



# Depression and anxiety in individuals with axial spondyloarthritis and nonspecific low back pain who are interested in non-pharmacological therapy options

# **Cross-sectional study**

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### **Abstract**

Psychological burden, such as depression and anxiety, may be associated with axial spondyloarthritis (axSpA) and poor prognosis of nonspecific low back pain (NSLBP). Non-pharmacological therapy is a substantial part of the management of both illnesses. Our study describes the psychological outcomes in patients with axSpA and NSLBP who were actively looking for non-pharmacological therapy. A total of 60 participants (34 with axSpA and 26 with NSLBP) were included in this cross-sectional study. Anxiety and depression were examined using the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI-II), respectively. The relationships between BAI and BDI-II and quality of life (EQ-5D), pain intensity (NRS pain), disease activity (AS disease activity score, ASDAS-CRP), and function (Bath AS Functional Index, BASFI) were determined. The intensity of anxiety and depression did not differ between patients with and without axSpA. In both, axSpA and NSLBP, BAI, and BDI-II scores were inversely correlated with EQ-5D, R = -0.268 (P < .05) and R = -0.486 (P < .0001), respectively. We found a variation in the relationship between pain intensity and psychological outcomes in NSLBP and axSpA. The pain intensity score was correlated with the BDI-II (R = 0.542, P = .001) and BAI (R = 0.489, P = .003) scores only in patients with axSpA. In patients with axSpA, BAI was inversely correlated with disease duration (R = -0.356, P = .039) and positively correlated with increased disease activity and poor function, ASDAS-CRP (R = 0.431, P = .012) and BASFI (R = 0.621, P < .0001) scores. The ASDAS-CRP score was positively correlated with BDI-II (R = 0.562, P = .001), and both disease activity and female sex were identified as risk factors for poor BDI-II outcomes in axSpA patients according to multiple regression analysis. Experiences of anxiety and depression seem to be similar for patients with axSpA and NSLBP in this selected group of participants. However, pain intensity may influence psychological outcomes, mainly in patients with axSpA. Disease activity, impaired function, and female sex were risk factors for anxiety and depression in patients with axSpA.

**Abbreviations:** AS = ankylosing spondylitis, ASDAS-CRP = AS disease activity score, axSpA = axial spondyloarthritis, BAI = Beck Anxiety Inventory, BASFI = Bath AS Functional Index, BDI-II = Beck Depression Inventory, bDMARDs = biologic disease modifying drugs, BMI = body mass index, CRP = C-reactive protein, DMARDs = disease modifying drugs, EQ-5D = 5-dimensional European Quality of Life questionnaire, LBP = low back pain, nr-axSpA = non-radiographic axial spondyloarthritis, NRS = numeric rating scale, NSAIDs = non-steroidal anti-inflammatory drugs, NSLBP = nonspecific low back pain.

Keywords: axial spondyloarthritis, depression, nonspecific low back pain, pain, supervised group-based physiotherapy

MH and AL contributed equally to this work.

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### 1. Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disorder affecting the axial skeleton, peripheral joints, entheses, and several extra-articular locations, such as the uvea, skin, or bowel.<sup>[1]</sup> All axSpA disease manifestations, particularly the daily experience with pain and stiffness, have a serious impact on the mobility of patients and their quality of life. AxSpA diagnosis comprises two subgroups of the disease classified by the Assessment of SpondyloArthritis International Society: non-radiographic (nr)-axSpA and ankylosing spondylitis (AS).<sup>[2]</sup> Both of these subgroups express similar disease burdens, such as disease activity requiring adequate therapy,<sup>[3]</sup> but patients with AS express higher levels of systemic and local inflammatory changes, worse functional impairment, increased uveitis occurrence<sup>[4]</sup> and radiographic changes in the sacroiliac joints.<sup>[5]</sup>

With regard to disease onset in early adulthood and the chronic course of the disease, the impact on disease outcomes has been demonstrated by several comorbidities, such as cardiovascular or neurological diseases. [6] Psychological distress has not been associated with the outcomes of axSpA for a long time; however, in 1993, Barlow et al uncovered depressive symptoms in one-third of AS patients.<sup>[7]</sup> Further studies demonstrated a very close relationship between two psychological difficulties, depression and anxiety, and disease activity and mobility in AS patients.[8] Importantly, depression has been identified as a risk factor for impaired mobility and reduced quality of life in axSpA patients.<sup>[9]</sup> Depression appears to occur more frequently in AS patients than in healthy subjects.[10] The incidence of depressive disorder in AS seems to be 2.2 times higher than in the general population,[11] and depression may accompany axSpA in 11% to 64% of patients without any significant differences between the two radiographic forms. [12] Similarly, increased anxiety has been found in 16% to 20% of patients with axSpA and has been associated with higher disease activity. [13,14]

