



Patients with Axial Spondyloarthritis are Great Consumers of Healthcare Resources, Especially Young and Women: Results from the Spanish Atlas

Marco Garrido-Cumbrera · Eduardo Collantes-Estévez ·
Victoria Navarro-Compán · Pedro Zarco-Montejo · Carlos Sastre ·
José Correa-Fernández · Jordi Gratacós

Received: September 15, 2022 / Accepted: February 13, 2023
© The Author(s) 2023

ABSTRACT

Introduction: This study aimed to assess high healthcare utilization over 1 year in patients with axial spondyloarthritis (axSpA) and factors associated with increased healthcare utilization.

Methods: A total of 530 unselected patients with axSpA from the Atlas of Axial Spondyloarthritis in Spain—who had used at least one healthcare resource—were included in the present study. Total health care utilization was obtained from the total number of healthcare visits, medical tests, hospital admissions and emergency visits, during the 12 months prior to the survey. Linear regression was used to

analyse possible factors associated with higher healthcare utilization.

Results: A total of 530 patients with axSpA participated in this study: mean age was 45.3 years and 51.1% were female. In the previous 12 months, 77.9% ($n = 530$) used at least one healthcare resource, with the median healthcare utilization at 25. In the multiple linear regression, the only categorical factor associated with higher healthcare utilization was female gender ($\beta = 12.854$), while the continuous factors associated with higher healthcare utilization were higher disease activity ($\beta = 3.378$), longer diagnostic delay ($\beta = 0.959$), younger age ($\beta = -0.737$) and greater functional limitation ($\beta = 0.576$).

M. Garrido-Cumbrera (✉)
Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain
e-mail: mcumbrera@us.es

M. Garrido-Cumbrera
Spanish Federation of Spondyloarthritis Associations (CEADE), Madrid, Spain

E. Collantes-Estévez
Reina Sofia University Hospital, Cordoba, Spain

E. Collantes-Estévez
Maimonides Biomedical Research Institute of Cordoba (IMIBIC), University of Cordoba, Cordoba, Spain

V. Navarro-Compán
University Hospital La Paz, IdiPAZ, Madrid, Spain

P. Zarco-Montejo
Hospital Fundación Alcorcón, Madrid, Spain

C. Sastre
Novartis Spain, Barcelona, Spain

J. Correa-Fernández · J. Gratacós
Hospital Universitari Parc Taulí, Sabadell, Spain

J. Gratacós
I3PT, Medicine Department UAB, Barcelona, Spain

M. Garrido-Cumbrera
Axial Spondyloarthritis International Federation (ASIF), London, UK

Conclusion: Half of patients with axSpA used 25 or more healthcare resources during 1 year. Higher healthcare utilization was associated with younger age, female gender, greater disease activity, higher functional limitation and longer diagnostic delay. Optimal monitoring of patients with axSpA may help to reduce their healthcare utilization.

Keywords: Axial spondyloarthritis; Healthcare utilization; Gender differences; Diagnostic delay

Key Summary Points

Why carry out this study?

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease with a high diagnostic delay that may be due to visiting several specialists until referral to a rheumatologist.

The aim of this study is to assess healthcare utilization and its associated factors.

What was learned from the study?

The present study has shown the high use of healthcare resources by patients with axSpA in 1 year.

Higher healthcare utilization was associated with younger age, female gender, greater disease activity, functional limitation and a longer diagnostic delay.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that can cause chronic pain, structural damage and disability [1]. Delay in the diagnosis can lead to further progression of the disease and poorer functioning of patients [2]. This deterioration of the disease may increase the need for patients to visit different specialists and/or emergency services. With respect to the follow-up of patients by the

