause of their jobless status or not. 54 (62.8%) declared being unemployed due to axSpA, while 32 (37.2%) did not point to the condition as the cause of their unemployment. Of the inactive population, 26.5% were on temporary sick leave, 26.9% on permanent sickleave, 26.5% retired, 12.2% homemakers, 3.8% students, and 4.2% had taken early retirement . In our sample, only 127 patients were on temporary or permanent sick leave, of whom 124 responded whether their sick leave was due to axSpA, obtaining that in 111 of them it was due to axSpA (n= 111; 89.5%) and in 13 of them was due to other causes (n= 13; 10.5%). No statistically significant gender differences in unemployment rates were found (24.5% for females and 18.5% for males, p=0.133). However, females were more likely to be homemakers (22.1% vs 1.7% of males, p<0.001) and less likely to have their disability recognized as permanent sick leave (21.3% vs 32.8% of males, p<0.001).

Comparison between employed and unemployed

Baseline characteristics of those patients with axSpA in the active population were the following: the mean age was 42.9 years in the employed category (vs. 42.0 years in the unemployed), 48.9% male (vs. 40.0% in the unemployed), 47.1% with university education (vs. 23.3% in the unemployed), and 71.1% married (vs. 60.0% in the unemployed).

The unemployment status of Spanish axSpA patients was associated with lower educational attainment and a lower monthly income. No statistically significant differences were shown with respect to year of diagnosis and diagnostic delay. Unemployed respondents reported poorer disease outcomes in all areas assessed: disease activity, spinal stiffness, functional limitation, and psychological distress. The

differences in disease activity measured by BASDAI had both statistical and clinical significance. However, the most pronounced impact is found in the psychological stress score, to which is added an increase of almost twice the prevalence of anxiety and more than twice that of depression (Table 1).

In the univariate logistic analysis, being unemployed was associated with lower educational level (OR= 2.92), higher disease activity (OR= 1.37), higher spinal stiffness (OR= 1.21), higher functional limitation (OR= 1.05), worse mental health (OR= 1.15), and the presence of anxiety (OR= 2.02) and depression (OR= 2.69). In the first block of multivariable logistic analysis, the variable associated with unemployment was poorer mental health (OR= 1.16). In the second block, patients with poorer mental health and with a lower educational level were associated with unemployment (Table 2).

Work-related issues of employed patients

Of those employed in the active population, 313 answered the question that asked whether they had experienced work-related issues in the past 12 months. 170 (54.3%) declared having experienced work-related issues in the year prior to the survey. The most frequently reported work-related issues were difficulty fulfilling working hours, missing work for doctor appointments, and taking sick leave (Figure 2).

DISCUSSION

Employment rates

In the Atlas 2017 survey, 90 patients (out of 415 patients in the active population) reported an unemployed status that accounts for a total unemployment rate of 21.7%,

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according to ILO standards. In comparison to employed patients, the unemployed presented poorer disease outcomes: greater disease activity, spinal stiffness, functional limitation, psychological distress, and anxiety and depression diagnosis rates. In the multivariate analysis, only psychological distress and educational levels were independently associated with unemployment status.

The unemployment rate in the Spanish Atlas sample was almost three times higher than that of the general population (21.7% vs. 7.7%) (4). According to Eurostat, in 2016, youth unemployment (under 25) in Spain affects 45.8% being the second highest in the European Union (only after Greece with 47.4%). During the same year (2016) the total unemployment rate in Spain was 19.9%, i.e., less than half with respect to the under-25 age group. Therefore, we can affirm that unemployment in Spain disproportionately affects younger people (10). Compared to the general Spanish population, female patients experience an even higher unemployment rate (24.5% vs. 8.8%) and anequally significant difference in their male counterparts (18.5% vs. 6.7%) (4). Although no statistically significant gender differences in unemployment rates were found, women were more likely to be homemakers and less likely to have their disability recognized as permanent sick leave.

Disease burden of the unemployed

Those patients with axSpA who were unemployed had worse disease outcomes (higher disease activity, along with greater stiffness and functional limitation). Additionally, they reported higher levels of psychological stress and twice to thrice the rates of anxiety and depression than those in employment. Results in this line are also found in other countries (3). Moreover, those unemployed due to the disease reported even poorer disease outcomes. Furthermore, 62.8% of unemployed participants declared being

unemployed due to axSpA.. However, respondents who are unemployed due to axSpA had a longer diagnostic delay, greater BASDAI, functional limitation, and psychological distress through GHQ-12, as well as higher anxiety and depression rates (Supplementary Table 1).

British patients of working age who are unemployed have worse disease outcomes that those who work (11). Additionally, a study carried out in Argentina also found that unemployed patients, compared to those who are employed, retired and pensioners, had the worst quality of life and the highest depression scores of those groups (3). Another British study underscores the importance of depression in unemployed axSpA patients and encourages healthcare professionals to include depressive disorders in the focus of clinical intervention in this population (12). All of this evidence makes it clear that psychosocial factors related to unemployment may influence axSpA patients' health status (13), and these issues need to be addressed in parallel with the medical control of the disease.

Nevertheless, the crux is: are patients with more severe disease more likely to be unemployed or does unemployment lead to poorer health status? The cross-sectional nature of this study cannot answer this question. However, in the logistic regression analysis to examine the factors associated with unemployment, disease outcomes do not explain the variance when examined together with two factors that are independently associated: educational level and mental health through GHQ-12. These results are consistent with those of cohort studies on healthy individuals, which reports an independent effect of unemployment on poorer mental health, even controlling for other life stressors (14). Additional longitudinal research has reported a causal link between unemployment and physical health. The effect is not immediate, although it

gains momentum as years pass. Moreover, it is mediated by the age at which the person becomes unemployed, with a minimal effect at 30, moderate effect at 40, and severe effect at 50 (15). In the case of axSpA, a condition usually initiated in the third decade of life, the effect of unemployment on physical health would be dissimulated, which is consistent with the results found in our study. However, patients with later disease onset could be at higher risk of poorer prognosis if they find themselves unemployed for several years. Further research is needed to better assess the effects of unemployment in axSpA patients' health status.

Employment and work-related issues

Employed patients showed, compared with those who are unemployed, higher overall values of physical and psychological health. However, 58.1% reported experiencing psychological distress, 16.0% declared that they were suffering from anxiety, and 10% from depression. Thus, it is not striking that more than half of the employed patients who participated in the Atlas 2017 experienced work-related issues due to axSpA. Overall, our results are in line with the findings of a Dutch study of 142 AS patients, in which 53% reported experiencing an adverse influence by the condition on their work productivity (16). However, the presence of work-related problems due to axSpA in the Atlas sample (54.3%) is lower than the percentage obtained in the European Map of Axial Spondyloarthritis (EMAS) sample, in which 67.7% of employed patients reported at least one work-related problem (17). This comparison is interesting if we take into account that the methodology and the period in which the data were collected was quite similar in both samples, which would show that Spaniards report fewer work-related problems than their European counterparts (18).

