



# A Benchmarking Study Evaluating Axial Spondyloarthritis Burden in Spain and Other European Countries. Results from the Spanish Atlas and the European Map of Axial Spondyloarthritis (EMAS) Studies

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## Abstract

**Aim:** To compare the burden of disease in Spanish patients with axial spondyloarthritis (axSpA) vs other European countries (OEC).

**Methods:** Data from 2846 unselected patients from the European Map of Axial Spondyloarthritis (EMAS) and the Atlas of Axial Spondyloarthritis in Spain (Atlas) were collected through online surveys. Comparative analysis was carried out between Spanish patients (2016) and patients from 12 OEC (2017-2018). Socio-demographic characteristics, life habits, and patient-reported outcomes (Bath Ankylosing Spondylitis Disease Activity Index 0-10, spinal stiffness 3-12, functional limitation 0-54, the 12-Item General Health Questionnaire [GHQ-12] for psychological distress 0-12) were compared. Chi-square and Mann-Whitney tests were used for qualitative and quantitative variables respectively.

**Results:** 680 (23.9%) Spanish axSpA patients were compared to 2166 axSpA patients (76.1%) from OEC. Compared to Spain, the OEC group had a higher percentage of females (64.1% vs 52.5%;  $P < .001$ ) and university-educated participants (51.7% vs 36.9%;  $P < .001$ ). Spanish patients showed a greater diagnostic delay ( $8.5 \pm 7.7$  vs  $7.2 \pm 8.6$  years;  $P < .001$ ), visits to orthopedic specialists before diagnosis (56.9% vs 25.3%;  $P < .001$ ), human leukocyte antigen-B27 carriership (77.1% vs 70.1%;  $P = .003$ ), disease activity ( $5.7 \pm 2.0$  vs  $5.4 \pm 2.0$ ;  $P = .024$ ), and higher unemployment rates (21.7% vs 9.2%;  $P < .001$ ). Despite lower rates of diagnosed anxiety and depression, Spanish patients were at higher risk of psychological distress according to the GHQ-12 ( $5.7 \pm 4.5$  vs  $4.8 \pm 4.0$ ;  $P < .001$ ).

**Conclusion:** Compared to European axSpA patients, Spanish patients experience a longer diagnostic delay and greater psychological distress. Being wrongly referred to orthopedic specialists and facing a more precarious labor scenario appear as

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possible causal factors, highlighting the need to increase the number of rheumatologists, the training of healthcare professionals, and improving axSpA patients' working conditions.

#### KEYWORDS

ankylosing spondylitis, axial spondyloarthritis, diagnostic delay, employment status, patient-reported outcomes, psychological distress

## 1 | INTRODUCTION

Axial spondyloarthritis (axSpA) is a disease associated with a high degree of disease burden and disability,<sup>1</sup> and consequently with a high cost per patient to European national health systems.<sup>2-4</sup> This disease has been the focus of extensive research in recent decades. From this growing interest in axSpA, different research registries and cohorts have emerged at national levels in Europe. Some examples are the DANBIO,<sup>5</sup> DESIR,<sup>6</sup> GESPIC,<sup>7</sup> OASIS,<sup>8</sup> SPACE,<sup>9</sup> SWISS,<sup>10</sup> or REGISPONSER,<sup>11</sup> the objectives of which are to study the characteristics of axSpA and understand the clinical aspects to improve patient management and treatment. However, despite the relevant clinical value of these studies, which allowed researchers to reach a better understanding of the functioning of axSpA and related conditions, these records have some limitations in providing answers to further research questions. On the one hand, there is a trend in these studies to leave aside life spheres that are of key importance from the patient's perspective, such as work experience or mental health. On the other hand, most of these registries and cohorts have been carried out on a national level and it is therefore not possible to compare data between different countries.

The systematic study of other life spheres, also affected by the disease either in a direct or indirect way, escapes clinical studies almost entirely. To give an example, only the DESIR cohort study collects some data on the impact of axSpA on working life for the total study population, based on indirect measures such as absenteeism through sick leave or level of disability.<sup>6</sup> There is a wide research gap not only on the disease's impact on working life, but also in the association of the condition with poorer psychological health or the patient's perspective with respect to their own disease.