Back pain due to non-inflammatory reasons usually manifests as low back pain (LBP). LBP is a very common health problem, while it may occur in teenagers, [15] LBP is more prevalent during adulthood and in elderly populations. [16] Back pain may be generated by various spinal structures, such as ligaments and paravertebral muscles; biomechanical stress usually results in the onset of symptoms. The exact causes of LBP, however, may not be precisely determined, and the term nonspecific LBP (NSLBP) describes the pain or discomfort in the area of the posterior part of the body localized between the gluteal area and the lower ribs.[17] Although LBP may occur as one episode with full recovery within 6 weeks, in up to 23% of cases, chronicity may be found.[18] Psychosocial factors, including depression and anxiety, have been found to be more common in NSLBP patients<sup>[16]</sup> and could be predictors of chronicity, poor therapeutic response and disability.[19]

Although the back pain may be the dominant sign of both, axSpA and NSLBP, the pathological background is different. In axSpA but not in NSLBP, the inflammation is the key pathological moment inducing pain. On the other hand, the muscle imbalances as reaction to the primary pathologic event may be similar in both, axSpA and NSLBP. For axSpA and LBP, the beneficial effects of non-pharmacological therapeutic options, particularly physiotherapy, have been validated in several studies. [20,21] Although some axSpA and NSLBP patients are not comfortable with their active participations and do not use the physiotherapy, many of them actively look for opportunities to improve their health. As NSLBP may manifest as one or more episodes of back pain, axSpA is a chronic disease with consequences of quality life including mental health. Recently, in patients with axSpA, mild and moderate to severe depression have been associated with a lack of exercise and fulltime employment.[22]

In our study, we primary looked for the variation between psychological outcomes in patients with axSpA and those with back pain of non-inflammatory origin (NSLBP) who actively seek non-pharmacological therapy, such as group physiotherapy. Next, we performed the survey focused on the relationship between psychological outcomes, pain severity, and occupational habits in patients with both axSpA and NSLBP.

### 2. Methods

### 2.1. Study participants and design

This is a cross-sectional study. Patients with axSpA and NSLBP who responded to an announcement for group-based physiotherapy for individuals with back pain were, prior to the beginning the lessons, asked to participate. Individuals who agreed to participate were asked for inform consent and to complete a self-reported questionnaire.

The inclusion criteria for patients with axSpA were as follows: axSpA classification according to Assessment of SpondyloArthritis International Society. A complete medical history, including information on the sacroiliac joint radiographic pattern, was required.

The inclusion criteria for the NSLBP group (also called controls) were as follows: at least one episode of low back pain in the last 6 months with total recovery lasting at least 4 weeks' prior to the study. A physiotherapeutic or physician examination clarifying the origin of back pain was required.

The exclusion criteria were similar for both groups: osteoporosis, fractures, acute vertebral changes (such as bulging or rupture disks), other inflammatory disorders, history or current therapy for cancer, surgery (current for any medical reasons and the history of spine surgery for axSpA or other sources of back pain), diabetes mellitus type 1 and type 2, and chronic infection. People who reported having psychological problems that required intervention in the last 6 months were excluded.

The study and the informed consent form were evaluated by the Ethical Committee of the Faculty of Physical Education and Sport, Charles University in Prague (number 193/2017). This study followed the principles of the Declaration of Helsinki.

### 2.2. Characterization of the axSpA group

AxSpA patients (n = 34) were characterized by the following variables: age at the time of diagnosis, age at the time of first symptom onset, disease duration since diagnosis and since the first symptom occurred, HLA B27 positivity, current clinical signs (back pain, arthritis, and enthesitis), extra-articular manifestations (uveitis, idiopathic bowel disease, and psoriasis), current therapy (non-steroidal anti-inflammatory drugs [NSAIDs], conventional synthetic [cs] or biologic [b] disease modifying drugs [DMARDs]), and radiographic sacroillitis (AS, n = 25 and nr-axSpA, n = 9). Clinical data were extracted from the medical history of each patient by a rheumatologist. The serum C-reactive protein (CRP) levels, the AS disease activity score-CRP (ASDAS-CRP),<sup>[23]</sup> and the Bath AS Disease Functional Index (BASFI)<sup>[24]</sup> were included.

### 2.3. Questionnaires for both groups

The following parameters were included in the questionnaires: age at the time of study; sex; pain evaluation according to the numeric rating scale (NRS): range 0 (no pain) to 10 (severe pain); body mass index (BMI); addictions (smoking, alcohol intake, abuse of psychotropic drugs); information about regular sport activities and about physiotherapeutic care consumption (individual physiotherapy and/or spa therapy for 3 weeks) during the last 3 months; and finally, a quality of life assessment according to the 5-dimensional European Quality of Life questionnaire (EQ-5D).<sup>[25]</sup> The occupational questionnaire included the highest education level, job classification (white vs blue

collar), and the ability to work: employment rate and workload, the real-time hours of work during the last 7 days, and the influence of axSpA/back pain on work during the last 7 days as measured by the NRS [range 0: without influence—10: impossible to perform].