The fact that the most frequently reported work-related issues were difficulty fulfilling working hours underscores the importance of addressing presenteeism in axSpA patients. Presenteeism is the inability to focus on work due to disease and is a strong predictor of future absenteeism (19). For this reason, it is to be expected that in this sample the second and third most frequent work-related issues after difficulty fulfilling working hours were absenteeism-related (missing work for doctor appointments and taking sick leave). In fact, the work-related issues reported by the Spanish Atlas 2017 sample conform to a sort of continuum similar to that proposed by Beaton and colleagues (20). That is, almost half are fully employed and productive, followed by those working with presenteeism- and absenteeism-related limitations and, to a lesser extent, those taking sick leave; Finally, a minor but important percentage of patients see their career limited or, ultimately, lose their job.

This image shows that patients employed with axSpA face a "slippery slope" from work, where poorer work outcomes may increase over the years as their disease worsens, increasing the risk of mental disorders such as anxiety and depression in the process.

Early diagnosis and effective treatment should be key to stopping this process as early as possible. In addition, healthcare professionals should be encouraged to monitor the mental health of axSpA patients facing difficult work conditions.

Limitations

The Atlas 2017 is the largest effort to date to capture the patient perspective of people with axSpA in Spain. Proof of its interest is that is being replicated in more than 20 other countries of North America, South America, Europe, and Asia in the form of the International Map of Axial Spondyloarthritis (IMAS). However, it has several limitations. Firstly, the cross-sectional design of the survey does not allow the establishment of

causality between employment status and patient-reported outcomes. This impedes a sense of certainty as to whether the unemployment status of axSpA patients is leading to poorer disease prognosis and facilitating the apparition of mental disorders or if poorer disease outcomes and the presence of anxiety and depression push axSpA patients into their jobless situation. However, it is most likely both, and many unemployed patients could find themselves in a cycle of poorer disease outcomes that make it difficult for them to follow the treatment and establish healthy habits in their daily lives to prevent further disease progression. These results suggest the need for further longitudinal studies to confirm our data and underline the importance for a holistic approach to patient care. In addition, being an online survey, selection biases are inherent because patients with less Internet access are underrepresented and because during the recruitment process respondents were not selected. Furthermore, the lack of a control group to compare the data presented from Spain.

Secondly, all information in the Atlas 2017 was patient-reported, and even if participants were asked to state whether their diagnosis was clinician-provided, no confirmation by a healthcare professional could be obtained. In any case, patient recruitment was made through the Spanish Federation of Spondyloarthritis Associations (CEADE), so the chance of misguided diagnosis is unlikely. Lastly, the non-use of validated scales or indices to assess certain factors such as functional limitation, spinal stiffness or even work experience, when there are validated scales for this population such as the AS-WIS or BASFI (21), should be kept in mind. The reason for this originated during the preliminary phase of the survey's development when patients expressed their concern about not being able to report all aspects of their disease when other scales or indices were employed. In any case, a good Cronbach alpha value was obtained for the index chosen

for our study, which testifies to the internal reliability of these measures.

CONCLUSIONS

The present study shows significant differences between employed and unemployed patients with axSpA, with greater disease activity, spinal stiffness, functional limitation, and poorer mental health in those unemployed. Although, a high burden of disease could explain higher unemployment rates, the fact that unemployment status itself may influence the burden of disease should not be overlooked. Furthermore, axSpA patients who work endure several work-related issues connected to their disease. However, for unemployed patients the situation is even worse, with poorer disease outcomes and greater psychological distress.

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Table 1. Association between relevant parameters (sociodemographic and patient-reported outcomes) and active population (N= 415, unless specified)

Variable	Employed n = 325; 78.3% Mean ± SD or n(%)	Unemployed n = 90; 21.7% Mean ± SD or n(%)	p-value
Sociodemographic			
Age (years)	42.9 ± 8.6	42.0 ± 9.1	0.513
Gender (Male)	159 (48.9)	36 (40.0)	0.133
Education level			
No schooling	4 (1.2)	1 (1.1)	
Primary school	40 (12.3)	19 (21.1)	**0.001***
High school	128 (39.4)	49 (54.4)	
University qualification	153 (47.1)	21 (23.3)	
Marital status (Married)	231 (71.1)	54 (60.0)	0.051
Monthly Income (€), N= 225	890.4 ± 592.3	358.5 ± 377.7	**<0.001***
Axial spondyloarthritis-related			
Diagnostic Delay (years), N= 349	7.7 ± 7.6	8.0 ± 6.5	0.319
BASDAI (0-10), N= 263	5.2 ± 1.9	6.3 ±1.9	**<0.001***
Spinal Stiffness (3-12), N= 314	6.5 ± 2.6	7.8 ± 2.3	**<0.001***
Functional Limitation Index (0-54), N= 381	40.6 ± 10.1	45.0 ± 8.4	**<0.001***
Functional Limitation Index. High Limitation, N= 381	202 (68.5)	72 (83.7)	**0.014***
GHQ-12 (0-12), N= 302	4.9 ± 4.3	7.6 ± 4.2	**<0.001***
Comorbidities			
Anxiety	52 (16.0)	25 (27.8)	**0.011***
Depression	33 (10.2)	21 (23.3)	**0.001***
Sleep disorder	50 (15.4)	18 (20.0)	0.295

€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.

Table 2. Regression analysis for variables explaining associated unemployment (N= 176)

| | Univariable logistic analysis | | Multivariable logistic analysis | | | |
| | | | Block 1 | | Block 2 | |
	OR	CI 95%	OR	CI 95%	OR	CI 95%
BASDAI (0-10)	1.369	**1.165, 1.609**	1.119	0.863, 1.450	1.133	0.873, 1.472
Spinal Stiffness (3-12)	1.211	**1.088, 1.347**	1.102	0.949, 1.280	1.081	0.928, 1.260
Functional Limitation Index (0- 54)	1.053	**1.024, 1.083**	1.007	0.955, 1.062	1.014	0.961, 1.070
GHQ-12 (0-12)	1.154	**1.080, 1.232**	1.158	**1.041, 1.289**	1.153	**1.034, 1.286**
Anxiety. Yes	2.019	**1.167, 3.494**	1.114	0.402, 3.085	0.891	0.307, 2.586
Depression. Yes	2.693	**1.468, 4.940**	1.531	0.499, 4.696	1.829	0.580, 5.769
Education level. No university	2.923	**1.712, 4.990**	-	-	2.757	**1.142, 6.658**

BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.

