



# **Atlas of axial spondyloarthritis in Spain 2017**

PROFILE OF THE DISEASE

---

Published by:



Max Weber Institute  
c/ Norias, 123  
28221 Majadahonda (Madrid)  
E-mail: [imw@imw.es](mailto:imw@imw.es)

ISBN: 978-84-617-9086-9  
D.L.: M-7134-2017  
Madrid, April 2017





# **Atlas of axial spondyloarthritis in Spain 2017**

PROFILE OF THE DISEASE

---



# TABLE OF CONTENTS

<b>TABLE OF CONTENTS, TABLES, FIGURES AND MAPS</b>	<b>10</b>
<b>ACRONYMS</b>	<b>17</b>
<b>PREFACE</b>	<b>19</b>
<b>PROLOGUE</b>	<b>21</b>
<b>PARTICIPATING ENTITIES</b>	<b>23</b>
<b>1. INTRODUCTION AND STATE OF THE ART</b>	<b>27</b>
1.1 The need for an Atlas of Axial Spondyloarthritis in Spain	27
1.2 Definition of the disease	27
1.3 Diagnosis	28
1.4 The patient's perspective	29
<b>2. OBJECTIVES</b>	<b>31</b>
2.1 Overall objective	31
2.2 Specific objectives	31
<b>3. METHODOLOGY</b>	<b>31</b>
3.1 <i>Literature</i> review	31
3.2 Scientific committee and advisory committee	31
3.3 Survey of patients with axial spondyloarthritis	32
3.3.1 Questionnaire design	32
3.3.2 Implementation of the survey	33
3.4 Supplementary instruments	34
3.5 Statistical analysis	34
3.6 Qualitative analysis	35
3.7 Societal burden methodology for ankylosing spondylitis	36
3.7.1 Perspective and time horizon	36
3.7.2 Costs	36
3.7.2.1 Diagnostic costs	39
3.7.2.2 Direct healthcare costs	39
3.7.2.3 Direct non-healthcare costs	40
3.7.2.4 Indirect costs	41
3.7.2.5 Total costs	41
3.7.3 Sensitivity analysis	41
3.7.4 Scenario analysis	41
<b>4. LEGISLATION AND PLANNING WITH REFERENCE TO SPONDYLOARTHRITIS</b>	<b>44</b>
4.1 Planning in rheumatology	44
4.2 Planning in rare diseases	45
4.3 Guidelines for health professionals and training programmes that cover SpA	47

<b>5. SAMPLE PROFILE</b>	<b>50</b>
<b>6. DIAGNOSIS</b>	<b>55</b>
6.1. Personnel involved	55
6.2 Diagnostic tests	56
6.3 Diagnostic delay	56
6.4 Importance of other medical specialities	59
<b>7. PHYSICAL HEALTH, LIMITATIONS, COMORBIDITY AND DISABILITY</b>	<b>62</b>
7.1 Disease activity (BASDAI)	62
7.2 Stiffness by spinal column areas	63
7.3 Body area with inflammation	67
7.4 Limitations on activities of daily living	68
7.5 Comorbidity reported by patients with Ax-SpA	73
7.6 Disability in patients with Ax-SpA	74
<b>8. PSYCHOLOGICAL HEALTH</b>	<b>78</b>
8.1 Psychological health and its relationship with socio-demographic variables	78
8.2 Psychological health, disease activity and limitations in daily living	80
8.3 Psychological health and comorbidity	81
<b>9. HEALTHCARE</b>	<b>84</b>
9.1 Visits by speciality	84
9.2 Resource utilisation	85
9.3 Radiology by body area	87
<b>10. PHARMACOLOGICAL TREATMENT</b>	<b>90</b>
10.1 Pharmacological therapy	90
10.2 Use of anti-inflammatory drugs (NSAIDs)	91
10.3 Use of disease modifying antirheumatic drugs (DMARDs)	92
10.4 Use of biologics	94
10.5 Effects of pharmacological treatments on quality of life	98
<b>11. REHABILITATION THERAPIES, PHYSICAL ACTIVITY AND BAD HABITS</b>	<b>101</b>
11.1 Rehabilitation therapies	101
11.2 Physical therapy care	104
11.3 Physical activity	107
11.4 Beneficial activities	109
11.5 Bad habits	113
<b>12. EMPLOYMENT STATUS</b>	<b>117</b>
12.1 Employment status of the patient	117
12.2 Working patients	117
12.3 Patients on temporary sick leave	122
12.4 Patients on permanent sick leave or early retirement	124
12.5 Unemployed patients	125

12.6 Difficulties accessing employment	125
12.7 Choice of professional life	126
<b>13. SOCIETAL BURDEN OF ANKYLOSING SPONDYLITIS</b>	<b>128</b>
13.1 Introduction	128
13.2 Diagnostic costs	129
13.3 Prevalent patient costs	130
13.3.1 Total costs	130
13.3.1.1 Total cost per patient / year	130
13.3.1.2 Total cost per patient / year in relation to severity	131
13.3.1.3 Total cost per patient / year by sex	132
13.3.1.4 Total cost per patient / year in relation to the administration of biologics	132
13.3.1.5 Total cost of AS in Spain	133
13.3.2 Direct healthcare costs	133
13.3.2.1 Medical visits	133
13.3.2.2 Medical tests	134
13.3.2.3 Radiology	135
13.3.2.4 Use of emergency services	135
13.3.2.5 Hospital admissions	136
13.3.2.6 Medication	136
13.3.2.7 Total direct healthcare costs	137
13.3.3 Direct non-healthcare costs	138
13.3.3.1 Alternative treatments	138
13.3.3.2 Rehabilitation therapies and physical exercise	138
13.3.3.3 Total direct non-healthcare costs	139
13.3.4 Indirect costs	139
13.3.4.1 Losses in labour productivity	139
13.4 Health-related costs and quality of life	141
13.5 Sensitivity analysis	142
13.6 Scenario analysis	144
<b>14. HOPES AND FEARS</b>	<b>148</b>
14.1 Fears in relation to the disease	148
14.2 Patients' hopes	149
14.3 Objectives in relation to treatment	151
14.4 Patient communication with their doctor	153
<b>15. CONCLUSIONS AND RECOMMENDATIONS</b>	<b>155</b>
<b>APPENDIX: Unit prices</b>	<b>161</b>