## 2.4. Psychological questionnaires

Anxiety and depression were evaluated using the validated Czech versions of the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI-II) self-reported questionnaires. [26-29] Twenty-one questions were included in each questionnaire. The BAI reflects the signs of anxiety, such as dizziness and an inability to relax, and the BDI-II captures the emotional, cognitive, and somatic symptoms of depression. The levels of severity are characterized by a four-point Likert scale (0: not at all affected; 3: very significantly). The final sum determined the score, which ranged from 0 to 9, for those without anxiety, from 10 to 18 for those with mild to moderate anxiety, 19 to 29 for those with moderate to severe anxiety and 30 to 63 for those with severe anxiety. [27,30] A normal mood was characterized by a BDI-II score of up to 13, mild depression by a score from 4 to 19, moderate depression by a score from 20 to 28 and severe depression by a score of 29 to 63.

### 2.5. Statistical analysis

The data were expressed as means and confidence intervals. Qualitative variables were tested using the chi-squared or Fisher's exact tests. Differences between groups were analyzed using the non-parametric unpaired test and the Mann-Whitney *U* test. The Pearson correlation coefficient was used

for correlations, and symmetric measures for the correlation between the NRS pain score and the BAI and BDI-II scores in patients with axSpA and NSLBP. Multiple regression models were used to analyze the association between BDI and BAI and clinical variables. Statistical significance was set at P < .05. SPSS (IBM Corp., Armonk, NY) and GraphPad Prism 7 software were used for all analyses.

### 3. Results

### 3.1. Demographic data

The axSpA and NSLBP (control) groups were comparable in terms of the following variables: age at the time of study, BMI, EQ-5D, addiction, and physical activities; however, a male predominance was obvious in the axSpA group (76.5% vs 42.3%, P = .008, Table 1). Patients with AS and nr-axSpA differed significantly in terms of serum CRP levels (6.79 vs 2.77; P = .009) but not in the evaluated clinical variables or basic demographics (data not shown).

Two individuals (one axSpA patient and one control) had a history of cannabis experience (*P*= ns), but no axSpA patients or controls reported present psychotropic drug abuse (data not shown).

The axSpA and control groups did not significantly differ in terms of most of the variables, such as education, professional arrangement, and physical activities (Table 1).

### 3.2. Psychological outcomes in NSLBP and axSpA

**3.2.1.** Analysis of anxiety: the BAI. The anxiety measurements according to the BAI questionnaire reached a similar intensity

Table 1

Basic characteristics of the patients with axial spondyloarthritis and controls with non-specific low back pain.

		axSpA (n = 34)		Controls (n = 26)	P value
Age at the time of study	43.10	39.92–46.43	39.46	35.61–43.31	.135
Sex (% men)	76.5		42.3		.008
BMI	25.38	24.38-26.39	24.13	22.71-25.54	.119
EQ-5D	0.796	0.739-0.853	0.821	0.733-0.908	.188
Education and professional arrangement					
The levels of highest education: University (%)	47.1		34.6		.780
Employment rate: full-time job (%)	97.0		92.3		.574
Job classification: white collar (%)	82.4		92.3		.446
The real-time hours of work during the last 7 d	45.01	40.28-49.75	42.85	26.89-48.80	.634
AxSpA/back pain impact on work habits during the last 7 d* (NRS)	1.32	0.76-1.88	0.00	0.0-0.0	<.0001
Addiction					
Current smokers (%)	20.6		7.7		.275
Alcohol daily (no more than 5 cl of distillates or equivalent)	88.9		96.1		.388
Physical activity†					
Physiotherapy care (%)	38.2		23.1		.268
Sport activities (%)	41.2		50.0		.602
Disease characterization					
Pain during the last 7 d (NRS)	2.77	2.04-3.48	2.17	1.12-3.22	.144
AS vs nr-axSpA (%)	73.5 vs 26.5	5	NA		NA
HLA B27 positivity (%)	85.3		NA		NA
Extra-articular manifestations‡ (%)	44.2		NA		NA
Age at the first symptoms of axSpA	24.76	21.87-27.65	NA		NA
Age at the time of axSpA diagnosis	31.61	29.29-33.92	NA		NA
ASDAS-CRP	1.72	1.50-1.96	NA		NA
BASFI	0.63	0.36-0.91	NA		NA
Current therapy: bDMARDs/daily use of NSAIDs (%)	20.6/79.4		NA		NA

Data are expressed as the mean with the 95% confidence interval. The Mann–Whitney test or Fisher's exact test were used, P < .05 was classified as statistically significant.

AS = ankylosing spondylitis, AS = ankylosing spondylitis, ASDAS-CRP = ankylosing spondylitis (AS) disease activity score-C-reactive protein, axSpA = axial spondyloarthritis, BASFI = Bath AS Functional Index, bDMARDs = biologic disease modifying drugs, BMI = body mass index, EQ-5D = 5-dimensional European Quality of life questionnaire, nr-axSpA = non radiographic axSpA, nr-axSpA = non-radiographic axSpA, NRS = numeric rating scale, NSAIDs = non-steroidal antirheumatic drugs.

<sup>\*</sup>Due to vertebrogenic problems in the controls.

<sup>†</sup>During the last 3 months.

<sup>‡</sup>Psoriasis (11.7%), Inflammatory bowel disease (2.9%) and uveitis (38.0%).

for axSpA patients (3.79; 95% CI: 2.47–5.12) and controls (3.44; 95% CI: 1.76–5.13) (P = ns; data not shown). However, patients with nr-axSpA tended to have a higher BAI score (6.11; 95% CI: 2.15–9.10) than patients with AS and controls (P = .097; data not shown). BAI scores corresponding to mild to moderate anxiety were found in 5 (14.1%) axSpA patients and 3 (11.5%) controls (P = ns), data not shown.