rheumatologist, according to a previous study in the UK, most patients are seen at least once a year by a rheumatologist, of whom 23% three or more times a year, 43.2% twice a year and 26.9% only once a year [3]. However, other studies show that about half of the patients visit another physician, with an average of two visits per year [4]. One in three patients visit a general practitioner [5]. Furthermore, a high proportion of the patients either go to a physiotherapist or would like to go to a physiotherapist [3]. Patients with axSpA who visit healthcare professionals more frequently may have a specific profile, different from the rest of the patients. In this regard, a study in patients with axSpA in the UK showed that younger patients, female patients and patients with a shorter duration of disease were more likely to be under the care of a rheumatologist [3]. Furthermore, female patients were more likely to visit a physiotherapist than male patients were [5]. Those patients who require more frequent use of healthcare resources are likely to have higher disease activity. Accordingly, it has been shown that both patients who visit a general practitioner and/or physiotherapist present higher disease activity [5]. In addition, a study conducted in patients with axSpA showed a significant positive correlation between number of visits to the physiotherapist, number of hospitalizations and number of outpatient appointments in relation to disease activity [6]. Although the general population also needs to use healthcare resources, people with a chronic rheumatic disease, such as axSpA, may need more continuous care. In this context, compared to the general population, patients with axSpA present a higher rate of inpatient admissions (12% vs 6%), emergency visits (23% vs 15%) and outpatient visits (97% vs 81%) [7]. It should be highlighted that in Spain the population has universal access to the healthcare system (covering 99.1% of the population). Furthermore, in Spain, the underlying principles and objectives of its national health system continue to focus on universality, free access and equity [8].

Many studies have assessed healthcare utilization with the aim of estimating the costs of illness, but fewer studies have aimed to assess other factors that may be related to healthcare

utilization, such as socio-demographic factors or patient-reported outcomes. Therefore, the present study aims to assess the healthcare utilization and the factor associated with higher healthcare utilization.

METHODS

Study Design and Survey

Atlas 2017 is an initiative of the Spanish Federation of Spondyloarthritis Associations (CEADE), conducted 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. This cross-sectional study uses the opinion of a scientific committee and an advisory committee, made up of patient representatives, health researchers and healthcare professionals with experience conducting scientific studies on axSpA. The patients were recruited by the different patient associations belonging to CEADE. The questionnaire comprised of 116 items and four open-ended qualitative questions assessing aspects related to axSpA: socio-demographic, lifestyle habits, disease characteristics, and patient-reported outcomes, among other areas. Retrospective data from the Atlas of Axial Spondyloarthritis in Spain 2017 survey was analysed (May–August 2016). More information on the methodology of the Atlas of Axial Spondyloarthritis in Spain has been published and can be consulted in the seminal Atlas article [9].

Sample Selection and Recruitment

The inclusion criteria were unselected patients with aged 18 years or older, residents in Spain, with a self-reported clinician-provided diagnosis of axSpA, including ankylosing spondylitis or non-radiographic axSpA and who had visited a healthcare professional for axSpA in the 12 months prior to participation. Spanish legislation does not require ethics committee

approval for online survey studies as no personal patient data are collected. Additionally, all patients agreed to their participation through informed consent and were asked to provide explicit opt-in consent prior to participating in the Atlas survey. Participant data were anonymized. The present study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

Total Healthcare Utilization

Total healthcare utilization was assessed as the aggregate number of healthcare visits, medical tests, hospital admissions and emergency visits, all based on the last 12 months prior to the survey and due to axSpA disease (Fig. 1).

Total healthcare utilization was accessed by the following questions:

- Healthcare visits: Please indicate the number of spondylitis/spondyloarthritis-related medical appointments you have had in the past 12 months
- Medical tests: Please indicate the number of spondylitis/spondyloarthritis-related medical tests you have had in the past 12 months
- Hospital admission: How many times have you been admitted to hospital in the past 12 months as a result of your spondylitis/spondyloarthritis?
- Emergency visits: How many times have you used an emergency service in the past 12 months as a result of your spondylitis/spondyloarthritis?