# TABLE OF CONTENTS, TABLES, GRAPHS AND MAPS

## 3. METHODOLOGY

<b>Figure 1.</b>	Components of the economic and societal burden of AS.	37
------------------	---	----

## 4. LEGISLATION AND PLANNING WITH REFERENCE TO SPONDYLOARTHRITIS

<b>Figure 1.</b>	Planning and guides for healthcare professionals with reference to SpA	48
<b>Map 1.</b>	Planning that includes SpA in different regions	46

## 5. SAMPLE PROFILE

<b>Figure 1.</b>	Membership of associations among patients with Ax-SpA (N: 680)	51
<b>Figure 2.</b>	Distribution of Ax-SpA patients by educational level (N: 680)	52
<b>Figure 3.</b>	Percentage distribution of patients with Ax-SpA according to marital status (N: 680)	53
<b>Map 1.</b>	Distribution of people taking part in the survey with Ax-SpA in different ARs (N: 680)	50
<b>Map 2.</b>	Distribution of individuals surveyed with Ax-SpA by sex in different regions (N: 680)	51
<b>Table 1.</b>	Age of participants in the survey.	52
<b>Table 2.</b>	Distribution of Ax-SpA patients by age group.	52
<b>Table 3.</b>	Percentage distribution of Ax-SpA patients by income level (N: 422)	53

## 6. DIAGNOSIS

<b>Figure 1.</b>	Medical specialist consulted by patients with Ax-SpA before being diagnosed (N: 540)	55
<b>Figure 2.</b>	Most commonly used diagnostic tests	56
<b>Figure 3.</b>	Scatter diagram for value pairs for year of appearance of the first symptoms and years of diagnostic delay (N: 550)	58
<b>Table 1.</b>	Visits to each medical specialist by patients before being diagnosed	55
<b>Table 2.</b>	Mean age at first symptoms, at diagnosis and diagnostic delay	57
<b>Table 3.</b>	Diagnostic delay in years by percentiles (N: 552)	57
<b>Table 4.</b>	Mean diagnostic delay of Ax-SpA in relation to patient educational level	58
<b>Table 5.</b>	Mean diagnostic delay for Ax-SpA patients in relation to the year of onset of the first symptoms ( $\leq 2008$ and $\geq 2009$ )	60

## 7. PHYSICAL HEALTH, LIMITATIONS, COMORBIDITY AND DISABILITY

<b>Figure 1.</b>	Degree of significant/moderate stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA by sex (N: 506-532)	64
<b>Figure 2.</b>	Degree of significant/moderate stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA by age group (N: 506-532)	65
<b>Figure 3.</b>	Areas of the body where patients with Ax-SpA experienced inflammation (N: 526)	67
<b>Figure 4.</b>	Daily activities in which patients with Ax-SpA manifest some degree of limitation in times of crisis (N: 605)	68
<b>Figure 5.</b>	Frequency of taking part in activities by patients with Ax-SpA (N: 605)	71

<b>Figure 6.</b>	Assessment of personal relationships before suffering from Ax-SpA (N: 605)	71
<b>Figure 7.</b>	Adaptations made by patients since they suffered from Ax-SpA (N: 605)	72
<b>Figure 8.</b>	Comorbidity reported by patients with Ax-SpA (N: 368)	74
<b>Figure 9.</b>	Percentage distribution of patients with Ax-SpA by degree of disability (N: 280)	75
<b>Table 1.</b>	Level of BASDAI disease activity in the last week (N: 442)	62
<b>Table 2.</b>	Level of BASDAI disease activity in the last week (N: 442)	62
<b>Table 3.</b>	Disease activity level in the last week assessed using the BASDAI score for the different sexes (N: 442)	62
<b>Table 4.</b>	Disease activity level in the last week assessed using the BASDAI score by age group (N: 442)	63
<b>Table 5.</b>	Degree of stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA (N: 506-532)	64
<b>Table 6.</b>	Degree of overall stiffness in patients with Ax-SpA according to age group (N: 494)	66
<b>Table 7.</b>	Degree of overall stiffness in patients with Ax-SpA by sex (N: 494)	66
<b>Table 8.</b>	Descriptive statistics for the index of overall limitation as a result of Ax-SpA in times of crisis (N: 605)	69
<b>Table 9.</b>	Index of overall limitation (low, medium and high) as a result of Ax-SpA in times of crisis (N: 605)	69
<b>Table 10.</b>	Index of overall limitation as a result of Ax-SpA by age group in times of crisis (N: 605)	70
<b>Table 11.</b>	Descriptive statistics for the degree of disability recognised in patients with Ax-SpA (N: 280)	75