Supplementary Table 1. Association between relevant parameters (sociodemographic and patient-reported outcomes) in patients whose unemployment was due to axSpA vs. patients whose unemployment was due to other causes (N= 86, unless specified)

Variable	Mean ± SD or n (%)		p-value
	Unemployed due to axSpA n= 54; 62.8%	Unemployed due to other causes n= 32; 37.2%	
Sociodemographic			
Age (years)	42.0 ± 8.5	40.8 ± 10.1	0.442
Gender (Male)	22 (40.7)	13 (40.6)	0.992
Education level (University)	13 (24.1)	7 (21.9)	0.125
Marital status (Married)	29 (53.7)	24 (75.0)	0.113
Monthly Income (€), N= 45	422.6 ± 471.7	311.7 ± 223.9	0.668
Axial spondyloarthritis related			
Diagnostic Delay (years), N= 73	9.8 ± 7.0	5.9 ± 5.2	**0.022***
Year of diagnosis, N= 75	2,006.2 ± 10.1	2,009.0 ± 8.0	0.201
BASDAI (0-10), N= 62	6.8 ± 1.8	5.4 ± 1.6	**0.003***
Spinal Stiffness (3-12), N= 66	8.1 ± 2.2	6.8 ± 2.1	0.065
Functional Limitation Index (0-54), N= 82	47.0 ± 7.0	41.6 ± 9.8	**0.008***
GHQ-12 (0-12), N= 65	8.3 ± 4.2	6.0 ± 4.3	**0.021***
Comorbidities			
Anxiety	21 (38.9)	3 (9.4)	**0.003***
Depression	18 (33.3)	2 (6.3)	**0.004***
Sleep disorder	15 (27.8)	4 (12.5)	0.099

€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.

Title: Understanding the Disease Burden of Unemployed Patients with Axial

Spondyloarthritis. Results of the Spanish Atlas 2017

Running head: Unemployed axSpA Patients' Burden

Authors:

Marco Garrido-Cumbrera, Prof. PhD. ORCID Id 0000-0001-9727-1189

Eduardo Collantes-Estevez, MD. ORCID Id 0000-0002-7647-6289

Victoria Navarro-Compán, MD. ORCID Id 0000-0002-4527-852X

Pedro Zarco-Montejo, MD. ORCID Id 0000-0002-3039-187X

Carlos Sastre, MSc. ORCID Id 0000-0002-1577-7838

José Correa-Fernández, MSc. ORCID Id 0000-0002-7788-5391

Sergio Sanz-Gómez, MSc. ORCID Id 0000-0001-6801-0836

Pedro Plazuelo-Ramos, Mr. ORCID Id N/A

Jordi Gratacos, MD. ORCID Id 0000-0002-7647-6289

Corresponding author: Marco Garrido Cumbrera, Centro Internacional. Av de la Ciudad Jardín, 20, 22, 41005 Sevilla (Spain); phone number +34 955 420 796; mcumbrera@us.es

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ABSTRACT

Objective: To evaluate differences in sociodemographic factors and patient-reported outcomes (PROs) between unemployed and employed axSpA patients and to explore work-related issues.

Methods: Data through online survey from 680 unselected patients of the Spanish Atlas of Axial Spondyloarthritis (2016) were analysed in 2017. Active workforce participants were divided into employed and unemployed according to International Labour Organization standards. Sociodemographic characteristics, Patient-reported Outcomes (PROs) [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and psychological distress [through General Health Questionnaire GHQ-12 (0-12)] were assessed. Logistic regression analysis was used to evaluate the association with unemployment status.

Results: 415 (63.6%) patients were categorised in the active population, of which 325 (78.3%) were employed and 90 (21.76%) unemployed. 62.8% (N = 54) of unemployed declared that their joblessness was due to axSpA. Of the employed, 170 (54.3%) reported work-related issues in the year prior to the survey, being the most frequent "difficulty fulfilling working hours" (44.1%), "missing work for doctor appointments" (42.9%), and "taking sick leave" (37.1%). Being unemployed was associated with lower educational level (OR= 2.92), disease activity (OR= 1.37), spinal stiffness (OR= 1.21), functional limitation (OR= 1.05), worse mental health (OR= 1.15), anxiety (OR= 2.02) and depression (OR= 2.69) in the univariable models; and only with lower educational level (OR= 2.76) and worse mental health (OR= 1.15) in the multivariable.

Conclusions: Results show significant differences between employed and unemployed axSpA patients. Employed axSpA patients endure many problems at work related to

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their condition, though unemployed patients present worse disease outcomes associated with greater psychological distress.

SIGNIFICANCE AND INNOVATIONS

- AxSpA is related to a high level of unemployment. A majority of participants report that the condition is the cause of their jobless status.

- More than half of employed patients reported work-related issues, with difficulty fulfilling working hours" (44.1%), "missing work for doctor appointments" (42.9%), and "taking sick leave" (37.1%) being the most frequent.

- Unemployed axSpA patients present worse disease outcomes to those employed, associated with greater psychological distress and lower educational level.

INTRODUCTION

Axial Spondyloarthirtis (axSpA) is a disease that has a significant impact on working life. The increase in disease activity is related to work productivity loss (1). As the age of disease onset is usually the third decade of life, at the peak of patients' productive capacity, the gradual and progressive loss of work productivity affects the work performance and employment possibilities of patients with axSpA (2). In any case, unemployment seems to be associated with even poorer disease outcomes in axSpA (3). For the case of Spain, this impact may be magnified by the fact that the country has one of the highest unemployment rates in the Eurozone (4).

The extensively demonstrated interactions between increased disease activity and disruption of patients' working lives stimulate the focus on the development of comprehensive and holistic treatments for axSpA (5). The ASAS/EULAR

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recommendations state that work productivity losses should be taken into account when assessing the cost-effectiveness of treatments (6). Consequently, it is important to evaluate the working life of people with axSpA in all its aspects: employment status, unemployment rates, work-related problems, in addition to the determinants of these problems in terms of the sociodemographic characteristics of patients and their disease outcomes.

The aim of this study is to compare employed and unemployed patients, and to assess the sociodemographic characteristics and patient- reported outcomes associated with unemployment status and define the work-related issues of employed axSpA patients.