Collected Data

The following factors were analysed:

1. Socio-demographic: age (in years), gender (male/female), educational level (no university/university), marital status (single/married/divorced or separated/widow) and patient organizations membership (yes/no).
2. BASDAI (Bath Ankylosing Spondylitis Disease Activity Index): a validated self-administered questionnaire assessing disease activity in patients with axSpA. Possible

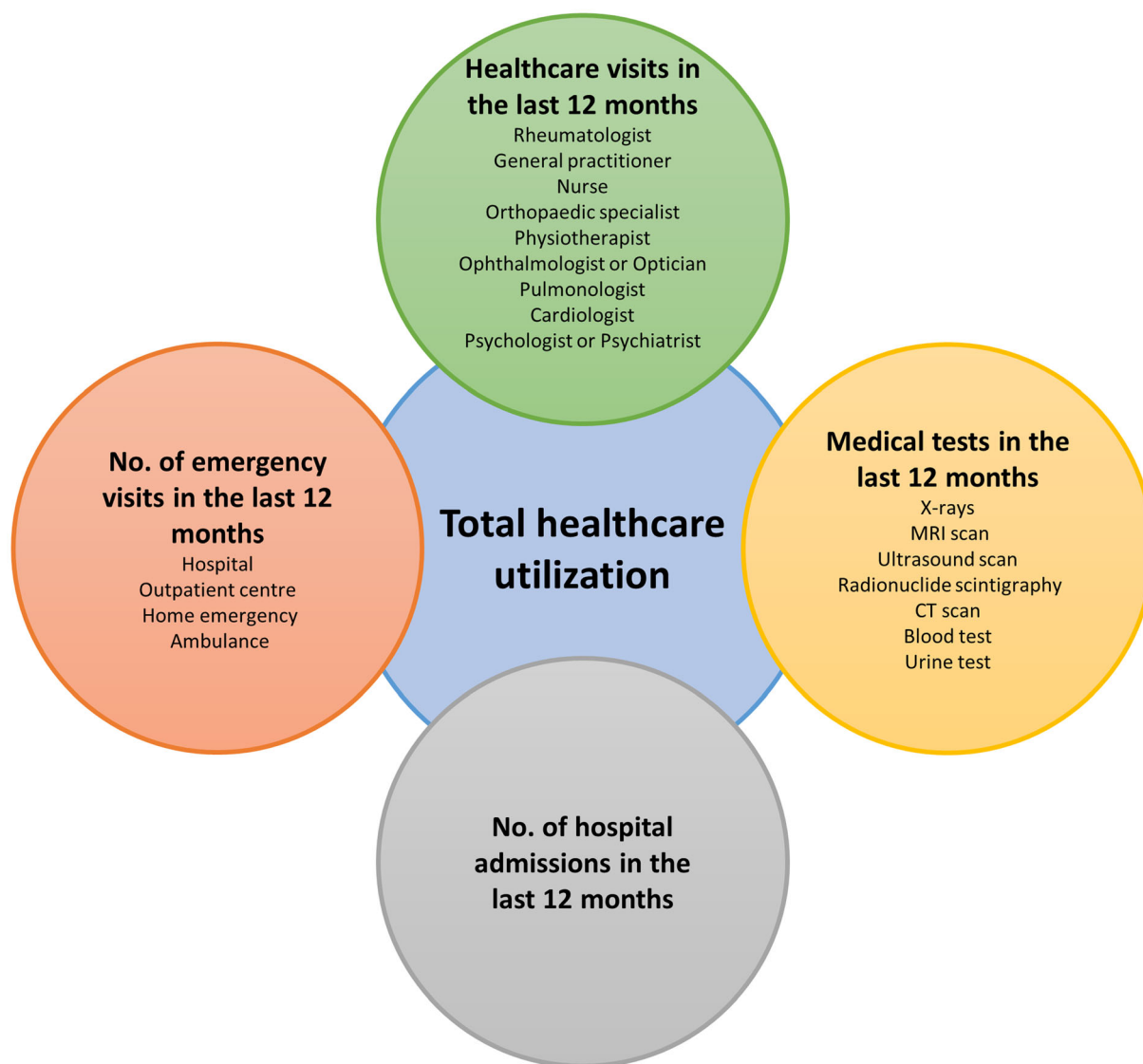


Fig. 1 Total healthcare utilization by patients with axSpA. *MRI* magnetic resonance imaging, *CT* computed tomography

scores range from 0 (no activity) to 10 (maximum activity) [10].