Additionally, despite the rigor of the studies presented, they utilize different methodologies in terms of sample inclusion criteria, sampling method and variables collected, so a comparison of the disease characteristics and status of patients with axSpA between European countries is not possible. Some studies are international, like the OASIS. However, its scope covers only 3 countries of similar geographical and socio-economic conditions (France, Belgium, and the Netherlands).<sup>8</sup> Even if great efforts are being made in order to carry out joint studies of different registries that allow for greater generalizability of results, this research is still subject to problems due to the different methodologies used by said registries, leading to sample bias<sup>12</sup> or lack of comparability of the relevant indicators for axSpA patients' health.<sup>13</sup>

All of these reasons made it necessary to conduct a study on axSpA from the patient's perspective, collecting representative country samples under 1 common methodology, thereby allowing comparisons of national data in relation to a European framework. That is one of the main objectives of the European Map of Axial Spondyloarthritis (EMAS), upon which data for this study is based.

Benchmarking studies in axSpA may provide evidence of disparities, making it necessary to improve the healthcare and management of these patients. The aim of this study is to analyze the burden of the disease in axSpA patients in Spain compared with that of patients from other European countries (OEC) in terms of sociodemographic characteristics, diagnostic journey, disease activity, function, and psychosocial wellbeing.

## 2 | MATERIALS AND METHODS

### 2.1 | The Atlas and EMAS working groups

The Atlas of Axial Spondyloarthritis in Spain is an initiative of the Spanish Federation of Spondyloarthritis Associations (CEADE), carried out by the Health & Territory Research (HTR) group of the University of Seville and the Max Weber Institute, with the collaboration of the Spanish Society of Rheumatology (SER), and the support of Novartis Spain. Results from the Atlas raised international interest and thus, an equivalent research following the same methodology was carried out. This extension of the project to OEC was addressed as EMAS, and it was also led by HTR in collaboration with the Axial Spondyloarthritis International Federation (ASIF), along with patient organizations in participating countries, and the support of Novartis headquarters. The EMAS project continues expanding, being currently carried out in additional countries in Africa, America, Asia, and Europe under the new brand International Map of Axial Spondyloarthritis (IMAS). More information about the Atlas<sup>14</sup> and EMAS<sup>15</sup> can be found in their seminal studies.

### 2.2 | Design and survey development

The Atlas of Axial Spondyloarthritis in Spain is a cross-sectional study gathering data through an online survey of 680 unselected patients with self-reported axSpA diagnosis.<sup>14</sup> This Spanish survey was adapted into the EMAS survey, which recruited an additional 2166 axSpA patients from 12 different European countries other than Spain: Austria,



Belgium, France, Germany, Italy, the Netherlands, Norway, Russia, Slovenia, Sweden, Switzerland, the United Kingdom. To develop the EMAS questionnaire, the steering committee and participating countries were asked to assess and modify questions for local relevance, with guidance to only make essential changes in order to maintain consistency between the Atlas and EMAS studies, on a pan-European level. The EMAS questionnaire was developed in English and subsequently translated into the languages of the other European countries involved (Dutch, French, German, Italian, Russian, Swedish, and Slovenian). The final EMAS patient questionnaire included 108 items of the original 116 of the Atlas, related to 12 different areas: socio-demographic and anthropometric characteristics, disability and performance, work life, daily life, lifestyle habits, diagnostic process, healthcare resource use, treatment, other disorders/diseases, psychological health, disease outcomes, and patient experience of living with the disease. All indicators collected for the EMAS survey were patient-reported outcomes.

In addition, a range of supplementary indices were collected in the questionnaire to assess specific areas.

1. BASDAI (Bath Ankylosing Spondylitis Disease Activity Index): a validated self-administered questionnaire assessing disease activity in axSpA patients.<sup>16</sup>
2. Spinal Stiffness Index: this index assessed the degree of stiffness experienced in the spinal column, distinguishing between the cervical, dorsal, and lumbar areas. The scale ranges from 3 (no stiffness) to 12 (maximum level of stiffness).<sup>14</sup>
3. Functional Limitation Index: it assessed the degree of functional limitation in 18 activities of daily life through a 4-point Likert scale (0 to 3). Total scores range from 0 (no limitation) to 54 (maximum level of functional limitation).<sup>14</sup>
4. GHQ-12 (The 12-Item General Health Questionnaire): this validated scale evaluates psychological distress using 12 questions. The cut-off point of 3 implied those with a score of 3 or more may be experiencing psychological distress.<sup>17</sup>