METHODS

Working Group

Atlas 2017 is an initiative of the Spanish Coordinator of Patient Associations of Spondyloarthritis (CEADE), carried out by the research group Health & Territory Research (HTR) of the University of Seville and the Max Weber Institute, with the collaboration of the Spanish Society of Rheumatology (SER) and supported by Novartis Farmacéutica Spain. Further information on the methods of the Atlas 2017 study can be consulted in its seminal article (7).

Design and Survey Development

A patient questionnaire was designed for individuals suffering from axSpA based on expert opinion of a panel of rheumatologists and patients with axSpA and a broad literature review. The questionnaire was composed of 116 items and four open-ended qualitative questions. The dissemination of the patient questionnaire for the recruitment of a sufficient representative sample size was made through general and specific press releases to the medical community, emails to axSpA patient association

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members, websites, social networks, and patient meetings (7). A total of 838 patients with axSpA anonymously accessed the online questionnaire between May 1 and August 15, 2016. After the validation and normalizsation of the information, the sample consisted of a total of 680 patients who responded to the majority of the questionnaire (completion rate was higher than 75%). All participants signed an opt-in consent form prior to their participation in the survey. As it was a non-interventional study, no further approval by an ethics committee was required.

Sample selection and recruitment

The inclusion criteria required participants to: be aged ≥18 years, resident in Spain, having received a self-reported clinician-provided diagnosis of axSpA, including Ankylosing Spondylitis or non-radiographic axSpA, and having visited a healthcare professional for axSpA in the 12 months prior to participation. Further selection for specific analysis are depicted in Figure 1.

Working life variables in the Atlas 2017

In relation to the working life variables, participants were asked about their employment status through a multiple-choice question in which they could choose one option between employed, unemployed, on temporary sick leave, on permanent sick leave, retired, early retired, student and homemaker.

A section of the Atlas 2017 questionnaire was only available for those reporting "employed" as their employment status for the assessment of work-related issues in the year prior to the survey. Survey respondents could state if they had experienced work-related issues in the past 12 months via a yes/no question. Those reporting yes could choose all work-related issues applicable to them in the year prior to the survey from the following list: 'I asked for some days off/leave of absence'; 'I took sick leave'; 'I

reduced my working hours'; 'I missed work only for the time my doctor's appointment took'; 'It has been difficult for me to fulfil working hours'; 'I have occasionally changed my work shift'; 'My professional life has suffered (e.g. missed promotion)'; 'I had to give up my previous job'. This list was developed with patient research partners in order to best reflect the actual impact of the condition in the workplace.

Finally, two yes/no questions were open to all participants: 'Do you think it is or it would be difficult for you to find a job because of your Spondylitis/Spondyloarthritis?' and 'Do you think your current or past work choice was in any way determined by your Spondylitis/Spondyloarthritis?'

Labor force and employment rates

The unemployment of people with axSpA has been the focus of much research. However, methodological differences when defining the employment ratio of different countries has led to inconsistent conclusions, often within the same population (8). In order to provide reliable indicators that allow comparison between countries, we calculate the unemployment rate following the indications of the International Labour Organization (ILO), endorsed by other institutions such as EUROSTAT.

Therefore, participants were classified according to whether they were part of the labor force (active population) or the economically inactive population. The labor force was composed of those who are employed or unemployed of working age (15-64years old). Respondents who indicated that they are on temporary sick leave, permanent sick leave, retired, early retirement, students or homemakers were

considered inactive. Employment and unemployment rates were calculated by comparing employed and unemployed participants within the labor force.

Supplementary indices

In addition, a range of supplementary measures were collected in the questionnaire to

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assess the specific domains of the disease:

1. BASDAI (Bath Ankylosing Spondylitis Disease Activity Index): A validated self-administered questionnaire assessing disease activity in patients with axSpA. Possible scores range from 0 (no activity) to 10 (maximum activity). The Cronbach's alpha score for the BASDAI was 0.879 for this study (7).

2. Spinal Stiffness Index: This index, developed specifically for this study, assesses the degree of stiffness experienced by patients in the spinal column, distinguishing between the cervical, dorsal, and lumbar areas. Possible responses range from least to most affected (1: without stiffness, 2: mild stiffness, 3: moderate stiffness, and 4: severe stiffness), total scores are obtained by adding together the responses for each area of the spine without weighting, resulting in a scale ranging from 3 to 12. This index showed an acceptable internal reliability (Cronbach Alpha =0.79) (7).

3. Functional Limitation Index: This index, developed specifically for this study, assesses the degree of functional limitation in 18 activities of daily life (dressing, bathing, showering, tying shoelaces, moving about the house, climbing stairs, getting out of bed, using the bathroom, shopping, preparing meals, eating, household cleaning, walking down the street, using public transportation, driving, going to the doctor, doing physical exercise, having sex). Each of these 18 activities was assigned as 0 for no limitation, 1 low limitation, 2 medium limitation, and 3 high limitation, resulting in values between 0 and 54. A total score between 0 and 18 was considered low limitation, between 18 and 36 medium limitation and between 36 and 54 high limitation. Cronbach Alpha of 0.97 demonstrated excellent internal reliability (7).

4. GHQ-12 (The 12-item General Health Questionnaire): This questionnaire evaluates psychological distress using 12 questions. For the present study, these were

transformed into a dichotomous score (0-0-1-1), called the GHQ score, to eliminate any bias resulting from the tendency of respondents to choose answers 1 and 4 or 2 and 3. The cut-off point of 3 implied those with a score of 3 or more may be experiencing psychological distress (9).

Statistical analysis

Sociodemographic characteristics, and Patient-reported Outcomes (PROs) [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and psychological distress (0-12, General Health Questionnaire GHQ-12)] were compared between employed and unemployed participants through bivariate analysis. The X^2 test was used for qualitative variables and the Mann-Whitney test for quantitative variables. Signification level was set at 0.05.

Univariable logistic regression analysis was used to evaluate the association between the independent variables and the dependent variable (0 = employed; 1 = unemployed). The variables introduced in the models as independent were those that showed a statistically significant association in the bivariate analysis: educational level, BASDAI (0-10), Spinal Stiffness (3-12), Functional Limitation Index (0-54), GHQ-12, anxiety and depression. A hierarchical logistic regression was carried out in two blocks using the "enter" method. In the first block, patient reported-outcomes [BASDAI (0-10), Spinal Stiffness (3-12), Functional Limitation Index (0-54), GHQ-12, self-reported diagnosis of anxiety and depression] were included. In the second block, educational level (reference category: no universitylevel) was entered in the model.