3. Spinal stiffness index: this index assesses the degree of stiffness in the spinal column (cervical, dorsal, and lumbar areas). Possible score range from 3 (no stiffness) to 12 (maximum stiffness) [9].
4. Functional limitation index: this index 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). Possible score range from 0 (low limitation) to 54 (maximum limitation) [9].
5. GHQ-12 (The 12-item General Health Questionnaire): this questionnaire 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 [11].

Statistical Analysis

Out of the 680 patients who made up the total sample of the Spanish Atlas survey, only 77.9% of patients ($n = 530$)—who had used at least one healthcare resource as a result of axSpA in the last 12 months—were included in the present study. The results are presented as summary statistics, with mean and standard deviation for continuous variables, and frequency and percentages for categorical variable. Mann–Whitney and Pearson’s correlation tests were used to analyse possible associations between socio-demographic (age, gender, educational level, marital status and patient organizations membership) and patient-reported outcomes (disease activity measured by BASDAI (0–10), mental health measured by GHQ-12 (0–12), functional limitation index (0–54), spinal stiffness index (3–12) and diagnostic delay) with respect to total healthcare utilization. Simple and multiple linear regression was used to analyse possible factors associated with total healthcare utilization. Data analysis was conducted using SPSS 25.0.

RESULTS

Baseline Characteristics

A total of 530 patients with axSpA participated in this study: the mean age was 45.3 years, 51.1% were female, 39.6% had a university degree and 70.6% were married. Patients presented a mean score (standard deviation) of 5.7 (± 2.0) for BASDAI, 42.6 (± 9.8) for functional limitation and 8.7 (± 7.7) for diagnostic delay.

Healthcare Utilization

In the previous 12 months prior to the survey, 77.9% ($n = 530$) used at least one healthcare resource (median healthcare utilization was 25.0); 75.3% visited a rheumatologist at least once ($n = 512$, mean number of visits 4.4), 55.6% a general practitioner ($n = 378$, mean number of visits 9.4) and 33.5% a physiotherapist ($n = 228$, mean number of visits 20.1). With

respect to medical tests undergone in the last 12 months prior to the survey, 75.3% underwent at least one x-ray test ($n = 512$, mean number of tests 4.4), 71.2% a blood test ($n = 484$, mean number of tests 4.5), 51.3% a urine test ($n = 349$, mean number of tests 3.7) and 31.5% an MRI scan ($n = 214$, mean number of tests 2.2). Furthermore, 7.9% of patients were admitted to hospital ($n = 54$, mean number of hospitalizations 2.2) and 23.1% visited an outpatient centre ($n = 157$, mean number of outpatient visits 5.5; Table 1).

Socio-demographic Factors and Healthcare Utilization

Younger age ($r = -0.195$, $p < 0.001$) and female gender (52.0 vs 32.2 for male gender, $p < 0.001$) were associated with higher healthcare resource utilization. These younger patients correlated significantly with more visits to a rheumatologist, general practitioner and psychologist/psychiatrist, more X-rays, MRI scans, blood tests and urine tests, more hospital admissions and more emergency hospital visits. Compared to men, women visited significantly more rheumatologists, general practitioners and clinical nurses, had more frequent X-rays, MRI scans, blood tests and urine tests, and made more visits to outpatient clinics (Table 2). In the multiple linear regression, female gender ($\beta = 12.854$) and younger age ($\beta = -0.737$) were associated with higher healthcare resource utilization (Table 3).

Patient-reported Outcomes and Healthcare Utilization

Regarding the impact of patient-reported outcomes, those with higher healthcare utilization presented higher disease activity ($r = 0.290$, $p < 0.001$), poorer mental health ($r = 0.257$, $p < 0.001$), greater functional limitation ($r = 0.283$, $p < 0.001$) and longer diagnostic delay ($r = 0.151$, $p < 0.001$; Table 2). In the multiple linear regression, factors associated with higher healthcare resource use were higher disease activity ($\beta = 3.378$), greater functional

Table 1 Descriptive analysis of healthcare visits, tests, hospital admissions and emergency visits ($n = 680$, unless specified otherwise). MRI magnetic resonance imaging, CT computed tomography; SD standard deviation