### 2.3 | Sample selection and recruitment

Sample selection inclusion criteria for both the Atlas and EMAS studies were the same: to be aged  $\geq 18$  years, resident in any of the 13 participating European countries, have a diagnosis of axSpA, including ankylosing spondylitis (also known as radiographic axSpA) and non-radiographic axSpA, and to have paid an axSpA-related visit to a healthcare professional in the 12 months prior to participation.

Participants from the Atlas were recruited from January to March 2016. Survey dissemination of the Atlas was made through press releases, e-mails and website and social media announcements. EMAS participants were recruited between July 2017 and March 2018 by Ipsos SA (formerly GfK) through its online panel of respondents. This firm ensures that patients are fully validated through their connected healthcare professionals around the world who refer patients for research. In Austria, Norway, Slovenia, Sweden, the Netherlands, Italy, Russia, and Spain, patient organizations supported recruitment by distributing the

survey link to their members. The questionnaire was completed via an online platform for survey data collection. In addition, the database from the Atlas<sup>18</sup> was adapted to fit the EMAS database in order to allow comparisons between Spanish and the OEC axSpA patients.

### 2.4 | Statistical analysis

Socio-demographic characteristics, life habits, and patient-reported outcomes (BASDAI, spinal stiffness, functional limitation and psychological distress through GHQ-12) were compared between Spanish and OEC axSpA patients. Chi-square test was used for qualitative variables and Mann-Whitney test for quantitative variables. All analyses were carried out using the Statistics Package for Social Sciences (SPSS) v. 25.0.

## 3 | RESULTS

The Spanish sample was characterized by a slightly higher age and lower presence of women than in the OEC sample. The number of people with university studies and the overall income level was lower than the European average. Regarding harmful lifestyle habits, compared to the OEC, a higher percentage of Spanish axSpA patients declared that they smoke. However, although both groups followed a similar trend regarding regular alcohol consumption (more than twice a week), the Spanish sample less frequently reported moderate consumption (between 1 and 2 times a week) and more participants reported occasional drinking or abstinence compared to their European counterparts (Table 1).

The average mean age of onset of first symptoms of Spanish axSpA participants was more than 3 years lower than in the OEC, overall disease duration was reported to be around 4 years longer, and diagnostic delay more than 1 year greater. As for patient-reported outcomes, the Spanish sample also reported a higher rate of human leukocyte antigen (HLA)-B27 positivity. Moreover, the Spanish sample had a slightly higher BASDAI score. However, BASDAI differences were not clinically relevant according to rheumatologic standards. Additionally, Spanish axSpA patients declared a much greater functional limitation than the OEC. They also reported half the rate of inflammatory bowel disease than the OEC (Table 2).

A total of 21.7% of the Spanish sample in the active population was unemployed, while for OEC this figure drops to 9.2%. Moreover, unemployed patients were asked whether they considered that they had to leave or lost their job due to axSpA, to which 62.8% of Spanish and 65.3% of OEC respondents answered "yes". Furthermore, 95.5% of Spanish axSpA patients stated that their disease made it or would make it difficult to find a job compared to 70.3% of the OEC. However, in the case of Spanish patients who had a job, they reported fewer work-related issues, and less need for workplace adaptation than their European counterparts. Although the reported prevalence of mental disorders (anxiety, depression, and sleep disorders) was significantly lower in the Spanish sample compared to the OEC, the average GHQ-12 score was higher in Spanish axSpA patients. Finally,