RESULTS

Labor force distribution

680 people participated in the Atlas 2017 survey. Of those, 653 reported their employment status. All 653 met the conditions to be considered in either the active or inactive population following ILO classification. 415 (63.5%) were part of the labor force while the rest 238 (36.5%) were economically inactive population.

Of the labor force, 325 (78.3%) were employed and 90 (21.7%) unemployed. 62.8% of those unemployed declared that axSpA was the cause of leaving or losing their job Of the 90 unemployed participants, 86 reported whether axSpA was the cause of their jobless status or not. 54 (62.8%) declared being unemployed due to axSpA, while 32 (37.2%) did not point to the condition as the cause of their unemployment. Of the inactive population, 26.5% were on temporary sick leave, 26.9% on permanent sick leave, 26.5% retired, 12.2% homemakers, 3.8% students, and 4.2% had taken early retirement (Table 1). In our sample, only 127 patients were on temporary or permanent sick leave, of whom 124 responded whether their sick leave was due to axSpA, obtaining that in 111 of them it was due to axSpA (n= 111; 89.5%) and in 13 of them was due to other causes (n= 13; 10.5%). No statistically significant gender differences in unemployment rates were found (24.5% for females and 18.5% for males, p=0.133). However, females were more likely to be homemakers (22.1% vs 1.7% of males, p<0.001) and less likely to have their disability recognized as permanent sick leave (21.3% vs 32.8% of males, p<0.001).

Comparison between employed and unemployed

Baseline characteristics of those patients with axSpA in the active population were the following: the mean age was 42.9 years in the employed category (vs. 42.0 years in the unemployed), 48.9% male (vs. 40.0% in the unemployed), 47.1% with university education (vs. 23.3% in the unemployed), and 71.1% married (vs. 60.0% in the unemployed).

The unemployment status of Spanish axSpA patients was associated with lower educational attainment and a lower monthly income. No statistically significant differences were shown with respect to year of diagnosis and diagnostic delay. Unemployed respondents reported poorer disease outcomes in all areas assessed: disease activity, spinal stiffness, functional limitation, and psychological distress. The differences in disease activity measured by BASDAI had both statistical and clinical significance. However, the most pronounced impact is found in the psychological stress score, to which is added an increase of almost twice the prevalence of anxiety and more than twice that of depression (Table 21).

In the univariate logistic analysis, being unemployed was associated with lower educational level (OR= 2.92), higher disease activity (OR= 1.37), higher spinal stiffness (OR= 1.21), higher functional limitation (OR= 1.05), worse mental health (OR= 1.15), and the presence of anxiety (OR= 2.02) and depression (OR= 2.69). In the first block of multivariable logistic analysis, the variable associated with unemployment was poorer mental health (OR= 1.16). In the second block, patients with poorer mental health and with a lower educational level were associated with unemployment (Table 32).

Work-related issues of employed patients

Of those employed in the active population, 313 answered the question that asked whether they had experienced work-related issues in the past 12 months. 170 (54.3%) declared having experienced work-related issues in the year prior to the survey. The most frequently reported work-related issues were difficulty fulfilling working hours, missing work for doctor appointments, and taking sick leave (Table 4Figure 2).

DISCUSSION

Employment rates

In the Atlas 2017 survey, 90 patients (out of 415 patients in the active population) reported an unemployed status that accounts for a total unemployment rate of 21.76%, according to ILO standards. ~~Among these, 62.8% reported that the axSpA had been the main cause of their unemployment, compared to 37.2% who stated that the disease had not influenced it.~~ In comparison to employed patients, the unemployed presented poorer disease outcomes: greater disease activity, spinal stiffness, functional limitation, psychological distress, and anxiety and depression diagnosis rates. In the multivariate analysis, only psychological distress and educational levels were independently associated with unemployment status.

The unemployment rate in the Spanish Atlas sample was almost three times higher than that of the general population (21.76% vs. 7.7%) (4). According to Eurostat, in 2016, youth unemployment (under 25) in Spain affects 45.8% being the second highest in the European Union (only after Greece with 47.4%). During the same year (2016) the total unemployment rate in Spain was 19.9%, i.e., less than half with respect to the under-25 age group. Therefore, we can affirm that unemployment in Spain disproportionately affects younger people (10). Compared to the general Spanish population, female patients experience an even higher unemployment rate (24.5% vs. 8.8%) and anequally significant difference in their male counterparts (18.5% vs. 6.7%) (4). Although no statistically significant gender differences in unemployment rates were found, women were more likely to be homemakers and less likely to have their disability recognized as permanent sick leave. ~~This shows that the gender composition of the sample can~~

affect work disability rates. The Spanish REGISPONSER study showed that in a sample of patients with AS in which 77% were men, the rate of permanent sick leave was 25% (10). In our study, with 47.5% men, only 9% of the total sample reported being on permanent sick leave. Therefore, the different gender distribution in both studies could be the reason behind a much lower percentage of patients on permanent sick leave in our study. However, a similar study to the Atlas 2017 carried out in the USA found that women reported that their disease interfered more frequently with their normal work (30.7% vs. 23.1% of men; p < 0.05) (11).

Disease burden of the unemployed

Those patients with axSpA who were unemployed had worse disease outcomes (higher disease activity, along with greater stiffness and functional limitation). Additionally, they reported higher levels of psychological stress and twice to thrice the rates of anxiety and depression than those in employment. Results in this line are also found in other countries (3). Moreover, those unemployed due to the disease reported even poorer disease outcomes. Furthermore, 62.8% of unemployed participants declared being unemployed due to axSpA. Of the 90 unemployed participants, 86 reported whether axSpA was the cause of their jobless status or not. 54 (62.8%) declared being unemployed due to axSpA, while 32 (37.2%) did not point to the condition as the cause of their unemployment. There was no difference regarding sociodemographic characteristics between those who were unemployed due to axSpA and those who were not. However, respondents who are unemployed due to axSpA had a longer diagnostic delay, greater BASDAI, functional limitation, and psychological distress through GHQ-12, as well as higher anxiety and depression rates (Supplementary Table 1).

British patients of working age who are unemployed have worse disease outcomes that

those who work (11). Additionally, a study carried out in Argentina also found that unemployed patients, compared to those who are employed, retired and pensioners, had the worst quality of life and the highest depression scores of those groups (3). Another British study underscores the importance of depression in unemployed axSpA patients and encourages healthcare professionals to include depressive disorders in the focus of clinical intervention in this population (12). All of this evidence makes it clear that psychosocial factors related to unemployment may influence axSpA patients' health status (13), and these issues need to be addressed in parallel with the medical control of the disease.