## 8. PSYCHOLOGICAL HEALTH

<b>Figure 1.</b>	Mental health problems (GHQ-12) in patients with Ax-SpA by gender	79
<b>Figure 2.</b>	Mental health problems (GHQ-12) in patients with Ax-SpA by age group	80
<b>Table 1.</b>	Mental health problems (GHQ-12) in patients with Ax-SpA by gender and age group	79
<b>Table 2.</b>	Relationship between poor mental health (GHQ-12) and disease activity (BASDAI) in patients with Ax-SpA	80
<b>Table 3.</b>	Risk of poor mental health (GHQ-12) in relation to a comorbidity with emotional disturbances (depression, anxiety and sleep disorders) in patients with Ax-SpA	81
<b>Table 4.</b>	Mental health problems (GHQ-12) in relation to visits to psychologists and psychiatrists in patients with Ax-SpA	82
<b>Table 5.</b>	Mental health problems (GHQ-12) in relation to membership of an SpA association	82

## 9. HEALTHCARE

<b>Figure 1.</b>	Percentage of patients with Ax-SpA visiting specialists during the last 12 months (N: 552)	84
<b>Figure 2.</b>	Attendance at emergency departments during the last 12 months (N: 552)	85
<b>Figure 3.</b>	Monitoring tests performed during the last 12 months (N: 552)	86
<b>Figure 4.</b>	Radiography by body region over the last 12 months (N: 552)	88
<b>Table 1.</b>	Frequency of visits to medical specialists by patients with Ax-SpA in the last 12 months (N: 552)	85

<b>Table 2.</b>	Attendance at emergency departments during the last 12 months (N: 552)	86
<b>Table 3.</b>	Frequency of monitoring tests in the last 12 months (N: 552)	87
<b>Table 4.</b>	Radiography by body region over the last 12 months (N: 552)	88

## 10. PHARMACOLOGICAL TREATMENT

<b>Figure 1.</b>	Total patients consuming NSAIDs, biologics and DMARDs and those who did not use any drugs.	90
<b>Figure 2.</b>	Percentage of drug use distinguishing between patients taking a single drug (biologics, NSAIDs or DMARDs) and those combining more than one or all those available (N: 461).	90
<b>Figure 3.</b>	Percentage distribution of patients taking NSAIDs in the past 12 months who have experienced side effects from these drugs (N: 372)	91
<b>Figure 4.</b>	Percentage of patients being treated with NSAIDs in the past 12 months who had been withdrawn from treatment (N: 372)	91
<b>Figure 5.</b>	Reason NSAID treatment was withdrawn from those taking these drugs in the last 12 months (N: 372)	92
<b>Figure 6.</b>	Percentage distribution of patients being treated with DMARDs in the last 12 months who had experienced side effects from these drugs (N: 193)	92
<b>Figure 7.</b>	Percentage distribution of patients receiving DMARDs in the last 12 months who had been withdrawn from the treatment (N: 193)	93
<b>Figure 8.</b>	Percentage distribution of patients receiving DMARDs in the last 12 months who had been withdrawn from treatment for various reasons (N: 193)	93
<b>Figure 9.</b>	Percentage distribution of patients according to the number of different biologics prescribed to date (N: 63)	95
<b>Figure 10.</b>	Assessment of the difference between taking a biologic drug and not taking it (N: 251)	95
<b>Figure 11.</b>	Patients who have changed consumption frequency in biological treatment in the last 12 months (N: 272)	96
<b>Figure 12.</b>	Percentage distribution of patients receiving biological treatment in the last 12 months who had their frequency modified for various reasons (N: 247)	96
<b>Figure 13.</b>	Change in biological treatment in the last 12 months (N: 272)	97
<b>Figure 14.</b>	Patients who changed treatment in the last 12 months, specifying the type of drug (N: 69)	97
<b>Table 1.</b>	Major improvement ( $\geq 6$ ) in different aspects related to quality of life in patients treated with biologics (N: 219), NSAIDs (N: 386) and DMARDs (N: 167)	98
<b>Table 2.</b>	Level of average improvement in different aspects related to the quality of life when consuming biologics and other medication	99

## 11. REHABILITATION THERAPIES, PHYSICAL ACTIVITY AND BAD HABITS

<b>Figure 1.</b>	Complementary treatments most used by people with Ax-SpA (N: 460)	102
<b>Figure 2.</b>	Percentage of patients who have attended a spa due to their illness in the last year (N: 583)	103
<b>Figure 3.</b>	Activities performed by people with Ax-SpA on a weekly basis (N: 545)	108
<b>Figure 4.</b>	Degree of cervical stiffness in relation to the performance of some beneficial activity	112