Variable	Spain mean ± SD; n (%)	OEC mean ± SD; n (%)	P value
<b>Sociodemographic</b>			
Age, years	45.7 ± 10.8	43.4 ± 12.6	<.001*
Gender, female	357 (52.5)	1389 (64.1)	<.001*
<b>Marital status</b>			
Single	126 (18.5)	475 (21.9)	.152
Married	486 (71.5)	1447 (66.8)	
Separated/divorced	60 (8.8)	213 (9.8)	
Widowed	8 (1.2)	31 (1.4)	
<b>Educational level</b>			
No schooling completed	9 (1.3)	23 (1.1)	<.001*
Primary school	119 (17.5)	144 (6.6)	
High school	301 (44.3)	880 (40.6)	
University	251 (36.9)	1119 (51.7)	
Monthly income (euros) per household member	823.2 ± 656.4; n = 333	1173.5 ± 928.8; n = 1956	<.001*
Patient organization, member	301 (44.3)	806 (37.2)	.001*
<b>Anthropometric characteristics</b>			
<b>Body mass index</b>			
Underweight, < 18.5	17 (2.5)	91 (4.2)	.069
Normal weight, 18.5-24.9	309 (45.4)	943 (43.5)	
Overweight, 25-29.9	240 (35.3)	713 (32.9)	
Obese, > 30	114 (16.8)	419 (19.3)	
<b>Lifestyle habits</b>			
<b>Smoking</b>			
Non-smoker or socially <10 cigarettes/day	417 (71.3); n = 585	1679 (77.5)	<.001*
More than 10 cigarettes/day	24 (4.1); n = 585	111 (5.1)	
	144 (24.6); n = 585	376 (17.4)	
<b>Alcohol</b>			
Never or occasionally	503 (86.0); n = 585	1723 (79.5)	<.001*
1-2 times per week	37 (6.3); n = 585	292 (13.5)	
More than twice per week	45 (7.7); n = 585	151 (7.0)	

Abbreviation: OEC, other European countries.

\*P-value ≤ .05.

95.6% of the Spanish sample reported benefiting from public health insurance while for OEC this figure fell to 77.7% ( $P < .001$ ; Table 3).

With respect to EMAS data, Spanish patients show a systematically longer diagnostic delay than their European counterparts over the last 2 decades (Table 4).

## 4 | DISCUSSION

The results of the EMAS survey allow us to verify a series of unmet needs at the European level as well as particular needs of Spanish

patients, such as long diagnostic delay and psychosocial consequences including the deterioration of mental health and high impact of axSpA on working life.

### 4.1 | Country profiles

Despite the organizational heterogeneity of European health systems, some peculiarities of the Spanish health system can be highlighted. Spain has more physicians than the European average (381 vs 353 per 100 000 inhabitants).<sup>19</sup> In fact, this figure places Spain

**TABLE 1** Sociodemographic, anthropometric characteristics, and lifestyle habits (N = 680 for Spain and N = 2,166 for OEC, unless otherwise specify)



**TABLE 2** Disease characteristics and functioning (N = 680 for Spain and N = 2,166 for OEC, unless otherwise specify)

Variable	Spain mean $\pm$ SD; n (%)	OEC mean $\pm$ SD; n (%)	P value
<b>Diagnosis</b>			
Age at onset of first symptoms, years	24.4 $\pm$ 8.8; n = 555	27.2 $\pm$ 11.6	<.001*
Age at diagnosis, years	32.9 $\pm$ 9.6; n = 556	33.9 $\pm$ 11.9	.053
Diagnostic delay, years	8.5 $\pm$ 7.7; n = 550	7.2 $\pm$ 8.6; n = 2,102	<.001*
Disease duration, years	20.9 $\pm$ 12.2; n = 555	16.2 $\pm$ 12.3; n = 2,161	<.001*
<b>Extra-musculoskeletal manifestations</b>			
Uveitis	122 (17.9)	347 (18.2); n = 1,902	.860
Crohn's disease	21 (3.1)	133 (6.8); n = 1,961	<.001*
Ulcerative colitis	22 (3.2)	153 (7.7); n = 1,981	<.001*
<b>Human leukocyte antigen-B27</b>			
Positive	391 (77.1); n = 507	892 (70.1); n = 1,272	.003*
<b>Disease activity</b>			
BASDAI, 0-10	5.7 $\pm$ 2.0; n = 418	5.4 $\pm$ 2.0	.024*
BASDAI, <4	81 (19.4); n = 418	484 (22.3)	.179
BASDAI, $\geq$ 4	337 (80.6); n = 418	1682 (77.7)	
<b>Spinal stiffness index, 3-12</b>			
Overall spinal stiffness	7.5 $\pm$ 2.7; n = 494	7.8 $\pm$ 2.4	.009*
<b>Maximum degree of spinal stiffness</b>			
No stiffness	59 (10.9); n = 541	128 (5.9)	<.001*
Mild	102 (18.9); n = 541	369 (17.0)	
Moderate	182 (33.6); n = 541	752 (34.7)	
Severe	198 (36.6); n = 541	917 (42.3)	
<b>Functional limitation index, 0-54</b>			
Overall limitation	27.7 $\pm$ 13.2; n = 605	14.3 $\pm$ 11.8	<.001*
Low, 0-17	152 (25.1); n = 605	1383 (63.9)	<.001*
Medium, 18-35	282 (46.6); n = 605	660 (30.5)	
High, 36-54	171 (28.3); n = 605	123 (5.7)	