Nevertheless, the crux is: are patients with more severe disease more likely to be unemployed or does unemployment lead to poorer health status? The cross-sectional nature of this study cannot answer this question. However, in the logistic regression analysis to examine the factors associated with unemployment, disease outcomes do not explain the variance when examined together with two factors that are independently associated: educational level and mental health through GHQ-12. These results are consistent with those of cohort studies on healthy individuals, which reports an independent effect of unemployment on poorer mental health, even controlling for other life stressors (14). Additional longitudinal research has reported a causal link between unemployment and physical health. The effect is not immediate, although it gains momentum as years pass. Moreover, it is mediated by the age at which the person becomes unemployed, with a minimal effect at 30, moderate effect at 40, and severe effect at 50 (15). In the case of axSpA, a condition usually initiated in the third decade of life, the effect of unemployment on physical health would be dissimulated, which is consistent with the results found in our study. However, patients with later disease

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onset could be at higher risk of poorer prognosis if they find themselves unemployed for several years. Further research is needed to better assess the effects of unemployment in axSpA patients' health status.

Employment and work-related issues

Employed patients showed, compared with those who are unemployed, higher overall values of physical and psychological health. However, 58.1% reported experiencing psychological distress, 16.0% declared that they were suffering from anxiety, and 10% from depression. Thus, it is not striking that more than half of the employed patients who participated in the Atlas 2017 experienced work-related issues due to axSpA. Overall, our results are in line with the findings of a Dutch study of 142 AS patients, in which 53% reported experiencing an adverse influence by the condition on their work productivity (16). However, the presence of work-related problems due to axSpA in the Atlas sample (54.3%) is lower than the percentage obtained in the European Map of Axial Spondyloarthritis (EMAS) sample, in which 67.7% of employed patients reported at least one work-related problem (17). This comparison is interesting if we take into account that the methodology and the period in which the data were collected was quite similar in both samples, which would show that Spaniards report fewer work-related problems than their European counterparts (18).

The fact that the most frequently reported work-related issues were difficulty fulfilling working hours underscores the importance of addressing presenteeism in axSpA patients. Presenteeism is the inability to focus on work due to disease and is a strong predictor of future absenteeism (19). For this reason, it is to be expected that in this sample the second and third most frequent work-related issues after difficulty fulfilling

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working hours were absenteeism-related (missing work for doctor appointments and taking sick leave). In fact, the work-related issues reported by the Spanish Atlas 2017 sample conform to a sort of continuum similar to that proposed by Beaton and colleagues (20). That is, almost half are fully employed and productive, followed by those working with presenteeism- and absenteeism-related limitations and, to a lesser extent, those taking sick leave; Finally, a minor but important percentage of patients see their career limited or, ultimately, lose their job.

This image shows that patients employed with axSpA face a "slippery slope" from work, where poorer work outcomes may increase over the years as their disease worsens, increasing the risk of mental disorders such as anxiety and depression in the process. Early diagnosis and effective treatment should be key to stopping this process as early as possible. In addition, healthcare professionals should be encouraged to monitor the mental health of axSpA patients facing difficult work conditions.

Limitations

The Atlas 2017 is the largest effort to date to capture the patient perspective of people with axSpA in Spain. Proof of its interest is that is being replicated in more than 20 other countries of North America, South America, Europe, and Asia in the form of the International Map of Axial Spondyloarthritis (IMAS). However, it has several limitations. Firstly, the cross-sectional design of the survey does not allow the establishment of causality between employment status and patient-reported outcomes. This impedes a sense of certainty as to whether the unemployment status of axSpA patients is leading to poorer disease prognosis and facilitating the apparition of mental disorders or if poorer disease outcomes and the presence of anxiety and depression push axSpA patients into their jobless situation. However, it is most likely both, and many

unemployed patients could find themselves in a cycle of poorer disease outcomes that make it difficult for them to follow the treatment and establish healthy habits in their daily lives to prevent further disease progression. These results suggest the need for further longitudinal studies to confirm our data and underline the importance for a holistic approach to patient care. In addition, being an online survey, selection biases are inherent because patients with less Internet access are underrepresented and because during the recruitment process respondents were not selected. Furthermore, the lack of a control group to compare the data presented from Spain.

Secondly, all information in the Atlas 2017 was patient-reported, and even if participants were asked to state whether their diagnosis was clinician-provided, no confirmation by a healthcare professional could be obtained. In any case, patient recruitment was made through the Spanish Federation of Spondyloarthritis Associations (CEADE), so the chance of misguided diagnosis is unlikely. Lastly, the non-use of validated scales or indices to assess certain factors such as functional limitation, spinal stiffness or even work experience, when there are validated scales for this population such as the AS-WIS or BASFI (21), should be kept in mind. The reason for this originated during the preliminary phase of the survey's development when patients expressed their concern about not being able to report all aspects of their disease when other scales or indices were employed. In any case, a good Cronbach alpha value was obtained for the index chosen for our study, which testifies to the internal reliability of these ~~methods~~ measures.

CONCLUSIONS

The present study shows significant differences between employed and unemployed patients with axSpA, with greater disease activity, spinal stiffness, functional limitation,

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and poorer mental health in those unemployed. Although, a high burden of disease could explain higher unemployment rates, the fact that unemployment status itself may influence the burden of disease should not be overlooked. Furthermore, axSpA patients who work endure several work-related issues connected to their disease. However, for unemployed patients the situation is even worse, with poorer disease outcomes and greater psychological distress.

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Table 1. Employment status of survey respondents

Population	N	%	Employment status	N	%
Active population*	415	63.6	Employed	325	78.3
			Unemployed	90	21.6
			Total	**415**	**100.0**
Inactive population	238	36.4	Temporary sick leave	63	26.5
			Permanent sick leave	64	26.9
			Retired	63	26.5
			Homemakers	29	12.2
			Students	9	3.8
			Early retirement	10	4.2
			Total	**238**	**100.0**
Total	**653**	**100.0**			

*According to the ILO, the active population or labor force is the sum of persons between 15 and 64 years

Table 21. Association between relevant parameters (sociodemographic and patient-reported outcomes) and active population (N= 415, unless specified)