<b>Figure 5.</b>	Degree of dorsal stiffness in relation to the performance of some beneficial activity	112
<b>Figure 6.</b>	Degree of lumbar stiffness in relation to the performance of some beneficial activity	113
<b>Figure 7.</b>	Smoking by people with Ax-SpA (N: 585)	113
<b>Figure 8.</b>	Alcohol consumption by people with Ax-SpA (N: 585)	114
<b>Table 1.</b>	Monthly sessions of the main complementary treatments (N: 123)	102
<b>Table 2.</b>	Monthly expenditure on rehabilitation therapies or physical exercise for patients with Ax-SpA (N: 311)	104
<b>Table 3.</b>	Visits to a physiotherapist for people with Ax-SpA in the last 12 months (N: 680)	104
<b>Table 4.</b>	Visits to a physiotherapist for people with Ax-SpA by sex (N: 680)	105
<b>Table 5.</b>	Visits to a physiotherapist for people with Ax-SpA in the last 12 months by age group (N: 680)	105
<b>Table 6.</b>	Average BASDAI score in relation to visits to a physiotherapist for people with Ax-SpA (N: 442)	105
<b>Table 7.</b>	Visits to a physiotherapist for people with Ax-SpA in relation to their work situation	106
<b>Table 8.</b>	Visits to a physiotherapist by people with Ax-SpA in relation to monthly income in the home (N: 468)	106
<b>Table 9.</b>	Hours per week dedicated to different activities by people with Ax-SpA (N: 418)	109
<b>Table 10.</b>	Practice of beneficial activities for people with Ax-SpA (water aerobics, aquatic therapy, walking, meditation, swimming, pilates and yoga) (N: 680)	109
<b>Table 11.</b>	Practice of activities beneficial for people with Ax-SpA by sex (N: 680)	110
<b>Table 12.</b>	Practice of activities that are beneficial for people with Ax-SpA by age group (N: 680)	110
<b>Table 13.</b>	Practice of activities that are beneficial for patients with Ax-SpA (pilates, yoga, swimming, aquatic therapy, water aerobics and meditation) except for walking by monthly income level (N: 680)	111
<b>Table 14.</b>	Practice of activities that are beneficial for people with Ax-SpA in relation to membership of a patient association.	111

## 12. EMPLOYMENT STATUS

<b>Figure 1.</b>	Current employment status (N: 562)	117
<b>Figure 2.</b>	Workers: Main occupation (N: 264)	118
<b>Figure 3.</b>	Workers: Work problems due to AS in the past 12 months (N: 272)	119
<b>Figure 4.</b>	Workers: Paid/unpaid leave due to AS in the past 12 months (N: 145)	119
<b>Figure 5.</b>	Workers: Sick leave due to AS in the past 12 months (N: 145)	120
<b>Figure 6.</b>	Workers: Reduction in working hours due to AS in the past 12 months (N: 145)	120
<b>Figure 7.</b>	Workers: Problems related with work due to AS in the past 12 months (N: 109)	121
<b>Figure 8.</b>	Temporary sick leave: Main occupation (N: 23)	122
<b>Figure 9.</b>	Temporary sick leave as a consequence of AS (N: 41)	123
<b>Figure 10.</b>	Permanent sick leave or early retirement as a consequence of AS (N: 63)	124
<b>Figure 11.</b>	Difficulties accessing employment because of AS (N: 277)	125

<b>Figure 12.</b>	Choice of profession conditioned by AS (N: 505)	126
<b>Table 1.</b>	Workers: Number of hours per week in their main occupation (N: 273)	118
<b>Table 2.</b>	Workers: Number of days of paid/unpaid leave due to AS in the past 12 months (N: 17)	119
<b>Table 3.</b>	Workers: Number of days of sick leave due to AS in the past 12 months (N: 48)	120
<b>Table 4.</b>	Workers: Number of hours and days reduced per week due to AS in the past 12 months (N: 18-8)	121
<b>Table 5.</b>	Temporary sick leave: Number of hours per week in their main job (when not on sick leave) (N: 41)	122
<b>Table 6.</b>	Temporary sick leave: Number of months of temporary sick leave as a consequence of AS in the past 12 months (N: 35)	123
<b>Table 7.</b>	Permanent sick leave or early retirement: Number of months permanent sick leave or early retirement because of AS in the past 12 months (N: 40)	124
<b>Table 8.</b>	Unemployed patients: Number of months unemployed as a result of AS in the past 12 months (N: 44)	125

### 13. SOCIETAL BURDEN OF ANKYLOSING SPONDYLITIS

<b>Table 1.</b>	Cost/diagnosis: visits to medical professionals (N: 578)	129
<b>Table 2.</b>	Cost/diagnosis: diagnostic tests performed (N: 578)	129
<b>Table 3.</b>	Total cost of AS diagnosis per patient (N: 578)	130
<b>Table 4.</b>	Total cost of AS diagnosis in Spain	130
<b>Table 5.</b>	Costs per patient / year and cost distribution by type	131
<b>Table 6.</b>	Costs per patient/year according to severity (BASDAI scale)	132
<b>Table 7.</b>	Costs per patient/year by sex	132
<b>Table 8.</b>	Costs per patient/year in relation to the administration of biologics	133
<b>Table 9.</b>	Annual total cost of AS management in Spain	133
<b>Table 10.</b>	Cost/patient/year: AS-related medical visits in the last 12 months (N: 578)	134
<b>Table 11.</b>	Cost/patient/year: AS-related medical tests in the past 12 months (N: 578)	134
<b>Table 12.</b>	Cost/patient/year: breakdown of AS-related radiography in the last 12 months (N: 578)	135
<b>Table 13.</b>	Cost/patient/year: visits to emergencies related to AS in the last 12 months (N: 578)	136
<b>Table 14.</b>	Cost/patient/year: hospital admissions related to AS in the last 12 months (N: 578)	136
<b>Table 15.</b>	Cost/patient/year: AS-related medication in the last 12 months (N: 578)	136
<b>Table 16.</b>	Cost/patient/year: Direct healthcare costs (N: 578)	137
<b>Table 17.</b>	Distribution of Direct Healthcare Costs by type of cost	137
<b>Table 18.</b>	Cost/patient/year: Direct Healthcare Costs by type of financing (N: 578)	137
<b>Table 19.</b>	Cost/patient/year: main alternative treatments related to AS in the last 12 months (N: 578)	138
<b>Table 20.</b>	Cost/patient/year: rehabilitation therapies and physical exercise related to AS in the past 12 months (N: 578)	138
<b>Table 21.</b>	Cost/patient/year: Direct Non-Healthcare Costs (N: 578)	139