3.2.2. Analysis of depression: the BDI-II were equal in axSpA patients (4.18, 95% CI: 2.51–5.85) and controls (2.88, 95% CI: 1.35–4.42) (P = ns, data not shown). Both axSpA radiographic forms did not differ in terms of the BDI-II scores (data not shown). Only one (2.9%) axSpA patient reported BDI-II scores that indicated moderate to severe depression, but mild depression was uncovered in 7.7% of controls and 2.9% of axSpA patients (P = ns) (data not shown).

# 3.3. BAI and BDI-II scores in clinical variables of NSLBP and axSpA

3.3.1. The anxiety scores were influenced by disease duration, physical activity and function. For all responders, the age at the time of study, EQ-5D, and BMI were significantly inversely correlated with anxiety (R = -0.268, R = -0.399,

and R = -0.333, respectively, all P < .05 (Table 2). Among all participants, the BAI score was correlated with the BDI-II score (R = 0.536, P < .0001), and women showed an inclination toward higher levels of anxiety (R = 0.280, P = .040) (Table 2).

In axSpA patients, anxiety was associated with disease activity and impaired function, and the BAI score was significantly correlated with the ASDAS-CRP (R = 0.431, P = .012) and BASFI scores (R = 0.621, P < .0001). Although patients with axSpA with biologic disease modifying drugs (bDMARDs) compared to those on NSAIDs only, had slightly lower ASDAS-CRP values 1.57 (95% CI 1.061–2.079) vs 2.04 (95% CI 1.71–2.36), P = .04; we did not find any differences in BAI scores between these two groups. On the other hand, the BAI scores were negatively correlated with disease duration since axSpA diagnosis (R = -0.356, P = .039, Table 2). When a multiple regression model for the dependent variable (BAI score) was used, only the BASFI was significantly associated: the BAI increased by 2.86 as the BASFI increased by one unit (Table 3).

3.3.2. The relationship between depression and sex, quality of life and axSpA disease activity. In all responders, women were more likely to report worse BD-II scores (R = 0.337, P = .009), and the BDI-II scores were inversely correlated with quality of life (EQ-5D) (R = -0.486, P < .0001).

Table 2

The correlation of the BAI and BDI scores with demographic and clinical variables.

	BAI		BDI-II		
	Pearson correlation	Significance (2-tailed)	Pearson correlation	Significance (2-tailed)	Group
BAI			0.526**	<0.0001	all
BDI-II	0.526**	< 0.0001			all
Age at the time of the study	-0.268*	0.040	-0.029	0.827	all
Sex	0.280*	0.032	0.337**	0.009	all
EQ-5D	-0.399**	0.002	-0.486**	< 0.0001	all
BMI	-0.333**	0.010	-0.075	0.569	all
Disease duration since diagnosis	-0.356*	0.039	-0.179	0.311	axSpA
Disease duration since first symptoms	-0.083	0.643	0.0001	0.999	axSpA
EAMs	0.008	0.965	0.260	0.138	axSpA
ASDAS-CRP	0.431*	0.012	0.562**	0.001	axSpA
BASFI	0.621**	< 0.0001	0.288	0.098	axSpA

Pearson correlation was used for analysis. Sex and EAMs were analyzed as dichotomous variables as follows: men as 1, women as 2; EAMs negative as 0 and positive as 1.

ASDAS-CRP = ankylosing spondylitis (AS) disease activity score-C-reactive protein, axSpA = axial spondyloarthritis, BAI = Beck Anxiety Inventory, BASFI = Bath AS Functional Index, BDI-II = Beck
Depression Inventory, BMI = body mass index, EAMs = extraarticular manifestations, EQ-5D = 5-dimensional European Quality of life questionnaire, N = number of cases, NRS = numeric rating scale.

\*Correlation is significant at the 0.05 level (2-tailed).

Table 3

The multiple regression analysis for the dependent variable BAI scores and independent clinical variables in axSpA patients.

	<b>Unstandardized coefficients</b>		Standardized coefficients		
	В	Std. error	Beta	t	Significance
(Constant)	3.627	6.861		0.529	0.602
Age at the time of the study	-0.039	0.094	-0.096	-0.420	0.679
Sex	2.584	1.508	1.508	1.713	0.100
Disease duration since diagnosis	-0.179	0.122	0.122	-1.467	0.156
Disease duration since first symptoms	0.138	0.088	0.088	1.581	0.128
EAMs	-0.582	1.125	-0.075	-0.517	0.610
ASDAS-CRP	1.152	0.996	0.195	1.157	0.259
BASFI	2.859	0.736	0.589	3.886	0.001
EQ-5D	4.308	4.152	0.183	1.038	0.310
BMI	-0.350	0.226	-0.245	-1.550	0.135

ASDAS-CRP = ankylosing spondylitis (AS) disease activity score-C-reactive protein, axSpA = axial spondyloarthritis, BAI = Beck Anxiety Inventory, BASFI = Bath AS Functional Index, BMI = body mass index, EAMs = Extraarticular manifestations, EQ-5D = 5-dimensional European Quality of life questionnaire.