	<i>n</i> (%)	Mean \pm SD
Healthcare visits in the last 12 months		
Rheumatologist	512 (75.3)	4.4 \pm 3.9
General practitioner	378 (55.6)	9.4 \pm 16.4
Nurse	159 (23.4)	8.7 \pm 14.6
Orthopaedic specialist	115 (16.9)	3.4 \pm 4.0
Physiotherapist	228 (33.5)	20.1 \pm 28.9
Ophthalmologist/optician	198 (29.1)	2.9 \pm 3.3
Pulmonologist	56 (8.2)	2.2 \pm 1.6
Cardiologist	57 (8.4)	2.2 \pm 2.0
Psychologist/psychiatrist	129 (19.0)	11.1 \pm 20.0
Medical tests in the last 12 months		
X-rays	512 (75.3)	4.4 \pm 3.9
MRI scan	214 (31.5)	2.2 \pm 1.8
Ultrasound scan	102 (15.0)	1.9 \pm 1.3
Radionuclide scintigraphy	48 (7.1)	1.5 \pm 0.7
CT scan	22 (3.2)	1.3 \pm 0.6
Blood test	484 (71.2)	4.5 \pm 4.1
Urine test	349 (51.3)	3.7 \pm 3.1
No. of hospital admissions in the last 12 months	54 (7.9)	2.1 \pm 1.9
No. of emergency visits in the last 12 months		
Hospital	172 (25.3)	3.0 \pm 3.2
Outpatient centre	157 (23.1)	5.5 \pm 11.2
Home emergency	16 (2.4)	2.4 \pm 1.9
Ambulance	10 (1.5)	2.1 \pm 1.7
Total healthcare utilization	530 (77.9)	42.3 \pm 49.0

limitation ($\beta = 0.576$) and longer diagnostic delay ($\beta = 0.959$; Table 3).

DISCUSSION

The present study has demonstrated that younger age, female gender, greater disease

activity, higher functional limitation and longer diagnostic delay were associated with higher healthcare utilization by patients with axSpA. Furthermore, three quarters (77.9%) of patients with axSpA used at least one healthcare resource per year, with an average of 42.3 healthcare resource uses per year (including healthcare visits, medical tests, hospital

Table 2 Bivariate analysis of socio-demographic characteristics and patient-reported outcomes in relation to total healthcare utilization ($N = 530$, unless specified otherwise)

	Mean \pm SD or <i>r</i> correlation Total healthcare utilization	<i>P</i> value
Socio-demographic		
Age	- 0.195	< 0.001
Gender		
Male	32.2 \pm 31.1	< 0.001
Female	52.0 \pm 59.8	
Educational level		
No university	44.2 \pm 51.9	0.748
University	41.1 \pm 46.9	
Marital status		
Single	45.0 \pm 47.4	0.131
Married	41.3 \pm 49.4	
Separated/divorced	46.0 \pm 50.4	
Widowed	19.3 \pm 15.9	
Patient organization membership		
Yes	40.6 \pm 47.9	0.134
No	43.7 \pm 49.8	
Patient-reported outcomes		
BASDAI (0–10), $N = 411$	0.290	< 0.001
GHQ-12 (0–12), $N = 464$	0.257	< 0.001
Functional limitation (0–54), $N = 529$	0.283	< 0.001
Spinal stiffness (3–12), $N = 476$	0.032	0.489
Diagnostic delay, $N = 517$	0.151	< 0.001

admissions or emergency visits) and the median was 25. Therefore, half of the patients used 25 or more healthcare contact.

Healthcare Utilization

Our study shows that the proportion of patients who had at least one healthcare resource use per year was higher than that shown in a previous study of 612 British patients with axSpA (77.9% vs 59.0%) [5]. A possible explanation for this difference in healthcare utilization proportions may be a higher disease activity (5.7) of patients with axSpA in Spain in the Atlas study compared to the lower disease activity of patients with axSpA in the UK (4.6). In our study, one in three patients visited the physiotherapist (with an average of 20 visits per year). This makes sense as physiotherapeutic interventions for axSpA have been shown to be an integral part of disease management, being effective in inducing short-term improvement in spinal mobility [12].