<b>Table 22.</b>	Distribution of Direct Non-Healthcare Costs by type of cost	139
<b>Table 23.</b>	Cost/patient/year: annual labour productivity losses for patients with AS	140
<b>Table 24.</b>	Correlation between cost, disease activity (BASDAI) and mental health (GHQ-12) in patients with AS	141
<b>Table 25.</b>	Cost/patient/year: medication related to AS in the past 12 months. Comparison of base case versus sensitivity analysis (N: 578)	142
<b>Table 26.</b>	Distribution of Direct Healthcare Costs according to cost type. Comparison of base case versus sensitivity analysis	143
<b>Table 27.</b>	Costs per patient per year and distribution of the cost depending on type. Comparison of base case versus sensitivity analysis	143
<b>Table 28.</b>	Total annual cost of managing AS in Spain. Comparison of base case versus sensitivity analysis	144
<b>Table 29.</b>	Scenario analysis. Cost/patient/year: informal care as a consequence of AS	144
<b>Table 30.</b>	Scenario analysis. Cost/patient/year: investment in adaptations	145
<b>Table 31.</b>	Scenario analysis. Direct Non-Healthcare Costs: cost/patient/year and distribution according to cost type	145
<b>Table 32.</b>	Scenario analysis. Average cost/year for a patient with AS in Spain and the cost distribution by type	146

#### 14. HOPES AND FEARS

<b>Figure 1.</b>	Fears of people with EspA-ax in the survey	148
<b>Figure 2.</b>	Main fears of people with Ax-SpA (N: 399)	149
<b>Figure 3.</b>	Main hopes of people with Ax-SpA (N: 387)	150
<b>Figure 4.</b>	General objectives of people with Ax-SpA in relation to their treatment	151
<b>Figure 5.</b>	Main specific objectives of the respondents in relation to their treatment (N: 410)	152
<b>Figure 6.</b>	Patients with Ax-SpA that have spoken with their doctor about their personal goals (N: 464)	153

#### 15. CONCLUSIONS AND RECOMMENDATIONS

<b>Table 1.</b>	Unit prices: visits to healthcare professionals	161
<b>Table 2.</b>	Unit prices: diagnostic tests	161
<b>Table 3.</b>	Unit prices: use of emergency services	162
<b>Table 4.</b>	Unit prices: hospital admissions according to CIE9: 720.0 Ankylosing spondylitis	162
<b>Table 5.</b>	Unit prices: AS-related medication	162
<b>Table 6.</b>	Unit prices: alternative treatments	163
<b>Table 7.</b>	Unit prices: hourly rate for normal hours	163
<b>Table 8.</b>	Unit prices: informal care	163



## ACRONYMS

<b>Anti-TNFα</b>	Anti-Tumour Necrosis Factor	<b>HLA-B27</b>	Human Leukocyte Antigen-B27
<b>ARs</b>	Autonomous regions	<b>HTR</b>	University of Seville Health & Territory Research Group
<b>AS</b>	Ankylosing spondylitis	<b>INE</b>	Spanish National Statistics Institute
<b>ASAS</b>	Assessment of Spondyloarthritis International Society	<b>INSS</b>	National Institute of Social Security
<b>ASQoL Questionnaire</b>	Ankylosing Spondylitis Quality of Life questionnaire	<b>MASES</b>	Maastricht Ankylosing Spondylitis Enthesitis Score
<b>AV block</b>	Atrioventricular block	<b>MRI</b>	Magnetic resonance imaging
<b>Ax-SpA</b>	Axial spondyloarthritis	<b>MSSSI</b>	Ministry of Health, Social Services and Equality
<b>BASDAI</b>	Bath Ankylosing Spondylitis Disease Activity Index	<b>NMR</b>	Nuclear Magnetic Resonance
<b>BASFI</b>	Bath Ankylosing Spondylitis Functional Index	<b>Nr-axSpA</b>	Non-radiographic axial spondyloarthritis
<b>BASMI</b>	Bath Ankylosing Spondylitis Metrology Index	<b>NSAID</b>	Non-steroidal anti-inflammatory drug
<b>CEADE</b>	Spanish Coordinator of Spondyloarthritis Associations	<b>PCD</b>	Primary Care Doctor
<b>CES-D Questionnaire</b>	Questionnaire: Centre for Epidemiological Studies Depression Scale	<b>PsA</b>	Psoriatic arthritis
<b>CNO-11</b>	National Occupations Classification 2011	<b>RD</b>	Rare diseases
<b>DMARD</b>	Disease modifying antirheumatic drugs	<b>RNA</b>	Ribonucleic acid
<b>DNA</b>	Deoxyribonucleic acid	<b>SEMFYC</b>	Spanish Society of Family and Community Medicine
<b>EMA</b>	European Medicines Agency	<b>SER</b>	Spanish Rheumatology Society
<b>ENMT</b>	National School of Occupational Medicine	<b>SF-12 Questionnaire</b>	Questionnaire on quality of life related to health or perceived health
<b>ETN</b>	Etanercept	<b>SpA</b>	Spondyloarthritis
<b>EULAR</b>	European League Against Rheumatism	<b>TNF</b>	Tumour Necrosis Factor
<b>EUROSTAT</b>	European Statistics Office	<b>US</b>	University of Seville
<b>FSS Questionnaire</b>	Fear Survey Schedule questionnaire	<b>VAS</b>	Visual analogue scale
<b>GHQ</b>	Goldberg's General Health Questionnaire	<b>VNS</b>	Verbal numeric scale
<b>GRESSER</b>	Spanish Rheumatology Society Spondyloarthritis Study Group		