<sup>\*\*</sup>Correlation is significant at the 0.01 level (2-tailed).

Of all tested clinical variables in axSpA patients, only ASDAS-CRP was associated with poor BDI-II outcomes (R = 0.562, P = .001) (Table 2). When a multiple regression model for axSpA was performed, sex and ASDAS-CRP were identified as the most important factors influencing BDI-II scores; the BDI-II score increased by 5.23 when the patient was female and by 3.44 when the ASDAS-CRP increased by one unit (Table 4). On the hand, we did not find any significant differences between BDI-II between axSpA with bDMARDs compared to those on NSAIDs only (data not shown).

3.3.3. The pain evaluation in relation to anxiety and depression. Although the pain evaluation on the NRS was similar for axSpA patients and controls (Table 1), the association of the pain experience with anxiety and depression varied among axSpA patients and controls. When symmetric correlation measures between axSpA patients and controls were performed, the severity of pain was correlated with BDI-II (R = 0.542, P = .001) and BAI (R = 0.489, P = .003) only in axSpA patients (Table 5).

3.3.4. The variability of work habits in the axSpA and control groups. Although the education levels, professional arrangement, and total hours of work per week were similar in both groups, a significant disease impact on work habits was suggested in axSpA patients (Table 1). Moreover, only in axSpA patients was the total hours of work per week inversely correlated with BDI-II scores, pain severity, and disease activity (R = -0.560, R = -0.472, both P < .01 and R = -0.408, P = .02, respectively) (Table 6).

### 4. Discussion

This is the first study to evaluate the self-reported evaluation of depression and anxiety using the Beck Depression Inventory and Beck Anxiety Inventory in axSpA patients and persons with NSLBP who were actively looking for non-pharmacological therapy options. Although the axSpA patients and controls did not differ significantly in terms of their scores on the BAI and BDI-II questionnaires, an inflammatory disorder may influence the outcomes of anxiety and depression. Moreover, it seems that the experience of pain severity may be related to anxiety and depression, mainly in axSpA patients, but not in those without inflammation.

Our study demonstrated similar BAI and BDI-II scores for axSpA patients and NSLBP; mild anxiety was observed in up to 14% of axSpA patients and 11% of controls, but moderate depression was only observed in up to 3% of axSpA patients. Recently, higher incidence rates of depressive disorder and anxiety in AS compared to the general population have been

demonstrated in nationwide studies in Taiwan and Korea,[11,31] and the Swedish national cohort survey suggested that the incidence of anxiety disorders was the highest among the psychiatric diseases in AS patients.[32] In the general Czech population, the prevalence of mood affection, major depression, and anxiety has been calculated as 5.5%, 4.0%, and 7.3%, respectively; mood affections are comparable, but anxiety seems to be lower than in other European countries. [33] Although the prevalence of anxiety was found to be slightly higher and the prevalence of depression was lower in our tested axSpA patients and controls than has been described in the general Czech population<sup>[33]</sup> the real prevalence and incidence of anxiety and depression, particularly in axSpA patients, should be estimated in further studies in the non-selected axSpA population and supported by a diagnosis from specialists in the field of psychiatry and not only by data obtained from one questionnaire. Moreover, the patients who participated in our study were mostly fully employed, performed regular physical activities, and, in the case of the axSpA patients, did not have severe functional impairment. All these factors may influence the occurrence of psychological distress.

The higher prevalence of depression and anxiety in the common axSpA population, however, has been suggested in large European studies: 28% and 31% of mild and moderate to severe depression, respectively, have been found among 1736 participants in a German study using the WHO Well-Being Index, [22] and the recent data from the ATLAS cohort comprising 680 axSpA patients detected depression in 21% and anxiety in 28% of individuals using the 12-item General Health Questionnaire scale. [34] Although anxiety rather than depression seems to be more common in our study, patients with axSpA in our study seemed to be less depressed and suffered less anxiety than their European counterparts. Similar to our work, the studies applying the BDI-II and BAI questionnaires found that the median BDI-II score was 6 and moderate depression was only 9% among 43 axSpA patients, [35] and a higher prevalence of anxiety in AS patients than in healthy individuals was identified in two Turkish studies. [36,37] Our study, however, focused on a selected group of patients with axSpA, and NSLBP demonstrated that persons looking for additional options to improve their health, such as exercise, had comparable depressive and anxiety burdens, irrespective of whether they suffered from inflammatory disorders. Therefore, the results of our study should not be generalized to the common axSpA population but may indicate the advantages of an active patient approach to their health, at least to mental health.

The previously discussed association of impaired function and anxiety<sup>[13]</sup> and the inclination of patients with higher disease activity to have depressive experiences<sup>[13,22,34]</sup> were supported in our work. Higher disease activity<sup>[13]</sup> and the first year of axSpA diagnosis<sup>[34]</sup> have already been found to be risk factors

Table 4
The multiple regression analysis for the dependent variable BDI-II scores and independent clinical variables in axSpA patients.