Abbreviations: BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; OEC, other European countries.

\*P-value  $\leq$  .05.

among the 10 countries within the Organization for Economic Co-operation and Development (OECD) with the highest number of doctors per inhabitant.<sup>20</sup> However, in relation to the number of rheumatologists, it has been estimated that Spain has 2.0 per 100 000 inhabitants.<sup>21</sup> According to workforce planning models for the year 2021, the as yet unreached estimate required to meet the needs of rheumatic patients is 3.5 per 100 000 inhabitants for Spain (calculated for 2021), while for the United Kingdom the need is only 0.7 rheumatologists per 86 000 inhabitants (calculated for 1988).<sup>22</sup> In other healthcare systems the needed rates may be higher. For example, in Austria the needed rate has been established as 4.3 rheumatologists per 100 000 inhabitants (calculated for 2017).<sup>23</sup>

According to the data presented, the situation of Spanish patients with axSpA is more precarious than that of their European neighbors. On the one hand, Spanish statutory health insurance is universal in coverage and financed almost entirely through the public sector,<sup>24</sup>

with a private spending in health that could match that of the Russian Federation (both comprising less than 5%) while surpassing that of Norway (<1%), and being much lower than that of France (>10%).<sup>25</sup> On the other hand, it is important to acknowledge that compared to other EMAS participating countries, Spain is among the countries that spend a lower percentage of its gross domestic product (GDP) on health. In fact, 9.2% of Spain's total GDP is allocated to the health sector. This percentage surpasses only that of Italy (9.0%), Slovenia (8.5%), and Russia (5.6%), and differs by about 2% with the largest health investors: France (11.5%), Germany (11.2%) and Sweden (11.0%).<sup>26</sup>

Additionally, Spanish expenditure per capita on health is \$2354, the 3rd lowest among EMAS countries, only above Slovenia and Russia;<sup>27</sup> it is also 3rd with the lowest numbers of hospital beds per 100 000 inhabitants (297.28, while the Euro 28 average is 504.02).<sup>28</sup> Furthermore, in comparison with the OEC sample, Spanish axSpA patients were characterized by being less educated



Variable	Spain mean $\pm$ SD; n (%)	OEC mean $\pm$ SD; n (%)	P value
Employment status of labor force	n = 415	n = 1247	
Employed	325 (78.3)	1132 (90.8)	<.001*
Unemployed	90 (21.7)	115 (9.2)	
Employment status of economically inactive	n = 238	n = 804	
Temporary sick leave	63 (26.5)	241 (30.0)	.308
Permanent sick leave	64 (26.9)	228 (28.4)	
Retired	63 (26.5)	167 (20.8)	
Early retirement	10 (4.2)	33 (4.1)	
Homemaker	29 (12.2)	85 (10.6)	
Student	9 (3.8)	50 (6.2)	
Work-related issues due to axSpA	170 (54.3); n = 313	795 (71.6); n = 1111	<.001*
Workplace adaptation due to axSpA	116 (23.9); n = 485	1047 (48.3)	<.001*
axSpA influenced job choice	186 (33.8); n = 551	970 (49.1); n = 1976	<.001*
Difficulties finding a job due to axSpA	294 (95.5); n = 308	1240 (70.3); n = 1763	<.001*
Psychological health			
Sleep disorder	134 (19.7)	924 (45.5); n = 2033	<.001*
Anxiety	135 (19.9)	674 (33.1); n = 2038	<.001*
Depression	100 (14.7)	610 (30.0); n = 2034	<.001*
GHQ-12 score, 0-12	5.7 $\pm$ 4.5; n = 474	4.8 $\pm$ 4.0	<.001*
At risk for psychological distress, GHQ-12 $\geq$ 3	310 (65.4); n = 474	1314 (60.7)	.055
Disease-related perceptions			
Talked with your physician about treatment goals	338 (75.8); n = 446	1325 (64.6); n = 2050	<.001*
Main health insurance			
Public health insurance	526 (95.6); n = 550	1110 (77.7); n = 1428	<.001*
Private health insurance	22 (4.0); n = 550	214 (15.0); n = 1428	
Private care, self-pay	2 (0.4); n = 550	104 (7.3); n = 1428	