Socio-demographic Factors and Healthcare Utilization

The fact that younger patients were associated with a higher healthcare utilization could be due to the early onset of functional limitations in daily activities among these patients [13]. In this sense, a Dutch study reported that younger patients with Ankylosing Spondylitis (AS) more often withdrew from work than older patients [14]. Perhaps the disease is more uncontrollable and less well managed in younger patients with more acute symptoms than in older patients, with fewer acute symptoms and better managed. However, the possibility that younger people take more care of their personal health owing to increased health education cannot be ignored. In addition, our results show that women are associated with higher healthcare utilization, which may be because, compared to men, women with axSpA have higher disease activity and pain [15–17], severe extra-musculoskeletal manifestations [18], poor quality of life [17] and less adherence to treatment [19, 20].

Table 3 Linear regression analysis of socio-demographic and patient-reported outcomes according to total healthcare utilization ($N = 402$)

	Simple linear regression		Multiple linear regression	
	Beta	95% CI	Beta	95% CI
Age	- 0.884	- 1.266, - 0.503	- 0.737	- 1.190, - 0.283
Gender, female	19.792	11.600, 27.984	12.854	3.502, 22.207
BASDAI (0–10)	7.260	4.934, 9.586	3.378	0.571, 6.185
GHQ-12 (0–12)	2.724	1.786, 3.663	1.126	- 0.048, 2.300
Functional limitation (0–54)	1.418	1.007, 1.828	0.576	0.007, 1.145
Diagnostic delay	0.966	0.419, 1.512	0.959	0.374, 1.544

Patient-reported Outcomes and Healthcare Utilization

In the present study, patients with axSpA with a higher utilization of healthcare resources were associated with higher disease activity, greater limitation and a longer diagnostic delay. These results are in line with previous studies which demonstrated that patients with more visits to the general practitioner, the physiotherapist, and more hospital admissions or outpatient visits had higher disease activity [3, 5, 6]. Another factor associated with higher healthcare utilization was diagnostic delay; indeed, previous studies have shown that diagnostic delay resulted in increased healthcare costs and utilization [21, 22]. A similar study among European patients, including patients from the present Spanish Atlas study, showed that longer diagnostic delay was associated with younger age at symptom onset, female gender and higher number of healthcare professionals (HCPs) seen before diagnosis [23]. Furthermore, in our study, patients with higher healthcare utilization were associated with a higher functional limitation, which might make sense as Rafia et al.'s study showed a relationship between higher number of visits to the general practitioner and greater loss of function [5].

As we have shown, half of patients with axSpA used 25 or more healthcare resources during a year, representing a high level of utilization. In addition, the present study show

that young people and women are the two groups that use healthcare resources the most. In relation to patient-related outcomes, patients with active disease, with functional limitations in daily activities and with a longer diagnostic delay are the most frequent users. These results suggest that there are specific profiles of patients with axSpA who may need more specific follow-up to reduce their number of visits, such as women, young people and those with uncontrolled disease and functional limitations. From a socio-demographic point of view, these young patients who are making their debut in the disease typically do not have coping tools, which has a negative impact on their health status and the need for more healthcare; this also applies to women whose disease outcomes are poorer. Likewise, both young people and women represent groups for whom there is still the erroneous perception that they have a lower prevalence of axSpA, compared to men and the elderly [24, 25].

Strength and Limitations

The study is not free of limitations. Firstly, the cross-sectional design of the survey does not allow one to establish causality between healthcare utilization and socio-demographic and patient-reported outcomes factors. However, we might expect that those patients who use more healthcare resources have worse disease outcomes such as disease activity,

functional limitation and diagnostic delay. Secondly, the survey relied on self-reported data, and did not attempt to confirm participant diagnosis nor to support participant responses with clinician-reported assessments. Therefore, healthcare utilization may also suffer from response bias because patients may not accurately recall their use of healthcare [26]. Another limitation of the study is the missing values in the regression analyses, since these analyses work only with subjects with complete data. During the preliminary phase of survey development, patients expressed concerns about aspects of their disease that were not being adequately measured. Therefore, it was decided to develop the functional limitation index and the spinal stiffness index. Although an adequate Cronbach alpha value was obtained for both scales, the fact that these scales are not validated should be considered a limitation of the study.