	Unstandardized coefficients		Standardized coefficients		
	В	Std. error	Beta	t	Significance
(Constant)	-6.995	9.151		-0.764	0.452
Age at the time of the study	-0.035	0.125	-0.067	-0.279	0.783
Sex	5.514	2.012	0.495	2.741	0.012
Disease duration since diagnosis	-0.020	0.162	-0.030	-0.124	0.902
Disease duration since first symptoms	0.108	0.117	0.242	0.924	0.365
EAMs	1.223	1.500	0.123	0.815	0.423
ASDAS-CRP	3.441	1.328	0.456	2.590	0.016
BASFI	1.536	0.981	0.248	1.564	0.131
EQ-5D	5.227	5.538	0.174	0.944	0.355
BMI	-0.294	0.301	-0.161	-0.976	0.339

ASDAS-CRP = ankylosing spondylitis (AS) disease activity score-C-reactive protein, axSpA = axial spondyloarthritis, BASFI = Bath AS Functional Index, BDI-II = Beck Depression Inventory, BMI = body mass index, EAMs = Extraarticular manifestations, EQ-5D = 5-dimensional European Quality of life questionnaire.

The variability of the correlation between anxiety, depression and pain severity in axSpA patients and controls.

	Pearson R	SE	t statistic	Significance
Correlation of th	ne BAI scores and N	IRS pain scores	3	
axSpA	0.489	0.136	3.172	0.003
Controls	-0.184	0.171	-0.858	0.401
All	0.186	0.142	1.402	0.166
Correlation of th	ne BDI-II scores and	NRS pain scor	res	
axSpA	0.542	0.141	3.645	0.001
Controls	0.027	0.174	0.123	0.903
All	0.346	0.143	2.732	0.008

Symmetric measures, interval by interval Pearson's R was performed. Significant when P < .05.

The correlations between the total hours of work per week and anxiety, depression and other variables in axSpA patients and controls.

	axSp	axSpA patients		Controls		
	Pearson R	Significance	Pearson R	Significance		
BAI	-0.315	0.069	-0.184	0.378		
BDI-II	-0.560**	0.001	-0.148	0.471		
EQ-5D	0.237	0.178	-0.028	0.891		
NRS pain	-0.472**	0.005	0.138	0.528		
ASDAS-CRP	-0.408*	0.018	NA	NA		
BASFI	-0.030	0.866	NA	NA		

The Pearson correlation was used for the analysis.

ASDAS-CRP = ankylosing Spondylitis (AS) disease activity score-C-reactive protein, axSpA = axial  $spondyloar thritis, \, BAI = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BDI-II = Beck \, Anxiety \, Inventory, \, BASFI = Bath \, AS \, Functional \, Index, \, BASFI = Bath \, AS \, Functional \, Bath \, AS \, Fu$ Depression Inventory, EQ-5D = 5-dimensional European Quality of life questionnaire, NA = not analyzed NRS = numeric rating scale

for anxiety in patients with axSpA. In our study, although the duration of axSpA diagnosis was inversely correlated with the BAI score, only BASFI seemed to be a major factor for anxiety. In our study, worse outcomes for depressive mood status were found in axSpA patients with higher disease activity and for females. Females are more likely to develop depression than men in the general population.[38] In axSpA, previous studies are not consistent; Zou et al[13] did not find a female predominance regarding depressive outcomes evaluated by the Zung Self-Rating Depression Scale among 60 patients, but Park et al<sup>[11]</sup> determined the hazard ratio for females to be 1.60 in AS patients, and sex was not associated with moderate-to-severe depressive symptoms while controlling for other variables in Redeker's German study.[22] AxSpA clinical outcomes, however, may vary between men and women; structural changes are more common in males, but females usually assign higher degrees to the evaluation of self-reported disease activity,[39] have a lower response to biological therapy,[40] and may have a longer diagnosis delay.

The findings of our study highlight the importance of studies focused on the variability of experience with depression and anxiety in axSpA individuals treated with various pharmacological therapy options. As various levels of experience with depression in axSpA patients with and without biologic therapy have been suggested, [22,35,36] studies examining therapeutic approaches, including non-pharmacological options and psychotherapeutic support, for the best mental health of axSpA patients, particularly in females, are warranted.

Pain severity was associated with poor anxiety and depression outcomes only in patients with axSpA but not in patients with nonspecific low back pain in our study. Zou et al[13] did not find a correlation between self-reported anxiety and depression with pain evaluated using the visual analogue scale in patients with axSpA. In patients with low back pain, however, the pain intensity on the visual analogue scale was associated with increased symptoms of depression and anxiety on the subscales of the self-reported Brief Symptom Inventory[41] and the Hospital Anxiety and Depression Scale.[42] However, the pain intensity described in these studies was higher than that reported on the NRS scale in our patients with NSLBP. In our study, individuals with NSLBP were mostly seeking physiotherapy for their current back pain problems and did not have an acute exacerbation of their LBP. We can hypothesize that the current physical situation of the intensity of LBP symptoms may influence the additive effect of psychological distress on pain perception. However, in patients with axSpA, the pain may have been accompanied by psychological distress even in the group of patients with low disease activity or an active approach to non-pharmacological therapy because the pain may be due to the inflammatory origin of the disease.