Abbreviations: axSpA, axial spondyloarthritis; GHQ-12, The 12-Item General Health Questionnaire; OEC, other European countries.

\*P-value  $\leq$  .05.

and having a lower income level per household member. Low public investment coupled with low income levels means that Spanish axSpA patients face a disabling disease with limited resources.

The Spanish sample also had a lower representation of female members, slightly older and with a higher rate of membership to national patient organizations. These facts, in particular educational level, income and gender, may mediate the differences found in the burden of disease across Europe.

## 4.2 | Diagnostic delay

The Spanish sample shows an average diagnostic delay of 8.5 years and a median of 6 years, a figure higher than that reported by the

Spanish REGISPONER study (mean 6.3 years and median 3.0 years) conducted in 2007.<sup>11</sup> This could lead to the unlikely conclusion of an increase in diagnostic delay in Spain in recent years. However, a more plausible explanation would be the longer disease duration for participants in the Atlas study with respect to that of REGISPONER (6 years longer on average). Therefore, the Atlas study, although more recent, would be reporting a diagnostic delay in patients with longer disease duration.

Comparison of the Atlas and EMAS studies showed that the diagnostic delay in Spain was significantly longer than in the OEC, with an average of more than 18 months. This difference is even more significant when considering there is a higher percentage of HLA-B27 positive patients and a lower proportion of women in the Spanish sample, as these 2 characteristics have been associated with

**TABLE 3** Patient-reported outcomes for working life, psychological health, and disease-related perceptions (N = 680 for Spain and N = 2166 for OEC, unless otherwise specified)



**TABLE 4** Distribution of diagnostic delay of Spanish and European Map of Axial Spondyloarthritis patients through the decades

	OEC			Spain		
	n	Mean ± SD	Median [Q1, Q3]	n	Mean ± SD	Median [Q1, Q3]
≤1980	154	14.9 ± 14.2	10 [2, 27]	77	12.7 ± 11.3	9 [5, 16]
1981-1990	275	14.8 ± 10.9	15 [4, 25]	90	12.3 ± 8.3	11 [5, 19]
1991-2000	447	10.2 ± 7.6	10 [3, 17]	162	9.2 ± 6.8	8 [3, 15]
2001-2010	668	4.9 ± 4.0	4.5 [1, 8]	156	6.2 ± 4.2	6 [2, 9]
>2010	551	1.4 ± 1.5	1 [0, 2]	65	2.3 ± 1.9	2 [1, 4]
Total	2095	7.2 ± 8.6	4 [1, 10]	550	8.5 ± 7.7	6 [3, 12]

Abbreviation: OEC, other European countries; Q1, quartile 1; Q3, quartile 3.

a shorter diagnostic delay in other studies.<sup>29</sup> In fact, a meta-analysis conducted on the Spanish population finds that women with axSpA are diagnosed later.<sup>30</sup>

With respect to the diagnosis of axSpA in Spain, patients should first visit their general practitioner who, after clinical examination, would decide to refer them to a rheumatologist,<sup>18</sup> as in many OEC. Additional delay to diagnosis could be influenced by a higher percentage in the Spanish sample of referrals to orthopedic specialists (56.9% of Spanish axSpA patients visited orthopedic specialists prior to diagnosis, compared to only 25.3% in the OEC). However, when examining the total number of healthcare professionals visited before diagnosis, both Spain and the OEC reported a similar average of 2 visits to different physicians before diagnosis. It would be necessary throughout Europe to improve disease education related to inflammatory vs mechanical back pain among healthcare professionals, specifically among those responsible for referring patients to rheumatologists. More precisely, Spanish general practitioners should be better trained to identify suspicious cases of axSpA in order to refer them to a rheumatologist, rather than an orthopedic specialist.