## PREFACE

CEADE, as the Spanish Coordinator of Spondyloarthritis Associations, represents 22 associations and more than 4,000 members spread throughout Spain. Its aim is to improve patients' quality of life by helping them accept their condition, become informed and access the most effective medical treatment and rehabilitation.

This Atlas of Axial Spondyloarthritis in Spain 2017 was born out of CEADE and proof of this is the person, also a sufferer of the disease, who suggested that this important project be undertaken by the University of Seville. This took place when I was attending an EAS conference held in Seville in November 2014. Ever since then this project became one of my top priorities as President. Along the way it has gained the support of bodies such as the University of Seville, the Max Weber Institute, the SER and Novartis who have all made it possible.

The 2017 Atlas is the most ambitious and important project that CEADE has promoted and it represents a leap in quality as it has become the cornerstone on which CEADE's demands, and those of its local associations, are founded when dealing with the regional health authorities and the Spanish state. We want it to give the patient a voice that will be heard and for its scientific evidence to help us to set priorities. CEADE aims to improve the coordination of its participating associations both at the national and international level and with this type of document we aim to achieve this goal. We aim to make the impact of our disease visible as well as the limitations it produces in our physical and psychological health, in the performance of our work activity and in our family environment. We also hope to promote early diagnosis, quality healthcare, access to the most effective treatments and, ultimately, an improvement in our quality of life.

**Pedro Plazuelo**  
*President of CEADE*



## PROLOGUE

As a medical society, the mission of the Spanish Rheumatology Society (SER) is to provide its members with the necessary tools to improve the quality of life of patients with rheumatic diseases. We also try to be a guarantor of the highest quality of care in the treatment of the musculoskeletal system and systemic autoimmune diseases. In order to achieve this we not only set reference standards for the improvement of the quality of healthcare practice in rheumatology, but we also ensure their dissemination, monitoring, updating and on-going revision.

At SER and, more specifically, at the Spanish Rheumatology Society Spondyloarthritis Study Group (GRESSER) we are not strangers to the current reality of the people suffering from musculoskeletal and systemic autoimmune diseases. In relation to axial spondyloarthritis (Ax-SpA) we fully understand the needs of the people affected from a medical and social point of view.

The Atlas of Axial Spondyloarthritis in Spain project is a good example of our scientific society's commitment to patients. GRESSER has actively participated in developing this initiative in collaboration with a multidisciplinary group of professionals involved in the treatment and management of Ax-SpA, as well as with the patients themselves. For the development of the project, GRESSER helped describe the current situation regarding the management of this disease and, most importantly, we have had the opportunity to use the group's scientific knowledge and experience to propose various measures to improve diagnosis and control of the disease, in its different degrees of severity.

SER and GRESSER, in compliance with our strategic plan, will continue to promote initiatives such as this project and the implementation of actions involving continuous improvement in the management of spondyloarthritis, for the benefit of patients.

**Dr. José Luis Andréu Sánchez**  
*President of SER*



## PARTICIPATING ENTITIES

### PROMOTING ENTITY

#### **CEADE (Spanish Coordinator of Spondyloarthritis Patient Associations).**

- Pedro Plazuelo Ramos (President).

### WORK TEAMS

#### **Health & Territory Research (HTR) Group at the University of Seville.**

- Marco Garrido Cumbreira (Lecturer and Researcher).
- David Gálvez Ruiz (Lecturer and Researcher).
- Jorge Chacón García (Researcher).
- Olta Braçe (Researcher).

#### **Max Weber Institute**

- Renata Villoro Valdés (Researcher).
- María Merino Ventosa (Researcher).
- Almudena González Domínguez (Researcher).
- Yoana Ivanova Markova (Researcher).

### COLLABORATING ENTITIES

#### **Spanish Rheumatology Society Spondyloarthritis Study Group (GRESSER).**

- Victoria Navarro Compán (Rheumatologist).
- Eduardo Collantes Estevez (Rheumatologist).
- Zarco Montejo (Rheumatologist).
- Jordi Gratacós Masmitjà (Rheumatologist).

#### **SEMFYC (Spanish Society of Family and Community Medicine).**

- Fernando León Vázquez (Primary Care Doctor).

#### **University of Castilla-La Mancha**

- Álvaro Hidalgo Vega (Lecturer in Fundamentals of Economic Analysis).

#### **Novartis.**

- Àngels Costa Ferrer (Patient Relations Manager).
- Carles Blanch Mur (Early Access & Health Economics).

We are grateful to the **Spanish Rheumatology League (LIRE)** for its collaboration in this project.