Variable	Employed n = 325; 78.3% Mean ± SD or n(%)	Unemployed n = 90; 21.76% Mean ± SD or n(%)	p-value
Sociodemographic			
Age (years)	42.9 ± 8.6	42.0 ± 9.1	0.513
Gender (Male)	159 (48.9)	36 (40.0)	0.133
Education level No schooling Primary school High school (University qualification)	4 (1.2) 40 (12.3) 128 (39.4) 153 (47.1)	1 (1.1) 19 (21.1) 49 (54.4) 21 (23.3)	**0.001***
Marital status (Married)	231 (71.1)	54 (60.0)	0.051
Monthly Income (€), N= 225	890.4 ± 592.3	358.5 ± 377.7	**<0.001***
Axial spondyloarthritis-related			
Diagnostic Delay (years), N= 349	7.7 ± 7.6	8.0 ± 6.5	0.319
Year of diagnosis, N= 353	2,006.4 ± 9.6	2,006.9 ± 9.5	0.596
BASDAI (0-10), N= 263	5.2 ± 1.9	6.3 ±1.9	**<0.001***
Spinal Stiffness (3-12), N= 314	6.5 ± 2.6	7.8 ± 2.3	**<0.001***
Functional Limitation Index (0-54), N= 381	40.6 ± 10.1	45.0 ± 8.4	**<0.001***
Functional Limitation Index. High Limitation, N= 381	202 (68.5)	72 (83.7)	**0.014***
GHQ-12 (0-12), N= 302	4.9 ± 4.3	7.6 ± 4.2	**<0.001***
Comorbidities			
Anxiety	52 (16.0)	25 (27.8)	**0.011***
Depression	33 (10.2)	21 (23.3)	**0.001***
Sleep disorder	50 (15.4)	18 (20.0)	0.295

€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.

Table 32. Regression analysis for variables explaining associated unemployment
(N=176)

| | Univariable logistic analysis | | Multivariable logistic analysis | | | |
| | | | Block 1 | | Block 2 | |
	OR	CI 95%	OR	CI 95%	OR	CI 95%
BASDAI (0-10)	1.369	**1.165, 1.609**	1.119	0.863, 1.450	1.133	0.873, 1.472
Spinal Stiffness (3-12)	1.211	**1.088, 1.347**	1.102	0.949, 1.280	1.081	0.928, 1.260
Functional Limitation Index (0- 54)	1.053	**1.024, 1.083**	1.007	0.955, 1.062	1.014	0.961, 1.070
GHQ-12 (0-12)	1.154	**1.080, 1.232**	1.158	**1.041, 1.289**	1.153	**1.034, 1.286**
Anxiety. Yes	2.019	**1.167, 3.494**	1.114	0.402, 3.085	0.891	0.307, 2.586
Depression. Yes	2.693	**1.468, 4.940**	1.531	0.499, 4.696	1.829	0.580, 5.769
Education level. No university	2.923	**1.712, 4.990**	-	-	2.757	**1.142, 6.658**

BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General
Health Questionnaire.

Table 4. Frequencies of work-related issues reported by employed respondents (N = 170)

	N (%)
Difficulty fulfilling working hours	75 (44.1)
I missed work only for the time my doctor appointment took	73 (42.9)
I took sick leave	63 (37.1)
My professional life has suffered	31 (18.2)
I asked for some days off	21 (12.3)
Changed shift sometimes	21 (12.3)
I had to give up my previous job	13 (7.6)

Supplementary Table 1. Association between relevant parameters (sociodemographic

and patient-reported outcomes) *in patients whose unemployment was due to axSpA vs.*

patients whose unemployment was due to other causes ~~and unemployed category~~ *(N=*

86, unless specified)

Variable	Mean ± SD or n (%)		p-value
	Unemployed due to axSpA n= 54; 62.8%	Unemployed due to other causes n= 32; 37.2%	
Sociodemographic			
Age (years)	42.0 ± 8.5	40.8 ± 10.1	0.442
Gender (Male)	22 (40.7)	13 (40.6)	0.992
Education level (University)	13 (24.1)	7 (21.9)	0.125
Marital status (Married)	29 (53.7)	24 (75.0)	0.113
Monthly Income (€), N= 45	422.6 ± 471.7	311.7 ± 223.9	0.668
Axial spondyloarthritis related			
Diagnostic Delay (years), N= 73	9.8 ± 7.0	5.9 ± 5.2	**0.022***
Year of diagnosis, N= 75	2,006.2 ± 10.1	2,009.0 ± 8.0	0.201
BASDAI (0-10), N= 62	6.8 ± 1.8	5.4 ± 1.6	**0.003***
Spinal Stiffness (3-12), N= 66	8.1 ± 2.2	6.8 ± 2.1	0.065
Functional Limitation Index (0-54), N= 82	47.0 ± 7.0	41.6 ± 9.8	**0.008***
GHQ-12 (0-12), N= 65	8.3 ± 4.2	6.0 ± 4.3	**0.021***
Comorbidities			
Anxiety	21 (38.9)	3 (9.4)	**0.003***
Depression	18 (33.3)	2 (6.3)	**0.004***
Sleep disorder	15 (27.8)	4 (12.5)	0.099

€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.

Table 1. Association between relevant parameters (sociodemographic and patient-reported outcomes) and active population (N= 415, unless specified)

Variable	Employed n = 325; 78.3% Mean ± SD or n(%)	Unemployed n = 90; 21.7% Mean ± SD or n(%)	p-value
Sociodemographic			
Age (years)	42.9 ± 8.6	42.0 ± 9.1	0.513
Gender (Male)	159 (48.9)	36 (40.0)	0.133
Education level			
No schooling	4 (1.2)	1 (1.1)	**0.001***
Primary school	40 (12.3)	19 (21.1)	
High school	128 (39.4)	49 (54.4)	
University qualification	153 (47.1)	21 (23.3)	
Marital status (Married)	231 (71.1)	54 (60.0)	0.051
Monthly Income (€), N= 225	890.4 ± 592.3	358.5 ± 377.7	**<0.001***
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Functional Limitation Index. High Limitation, N= 381	202 (68.5)	72 (83.7)	**0.014***
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Comorbidities			
Anxiety	52 (16.0)	25 (27.8)	**0.011***
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Sleep disorder	50 (15.4)	18 (20.0)	0.295

€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-itemGeneral Health Questionnaire.