CONCLUSION

Half of patients with axSpA had 25 or more healthcare contacts during 1 year. Furthermore, higher healthcare utilization was associated with higher disease activity, greater functional limitation and longer diagnostic delay in younger and female patients with axSpA. Optimal monitoring of patients with axSpA can contribute to minimizing healthcare utilization in patients with axSpA and, in addition, reduce healthcare costs associated with the disease.

ACKNOWLEDGEMENTS

We would like to thank all patients and patient organizations who participated in the Atlas of Axial Spondyloarthritis in Spain.

Funding. The Atlas 2017 study was supported by Novartis Farmacéutica Spain, which in no means affected the analysis or interpretation of results. Funding for this study and its publication, including the journal's Rapid

Service Fee, were provided by Novartis Farmacéutica Spain.

Author Contributions. Marco Garrido-Cumbrera, Eduardo Collantes-Estévez, Victoria Navarro-Compán, Pedro Zarco-Montejo, Carlos Sastre, José Correa-Fernández, and Jordi Gratacós made substantial contributions to study conception and design and to the interpretation of the data. All authors contributed to the writing of the manuscript and approved the last version to be published.

Prior Presentation. The abstract of this paper was presented and published at the EULAR 2022 Congress in Copenhagen, Denmark, on June 1–4, 2022 under the following code: AB0810.

Disclosures. Dr Eduardo Collantes-Estévez, Dr Victoria Navarro-Compán and Dr Jordi Gratacós have received unrelated honoraria or research grants from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche, and UCB. Dr Carlos Sastre is an employee of Novartis Farmacéutica Spain. PhD. Marco Garrido-Cumbrera has received research grants from Novartis. MSc. José Correa-Fernández and Dr Pedro Zarco-Montejo have nothing to disclose.

Compliance with Ethics Guidelines. Spanish legislation does not require ethics committee approval for online survey studies as no personal patient data are collected. Additionally, all patients agreed to their participation through informed consent and were asked to provide explicit opt-in consent prior to participating in the Atlas survey. Participant data were anonymized. The present study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments and all participants gave their informed consent to participate in the study.

Data Availability. The data sets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Open Access. This article is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

- Braun J, Sieper J. Ankylosing spondylitis. *Lancet*. 2007. [https://doi.org/10.1016/S0140-6736\(07\)60635-7](https://doi.org/10.1016/S0140-6736(07)60635-7).
- Aggarwal R, Malaviya AN. Diagnosis delay in patients with ankylosing spondylitis: factors and outcomes—an Indian perspective. *Clin Rheumatol*. 2009;28(3):327–31.
- Derakhshan MH, Pathak H, Cook D, Dickinson S, Siebert S, Gaffney K. Services for spondyloarthritis: a survey of patients and rheumatologists. *Rheumatology*. 2018;57(6):987–96. <https://academic.oup.com/rheumatology/article/57/6/987/4907948>.
- Ward MM. Functional disability predicts total costs in patients with ankylosing spondylitis. *Arthritis Rheum*. 2002;46(1):223–31.
- Rafia R, Ara R, Packham J, Haywood K, Healey E. Healthcare costs and productivity losses directly attributable to ankylosing spondylitis. *Clin Exp Rheumatol*. 2012;30(2):246–53.
- Ara RM, Packham JC, Haywood KL. The direct healthcare costs associated with ankylosing spondylitis patients attending a UK secondary care rheumatology unit. *Rheumatology*. 2008;47(1):68–71.
- Walsh JA, Song X, Kim G, Park Y. Healthcare utilization and direct costs in patients with ankylosing spondylitis using a large US administrative claims database. *Rheumatol Ther*. 2018;5(2):463–74.
- Bernal E, Sandra D, Juan G-A, et al. Spain Health system review. *Health Syst Transit*. 2018;20(2). www.healthobservatory.eu
- Garrido-Cumbrera M, Navarro-Compán V, Zarco P, et al. Atlas of axial spondyloarthritis in Spain 2017: study design and population. *Reumatol Clin*. 2019;15(3):127–32.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol*. 1994;21(12):2286–91.
- Cano A, Sprafkin RP, Scaturro DJ, Lantinga LJ, Fiese BH, Brand F. Mental health screening in primary care: a comparison of 3 brief measures of psychological distress. *Prim Care Companion J Clin Psychiatry*. 2001;3(5):206–10.
- van Tubergen A, Landewe R, Wolter N, et al. Combined spa-exercise therapy is effective in patients with ankylosing spondylitis: a randomized controlled trial. *Arthritis Care Res*. 2001;45:430–8.
- Khan S, Shridharmurthy D, et al. The disease burden of axial spondyloarthritis: through a gendered lens. *Clin Rheumatol*. 2022;41(4):1115–24. <https://doi.org/10.1007/s10067-021-06008-8>.
- Boonen A, Chorus A, Miedema H, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2001;60(11):1033–9. <https://ard.bmj.com/content/60/11/1033>.
- Roussou E, Sultana S. Spondyloarthritis in women: differences in disease onset, clinical presentation, and Bath Ankylosing Spondylitis Disease Activity and Functional indices (BASDAI and BASFI) between men and women with spondyloarthritis. *Clin Rheumatol*. 2011;30(1):121–7. <https://doi.org/10.1007/s10067-010-1581-5>.
- Webers C, Essers I, Ramiro S, et al. Gender-attributable differences in outcome of ankylosing spondylitis: long-term results from the Outcome in Ankylosing Spondylitis International Study. *Rheumatology* 2016;55(3):419–28. <https://academic.oup.com/rheumatology/article/55/3/419/1793176>.
- Landi M, Maldonado-Ficco H, Perez-Alamino R, et al. Gender differences among patients with primary ankylosing spondylitis and spondylitis associated with psoriasis and inflammatory bowel