**ATLAS OF AXIAL SPONDYLOARTHRITIS**  
**IN SPAIN 2017:**  
PROFILE OF THE DISEASE





# 1. INTRODUCTION AND STATE OF THE ART

## 1.1 Need for an Atlas of Axial Spondyloarthritis in Spain

There is currently a wealth of information about spondyloarthritis from the clinical point of view and regarding the most appropriate pharmacological treatments. However, there is a shortage of information in relation to legislation and planning, existing resources for its treatment, the reasons for delays in diagnosis, the physical limitations and psychological state of patients, their employment situation, productivity losses and the costs associated with the management of the disease.

The Atlas of Axial Spondyloarthritis in Spain 2017: Investigation of the Disease is an initiative that originated with CEADE and has been carried out by the Health & Territory Research (HTR) Group at the University of Seville, the Max Weber Institute and with the collaboration of the Spanish Rheumatology Society (SER), the Rheumatology League and Novartis.

The objective of this initiative is to analyse the situation of people with Ax-SpA in Spain, creating a document that deepens knowledge of the disease and contributes new information aimed at improving patients' health-care and quality of life.

This report is based on the assessment of the status of people with Ax-SpA through a survey of patients, expert opinion, and analysis of various sources of information and indicators. This has allowed a broad brush estimation of patients' realities and the most appropriate types of treatment, in order to establish proposals and recommendations aimed at improving the quality of life of patients with Ax-SpA.

## 1.2 Definition of the disease

The term spondyloarthritis (SpA) describes a group of chronic inflammatory diseases that share clinical, pathogenic, genetic, radiological, epidemiological and therapeutic response characteristics, including inflammation of the spine and, in some people, of the joints of the arms and legs. It can also affect the skin, bowel and eyes. The main symptom in most patients is pain in the lower back. The terms "spondyloarthropathies" and "spondyloarthritis" are used interchangeably to refer generically to any of the diseases that make up the spondyloarthritis group, including: ankylosing spondylitis (AS), reactive arthritis (ReA), arthritis related with inflammatory bowel diseases (IBD), Crohn's disease, ulcerative colitis, psoriatic arthritis (PsA), undifferentiated spondyloarthritis (USpA), and juvenile-onset ankylosing spondylitis (JoAS).

Ax-SpA is a chronic inflammatory disease that mainly affects the joints of the spine and the sacroiliac joints, which tend to become fused together, limiting mobility (hence the term ankylosing, which comes from the Greek 'Ankylos' and means stiffening or fusion). The disease is characterised by the appearance of inflammatory pain in the spinal column that causes sufferers to wake in the second half of the night and that sometimes forces the patient to get up out of bed. Similarly, Ax-SpA is characterised by the presence of stiffness in the morning, due to the inflammation of the spinal column itself and this limits mobility for at least 30 minutes upon awakening. In the active phases this can last for hours, which results in an important decrease in physical function (1).

As for its clinical manifestation, the first thing a sufferer notices is lower back pain that is produced by the inflammation of the sacroiliac and vertebral joints. This pain is of an inflammatory type and manifests itself in an insidious, slow and gradual way, making it impossible to determine exactly when the symptom began. Most of the pain occurs when the affected person is at rest, improving with physical activity. This means that the pain is usually worst late at night and in the early hours of the morning, when the patient has already spent some time in bed. This forces the person to get up and walk about in order to relieve the pain. Over time, the pain and stiffness can progress to the dorsal spine and neck. The vertebrae become fused progressively, the column loses flexibility and becomes rigid, limiting movement. The rib cage may also be affected, causing pain in the joints between the ribs and the sternum and limiting the normal expansion of the chest making breathing difficult. Inflammation and pain may also occur in the joints of the hips, shoulders, knees, ankles, or in areas of the skeleton where the ligaments and tendons are attached to the bones (pain in the heel, Achilles tendon, etc.) (2).

Ax-SpA is a systemic disease, which means it can affect other body organs. In some people it can cause fever, loss of appetite, fatigue and even inflammation in organs such as the lungs and heart, although the latter occurs only very rarely. There may be a decrease in the functioning of the lungs due to a decrease in the elasticity of the chest. Inflammation of some parts of the eye (uveitis) is relatively common, it occurs in a quarter of people with Ax-SpA and manifests as ocular pain and redness ("red eye") (3).

The Spanish Rheumatology Society Spondyloarthritis Study Group (GRESSER) estimates the prevalence of these conditions to be around 1.9% of the general population. Currently available data indicate the incidence of the disease to be about 7 new cases per 100,000 inhabitants per year. Its prevalence varies according to ethnicity, geographic location and, above all, the frequency of HLA-B27 in the general population. In Europe, the prevalence of Ax-SpA ranges from 0.3% to 1.3%, which would be equivalent to the presence of at least half a million patients with Ax-SpA in Spain. It usually occurs in males between 20 and 30 years of age. It is less frequent in women and is usually less severe (4).

The onset of the disease in this age group (20-30 years), which is the start of a person's working life, often determines their future professional prospects. The inability of these patients to continue in their work considerably affects their social life (psycho-affective), as well as having economic repercussions, not only for the patient but for society in general. Some studies have shown that the overall unemployment rate is 25.3%, with 20.6% attributable to the disease itself, with this level being conditioned by being female, having a low educational level, living in rural areas as well as high rates of disease activity (5). This is why the disease has a huge impact on patients' quality of life as it affects their physical, psychological and social well-being (6).

## 1.3 Diagnosis

Early detection, diagnosis and treatment of chronic inflammatory rheumatic diseases should be one of the objectives of medicine and society in general if we want to improve the functional situation, reduce comorbidities and loss of the quality of life of these patients.