Table 2. Regression analysis for variables explaining associated unemployment (N=176)

	Univariable logistic analysis		Multivariable logistic analysis			
			Block 1		Block 2	
	OR	CI 95%	OR	CI 95%	OR	CI 95%
BASDAI (0-10)	1.369	**1.165, 1.609**	1.119	0.863, 1.450	1.133	0.873, 1.472
Spinal Stiffness (3-12)	1.211	**1.088, 1.347**	1.102	0.949, 1.280	1.081	0.928, 1.260
Functional Limitation Index (0- 54)	1.053	**1.024, 1.083**	1.007	0.955, 1.062	1.014	0.961, 1.070
GHQ-12 (0-12)	1.154	**1.080, 1.232**	1.158	**1.041, 1.289**	1.153	**1.034, 1.286**
Anxiety. Yes	2.019	**1.167, 3.494**	1.114	0.402, 3.085	0.891	0.307, 2.586
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Education level. No university	2.923	**1.712, 4.990**	-	-	2.757	**1.142, 6.658**

BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item GeneralHealth Questionnaire.
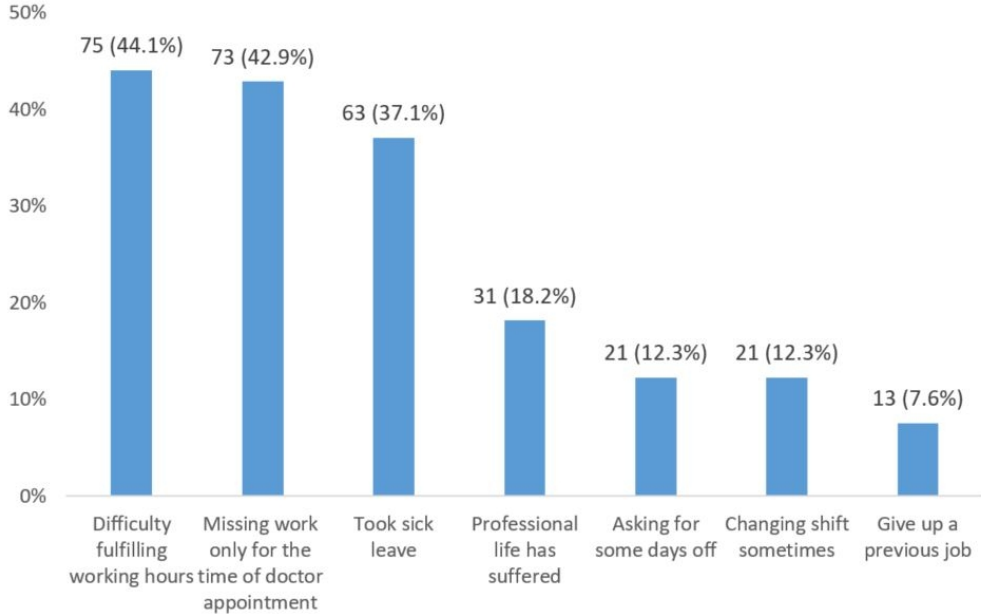
Figure 1. Frequencies of work-related issues reported by employed respondents (N = 170)
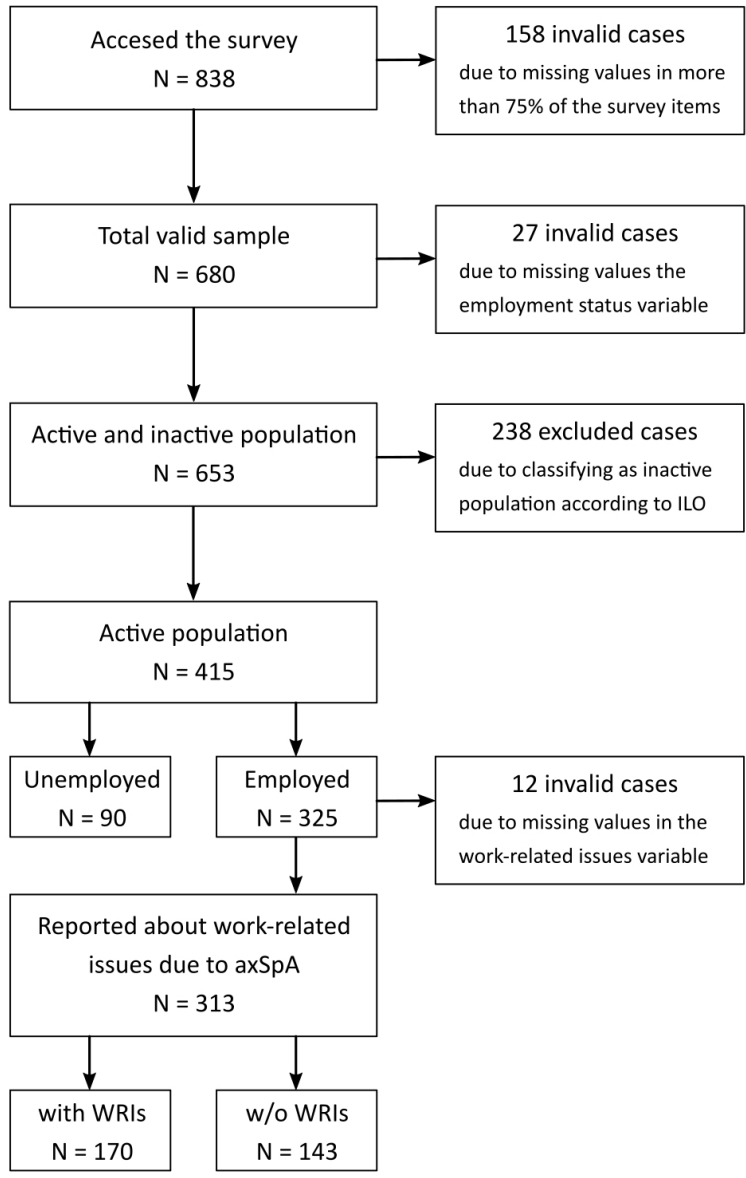
200x125mm (120 x 120 DPI)

Figure 2. Sample selection flowchart / WRIs: Work-related issues

343x530mm (72 x 72 DPI)

Supplementary Table 1. Association between relevant parameters (sociodemographic and patient-reported outcomes) in patients whose unemployment was due to axSpA vs. patients whose unemployment was due to other causes (N= 86, unless specified)

Variable	Mean ± SD or n (%)		p-value
	Unemployed due to axSpA n= 54; 62.8%	**Unemployed due to other causes** **n= 32; 37.2%**	
Sociodemographic			
Age (years)	42.0 ± 8.5	40.8 ± 10.1	0.442
Gender (Male)	22 (40.7)	13 (40.6)	0.992
Education level (University)	13 (24.1)	7 (21.9)	0.125
Marital status (Married)	29 (53.7)	24 (75.0)	0.113
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Axial spondyloarthritis related			
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Anxiety	21 (38.9)	3 (9.4)	**0.003***
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€: Euros; BASDAI: Bath Ankylosing Spondylitis Disease Activity Scale; GHQ-12: 12-item General Health Questionnaire.