Our study has several limitations. The first one resided in the selected individuals because healthy persons without any musculoskeletal problems and axSpA patients with relevant functional impairment and who were not active in looking to exercise were not included; thus, we could not determine if the active patients were less depressed and anxious than those without personal interests in the exercise therapeutic options. The next limitation is the number of axSpA patients and their clinical manifestation - most patients had lower disease activity and only 20% were treated by bDMARDs. The next limitation is the lack of a complex medical history for patients with NSLBP, because only the inclusion criteria were essential for inclusion in the study. The duration of the current episode of back pain, chronicity of LBP, and the number of relapses may influence pain evaluation and the association of low back pain with depression.[41,43] The next limitation was the questionnaires used for the study. The BDI-II and BAI are both well-established questionnaires for monitoring depression and anxiety. In axSpA patients, the surveys focused on psychological outcomes; however, many other questionnaires have been used,[10,12,13,22,34-36] and to date, no consensus has been reached regarding which is the best one for monitoring depression and anxiety.

### 5. Conclusion

Our study demonstrated a similar intensity of anxiety and depression evaluated by the self-reported BAI and BDI-II questionnaires in people looking for non-pharmacological therapeutic options for their disorders, inflammatory axSpA and non-inflammatory NSLBP. Although it is necessary to validate the results of our study, the positive approach for all therapeutic options seems to be beneficial for mental health in patients with musculoskeletal disorders, irrespective of inflammatory origin. On the other hand, the impact of daily experience with pain and the chronicity of axSpA may influence the relationship between pain intensity and psychological burden. Higher disease activity, impaired function, and the onset of the disease were associated with poorer psychological outcomes in patients with axSpA. Thus, adequate therapy to prevent impaired mobility and support disease remission is required for axSpA patient mental health.

### **Author contributions**

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<sup>\*</sup>Correlation is significant at the 0.05 level (2-tailed).

<sup>\*\*</sup>Correlation is significant at the 0.01 level (2-tailed).

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### References

- [1] Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet. 2017;390:73–84.
- [2] Sieper J, Rudwaleit M, Baraliakos X, et al. The assessment of spondyloarthritis international society (ASAS) handbook: a guide to assess spondyloarthritis. Ann Rheum Dis. 2009;68:ii1–44.
- [3] Sieper J, Hu X, Black CM, et al. Systematic review of clinical, humanistic, and economic outcome comparisons between radiographic and non-radiographic axial spondyloarthritis. Semin Arthritis Rheum. 2017;46:746–53.
- [4] Kiltz U, Baraliakos X, Karakostas P, et al. The degree of spinal inflammation is similar in patients with axial spondyloarthritis who report high or low levels of disease activity: a cohort study. Ann Rheum Dis. 2012;71:1207–11.
- [5] van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum. 1984;27:361–8.
- [6] Derakhshan MH, Goodson NJ, Packham JC, et al. Increased risk of hypertension associated with spondyloarthritis disease duration: results from the ASAS-COMOSPA study. J Rheumatol. 2019;46:701–9.
- [7] Barlow JH, Macey SJ, Struthers GR. Gender, depression, and ankylosing spondylitis. Arthritis Rheum. 1993;6:45–51.
- [8] Martindale J, Smith J, Sutton CJ, et al. Disease and psychological status in ankylosing spondylitis. Rheumatology (Oxford). 2006;45:1288–93.
- [9] Brionez TF, Assassi S, Reveille JD, et al. Psychological correlates of self-reported functional limitation in patients with ankylosing spondylitis. Arthritis Res Ther. 2009;11:R182.
- [10] Zhang L, Wu Y, Liu S, et al. Prevalence of depression in ankylosing spondylitis: a systematic review and meta-analysis. Psychiatry Investig. 2019;16:565–74.
- [11] Park JS, Jang HD, Hong JY, et al. Impact of ankylosing spondylitis on depression: a nationwide cohort study. Sci Rep. 2019;9:6736.
- [12] Zhao S, Thong D, Miller N, et al. The prevalence of depression in axial spondyloarthritis and its association with disease activity: a systematic review and meta-analysis. Arthritis Res Ther. 2018;20:140.
- [13] Zou Q, Jiang Y, Mu F, et al. Correlation of axial spondyloarthritis with anxiety and depression. Med Sci Monit. 2016;22:3202–8.
- [14] Chan CYY, Tsang HHL, Lau CS, et al. Prevalence of depressive and anxiety disorders and validation of the hospital anxiety and depression scale as a screening tool in axial spondyloarthritis patients. Int J Rheum Dis. 2017;20:317–25.
- [15] Balagué F, Pellisé F. Adolescent idiopathic scoliosis and back pain. Scoliosis Spinal Disord. 2016;11:27.
- [16] Fernandez-de-Las-Penas C, Alonso-Blanco C, Hernandez-Barrera V, et al. Has the prevalence of neck pain and low back pain changed over the last 5 years? A population-based national study in Spain. Spine J. 2013;13:1069–76.
- [17] Koes BW, van Tulder M, Lin CW, et al. An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. Eur Spine J. 2010;19:2075–94.
- [18] Balague F, Mannion AF, Pellise F, et al. Non-specific low back pain. Lancet. 2011;379:482–91.
- [19] Bair MJ, Robinson RL, Katon W, et al. Depression and pain comorbidity: a literature review. Arch Intern Med. 2003;163:2433–45.
- [20] Levitova A, Hulejova H, Spiritovic M, et al. Clinical improvement and reduction in serum calprotectin levels after an intensive exercise