More specifically, general practitioners need to be better trained in axSpA clinical patterns and the typical features of the disease, such as disease onset <45 years old, extra-articular manifestations and response to nonsteroidal anti-inflammatory drug treatment,<sup>31</sup> while also understanding that axSpA is not a disease exclusive to older men, affecting young people of both genders,<sup>32</sup> with the potential to manifest in both radiographic and non-radiographic forms.<sup>33</sup> This could be achieved by training medicine students in general practice consultations where they could encounter axSpA patients<sup>34</sup> or through training activities aimed at general practitioners and conducted by rheumatologists, as in the case of the ESPeranza program.<sup>35</sup> Moreover, general practitioners should have easier access to medical tests for detecting axSpA features, such as imaging of the sacroiliac joints or HLA-B27 testing, and procedures should be habilitated in order to allow preferential referral to the rheumatologist of suspected cases. Additionally, it would be of utmost importance for Spain to increase its rate of rheumatologists per 100 000 inhabitants to meet the healthcare demand. Nevertheless, optimizing collaboration between different specialties should shorten the patient journey to diagnosis, and ultimately effective treatment.

### 4.3 | Burden of the disease

The burden of disease reported by both samples was significant, declaring high levels of disease activity, spinal stiffness and functional limitation overall. However, Spanish axSpA patients reported an even higher BASDAI score than the EMAS OEC average, even higher than the values recorded by other Spain-based axSpA registries like the REGISPONER.<sup>11</sup> However, mean differences, although statistically significant, were not clinically relevant. Spanish patients also reported greater functional limitation. However, we cannot be sure whether this is due to longer disease duration or whether it is actually associated with the longer diagnostic delay of these patients.

### 4.4 | Working impact

Unemployment rates differ greatly from the Spanish general population (17.2%) to that estimated for the EU-28 (6.8%).<sup>36</sup> When employment status is examined for axSpA patients, an increase in unemployment rates is appreciated in both Spain and Europe despite both samples reporting a higher level of education than the general population.<sup>37</sup> However, Spanish axSpA patients' unemployment rates show a steeper increase than that of their European counterparts, and the unemployment gap becomes larger between both groups.

When examining employed patients, the Spanish were less likely to report interference of the disease in their work performance compared to the OEC. Spanish participants declared fewer work-related issues overall, fewer workplace adaptations, and a smaller influence of axSpA on work choice. This is striking, as research points to a strong relationship between problems and needs in working life and burden of disease.<sup>38</sup> If burden of disease is equivalent between Spain and OEC, interference of the condition at work should also be similar.

Therefore, it is more likely that work outcomes reported by the Spanish sample are due to a more precarious labor scenario (characterized by high unemployment rates, short-term duration jobs, low salaries, and gender inequalities), compared to the European Union context.<sup>39</sup> Thus, Spanish axSpA patients would not report an influence of axSpA on work choice in an already constrained market,



would not have access to as many workplace adaptations as in OEC, and would refrain from asking for sick days or reductions in working hours for fear of losing their job. Additional data from the Atlas and EMAS surveys would indicate that this fear may be common among those with the condition, especially in the Spanish context: if we consider what European axSpA patients stated about job hunting, 70% of OEC patients stated they found or expected to find difficulties in job searches, compared to 95% of the Spanish sample. This difficult labor scenario could be influencing the levels of psychological distress reported by Spanish survey participants as it has been noted how the financial crisis has been involved in the increased prevalence of mental disorders in Spain.<sup>40</sup>

#### 4.5 | Mental burden

The impact of axSpA on mental health is well documented.<sup>41,42</sup> The EMAS sample showed a high prevalence of mental health issues among axSpA patients, higher than those collected by the World Health Organization for the European region, which situates the prevalence of anxiety and depression in the general population below 5%.<sup>43</sup> However, Spanish axSpA patients showed particularities regarding their self-reported mental health, declaring lower rates of the mental disorders explored (anxiety, depression, and sleep disorders), while reporting much higher levels of psychological distress through the GHQ-12, a validated screening scale. The fact that Spanish participants reported fewer diagnosed mental disorders (anxiety, depression, and sleep disorders) than OEC axSpA patients, while ranking much higher in the GHQ-12 score, points to an underdiagnosis of mental disorders in Spain.