- disease in an iberoamerican spondyloarthritis cohort. *Medicine (Baltimore)*. 2016;95(51):e5652.
18. Zarco P, González CM, Rodríguez de la Serna A, et al. Extra-articular disease in patients with spondyloarthritis. Baseline characteristics of the spondyloarthritis cohort of the AQUILES Study. *Reumatol Clin*. 2015;11(2):83–9.
 19. Gremese E, Bernardi S, Bonazza S, et al. Body weight, gender and response to TNF- α blockers in axial spondyloarthritis. *Rheumatology*. 2014;53(5): 875–81.
 20. Lorenzin M, Ortolan A, Frallonardo P, Oliviero F, Punzi L, Ramonda R. Predictors of response and drug survival in ankylosing spondylitis patients treated with infliximab. *BMC Musculoskelet Disord*. 2015;16(1):1–8. <https://doi.org/10.1186/s12891-015-0620-4>.
 21. Sarah E G, Martin BJ, Buchanan RR, Schachna L. Burden of delay to diagnosis of ankylosing spondylitis. *ACR/ARHP Annu Sci Meet*. 2011. <https://acr.confex.com/acr/2011/webprogram/Paper22233.html>.
 22. Mennini FS, Viti R, Marcellusi A, Sciattella P, Viapiana O, Rossini M. Economic evaluation of spondyloarthritis: economic impact of diagnostic delay in Italy. *Clin Outcomes Res*. 2018;10:45.
 23. Garrido-Cumbrera M, Navarro-Compán V, Bundy C, et al. Identifying parameters associated with delayed diagnosis in axial spondyloarthritis: data from the European map of axial spondyloarthritis. *Rheumatology*. 2021;1:1–19.
 24. Polley HF, Slocumb CH. Rheumatoid spondylitis: a study of 1,035 cases. *Ann Intern Med*. 1947;26(2): 240–9. <https://doi.org/10.7326/0003-4819-26-2-240>.
 25. Feldtkeller E, Bruckel J, Khan MA. Scientific contributions of ankylosing spondylitis patient advocacy groups. *Curr Opin Rheumatol*. 2000;12(4): 239–47.
 26. Gorber SC, Tremblay MS, Gorber SC, Tremblay MS. Self-report and direct measures of health: bias and implications. 2016;369–76. https://doi.org/10.1007/978-3-319-29577-0_14.