- programme for patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis. Arthritis Res Ther. 2016;18:275.
- [21] Akodu AK, Akindutire OM. The effect of stabilization exercise on pain-related disability, sleep disturbance, and psychological status of patients with non-specific chronic low back pain. Korean J Pain. 2018;31:199–205.
- [22] Redeker I, Hoffmann F, Callhoff J, et al. Determinants of psychological well-being in axial spondyloarthritis: an analysis based on linked claims and patient-reported survey data. Ann Rheum Dis. 2018;77:1017–24.
- [23] van der Heijde D, Lie E, Kvien TK, et al. ASDAS, a highly discriminatory ASAS-endorsed disease activity score in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68:1811–8.
- [24] Calin A, Garrett S, Whitelock H, et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the bath ankylosing spondylitis functional index. J Rheumatol. 1994;21:2281–5.
- [25] Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol group. Ann Med. 2001;33:337–43.
- [26] Beck AT, Steer RA, Carbin MG. Psychometric properties of the beck depression inventory: twenty-five years of evaluation. Clin Psychol Rev. 1988;8:77–100.
- [27] Beck AT, Epstein N, Brown G, et al. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56:893–7.
- [28] Kamarádová D, Praško J, Látalová K, et al. Validizace české verze Beckova inventáře úzkosti. Čes Slov Psychiat; 2016;112:153–8.
- [29] Ptáček R, Raboch J, Vňuková M, et al. Beckova škála deprese BDI-II standardizace a využití v praxi. Čes Slov Psychiat. 2016;112:270–4.
- [30] Julian LJ. Measures of anxiety: state-trait anxiety inventory (STAI), beck anxiety inventory (BAI), and hospital anxiety and depression scale-anxiety (HADS-A). Arthritis Care Res (Hoboken). 2011;63:S467–72.
- [31] Shen CC, Hu LY, Yang AC, et al. Risk of psychiatric disorders following ankylosing spondylitis: a nationwide population-based retrospective cohort study. J Rheumatol. 2016;43:625–31.
- [32] Sundquist K, Li X, Hemminki K, et al. Subsequent risk of hospitalization for neuropsychiatric disorders in patients with rheumatic diseases: a nationwide study from Sweden. Arch Gen Psychiatry. 2008;65:501–7.
- [33] Formanek T, Kagstrom A, Cermakova P, et al. Prevalence of mental disorders and associated disability: results from the cross-sectional CZEch mental health Study (CZEMS). Eur Psychiatry. 2019;60:1–6.
- [34] Garrido-Cumbrera M, Delgado-Dominguez CJ, Galvez-Ruiz D, et al.; Atlas Working Group. The effect of axial spondyloarthritis on mental health: results from the Atlas. J Rheumatol. 2019;46:1284–9.
- [35] Milutinovic S, Veljkovic K, Zlatanovic M, et al. Depression/anxiety symptoms in axial spondyloarthritis and psoriatic arthritis patients in Serbia: a pilot study. Rheumatol Int. 2019;39:1595–605.
- [36] Yildirim T, Solmaz D, Emul M, et al. Affective temperament profile in ankylosing spondylitis patients using TEMPS-A. J Phys Ther Sci. 2017;29:394–400.
- [37] Esen SA, Karabulut Y, Esen I, et al. Effects of the disease characteristics and the treatment on psychological status in patients with rheumatoid arthritis and ankylosing spondylitis. Curr Rheumatol Rev. 2018;14:271–8.
- [38] Kuehner C. Why is depression more common among women than among men? Lancet Psychiatry. 2017;4:146–58.
- [39] de Jong H, Paramarta JE, de Winter J, et al. Differences between females and males in axial spondyloarthritis: data from a real-life cross-sectional cohort. Scand J Rheumatol. 2020;49:1–5.
- [40] Lubrano E, Perrotta FM, Manara M, et al. The sex influence on response to tumor necrosis factor-alpha inhibitors and remission in axial spondyloarthritis. J Rheumatol. 2018;45:195–201.
- [41] Mngoma N, Corbiere M, Stevenson J. Pain profiles and psychosocial distress symptoms in workers with low back pain. Physiother Can. 2008;60:239–45.
- [42] Wang HY, Fu TS, Hsu SC, et al. Association of depression with sleep quality might be greater than that of pain intensity among outpatients with chronic low back pain. Neuropsychiatr Dis Treat. 2016;12:1993–8.
- [43] Salt E, Wiggins AC, Rayens MK, et al. The relationship between life purpose with depression and disability in acute low back pain patients. Orthop Nurs. 2018;37:287–91.