#### 4.6 | Strengths and limitations

The EMAS project represents the largest axSpA patient survey to date, including 2846 respondents from 13 European countries. Its main objective was to understand the patient's perspective through a holistic approach using a questionnaire developed for patients by patients. As such, EMAS collected not only clinical characteristics of the disease but also the patient-reported impact on psychological health, daily activities, work, and lifestyle, all of which are considered relevant aspects by axSpA patients. The focus of its design added to its international scope, enables a head-to-head comparison of patient-reported outcomes at the pan-European level in areas that are often overlooked by research.

We acknowledge that EMAS has some limitations. First, the survey was based on self-reported data and did not attempt to confirm participant diagnosis, nor did it seek to support participant responses with clinician-reported assessments. Nevertheless, the characteristics of the sample matched those of previous cohorts including patients with confirmed axSpA, and as the aim of the survey was to better understand the patient perspective, direct feedback

was preferred. Second, as 1 of the inclusion criteria was to have had at least 1 visit to a rheumatologist in the last 12 months, the sample could be biased in excluding patients not requiring a follow-up appointment and thus, with controlled disease activity. In this way, this study could have overestimated the severity of some disease outcomes, especially those related to disease activity.

Additionally, non-validated indices were used for assessing functional limitations in daily activities and spinal stiffness. This was due to patients expressing their concern during the preliminary phase of the survey development about not being able to report relevant aspects of their disease not included in other scales or indices considered. In any case, Cronbach alpha values obtained for the indices employed in EMAS showed good reliability of these instruments in this sample.<sup>14</sup> Lastly, the 2 recruitment methods employed (GfK patient panel and patient organizations) resulted in differences in sample sizes between countries, naturally skewing the aggregated European data toward the experiences of patients in countries with a greater sample weight.

Despite these limitations, EMAS adopts a multidisciplinary approach, including the medical and patient community within the research team aiming to understand the patient experience from a holistic perspective.

### 5 | CONCLUSIONS

The EMAS results show how, compared to OEC, Spanish axSpA patients show longer diagnostic delay. The results highlight the need to improve the diagnostic pathway of axSpA patients as well as psychological care within the Spanish health system in order to deal with the high psychological distress levels reported by Spanish patients and the rates of underdiagnosed mood disorders suggested by the present study. Low numbers of rheumatology specialists, in addition to a high percentage of erroneous referrals to orthopedic specialists in Spanish patients, has highlighted the need to increase human resources for health in order to adapt international recommendations to the national context.

However, the unmet needs of Spanish axSpA patients are not only limited to the quality of health care. Compared to the EMAS sample, the Spanish cohort had much higher unemployment rates. Additionally, workers with axSpA with a similar burden of disease, as their European counterparts, receive less support in the workplace. All this could be affecting patients' levels of psychological distress.

Managing axSpA from a holistic approach, including the perspective of health psychologists, rehabilitation therapists, social workers, and related professions, should be key for clinical improvement and quality of life in these patients in Spain, as well as in Europe.

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## CONFLICT OF INTEREST

Dr Jordi Gratacós has received unrelated honoraria or research grants from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB. Dr Eduardo Collantes-Estévez has received unrelated honoraria or research grants from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB. Mrs Laura Christen is an employee of Novartis Pharma AG. Dr Carlos Sastre is an employee of Novartis Farmacéutica Spain. Dr Victoria Navarro-Compán has received unrelated honoraria or research grants from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB.

## AUTHORS' CONTRIBUTIONS

Marco Garrido-Cumbrera, Laura Christen, Sergio Sanz-Gómez, José Correa-Fernández and Victoria Navarro-Compán designed the study, José Correa-Fernández carried out data analysis. All authors contributed to interpretation of the data, helped to draft the manuscript and approved its final version to be submitted; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## ETHICS APPROVAL

The manuscript does not contain clinical studies.


## CONSENT TO PARTICIPATE

All participants were asked to provide explicit opt-in consent prior to participating in the survey.


## DATA AVAILABILITY STATEMENT

Data are available via the corresponding author upon reasonable request.

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