Diagnostic delay in the case of Ax-SpA prevents treatment in the initial phases, which is responsible to a great extent for a worsening in the disease, an increase in structural damage and loss of mobility (7,8). This is a result of its insidious onset, low prevalence and because it is not well recognised by doctors who are not specialists in rheumatology. Other reasons for a delay in diagnosis are due to a lack of awareness of this group of diseases by society and a lack of training in their diagnosis in some health professionals. This means that patients are forced to live with the disease for a number of years before they are diagnosed (9).

New criteria have recently been adopted that have facilitated the diagnosis of spondyloarthritis in the early stages of the disease (10). Combined with the use of new techniques such as magnetic resonance imaging, these criteria have facilitated diagnosis at the earliest stages of the disease before radiographic disorders occur. This has resulted in the concept of "non-radiographic axial spondyloarthritis", corresponding to those initial stages of the disease in which there has not yet been sufficient structural damage for it to be seen on conventional radiography.

## 1.4 The patient's perspective

One of the main contributions of the 2017 Atlas has been the incorporation of the patient's perspective on all aspects of coping with this disease: chronic pain/inflammation, physical, social, etc. Therefore, unlike other reports or research carried out on Ax-SpA, this report not only seeks to capture a series of clinical aspects and/or treatments related to patient health, but rather to reflect the patient's experience of the disease. And to do this for aspects as diverse as the objectives established for the treatment, the disease's psychological aspects, the patient's hopes and fears and even the treatments and resources used by each patient beyond those prescribed by their rheumatologist.

This philosophy is in line with the recommendations established by the international working group ASAS-EULAR (11) in relation to basing treatment and care decisions on a close relationship between the rheumatologist and the patient. This 'shared decision-making' refers to aspects such as the choice of a particular drug and even to many other stages of the process: defining treatment objectives, investigating potential barriers to achieving these objectives, choosing the best strategy for achieving those objectives, considering alternative strategies if the objective is not reached or if treatment is not tolerated.

## References

1. Kiltz U, van der Heijde D. Health-related quality of life in patients with rheumatoid arthritis and in patients with ankylosing spondylitis. *Clin Exp Rheumatol*. 2009;27(4 Suppl 55):S108-111.
2. Spanish Society of Rheumatology (SER). What is it? Ankylosing spondylitis [Internet]. Available on: <http://www.ser.es/wp-content/uploads/2015/09/espondilitis.pdf>
3. Cantini F, Nannini C, Cassara E, Kaloudi O, Niccoli L. Uveitis in Spondyloarthritis: An Overview. *J Rheumatol Suppl*. 2015;93(0):27-9.
4. Cañete J, Collantes E, Sueiro Fernández J, Juanola X. Espondiloartropatías. Press Kit [Internet]. Madrid; Available on: <http://www.gresser.es/PACIENTES/Espondiloartropatias.pdf>
5. Montacer Kchir M, Mehdi Ghannouchi M, Hamdi W, Azzouz D, Kochbati S, Saadellaoui K, et al. Impact of the ankylosing spondylitis on the professional activity. *Jt Bone Spine*. 2009;76(4):378-82.
6. Kotsis K, Voulgari P V, Drosos AA, Carvalho AF, Hyphantis T. Health-related quality of life in patients with ankylosing spondylitis: a comprehensive review. *Expert Rev Pharmacoecon Outcomes Res*. 5 December 2014;14(6):857-72.
7. Deodhar A, Mittal M, Reilly P, Bao Y, Manthena S, Anderson J, et al. Ankylosing spondylitis diagnosis in US patients with back pain: identifying providers involved and factors associated with rheumatology referral delay. *Clinical Rheumatology*. 2016;1-8.
8. Nakashima Y, Ohishi M, Okazaki K, Fukushi J-I, Oyamada A, Hara D, et al. Delayed diagnosis of ankylosing spondylitis in a Japanese population. *Mod Rheumatol*. May 2016;26(3):421-5.
9. Khan MA. Ankylosing spondylitis: introductory comments on its diagnosis and treatment. *Ann Rheum Dis*. December 2002;61 Suppl 3(suppl 3):iii3-7.
10. Rudwaleit M, Landewé R, van der Heijde D, Listing J, Brandt J, Braun J, et al. The development of Assessment of Spondylo Arthritis international Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. *Ann Rheum Dis*. 2009;68(6):770-6.
11. Van Der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van Den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. 2017;0:1-14.

## 2.OBJECTIVES:

### 2.1 Overall objective

The overall objective of the Atlas of Axial Spondyloarthritis in Spain 2017 is a better understanding of the reality of the people affected from an integrative perspective and based on scientific evidence, expert knowledge and the patients' own perspective.

### 2.2 Specific objectives

1. Identify the main barriers and difficulties in the diagnosis of Ax-SpA.
2. Evaluate healthcare for people with Ax-SpA.
3. Evaluate the use of pharmacological and non-pharmacological treatments in people with Ax-SpA.
4. Analyse the work situation and productivity losses of people with Ax-SpA.
5. Estimate the direct healthcare and non-healthcare costs derived from the disease.

## 3.METHODOLOGY

### 3.1 Literature review

A broad literature review was carried out on aspects related to the disease in the following areas: policy and legislation, socio-demographic characteristics, diagnosis, treatment, comorbidity, work situation, limitations and psychological state. In addition to the review of the scientific literature, available databases were also consulted, as well as planning and legislation documents with reference to SpA, both at a national and autonomous region level.

### 3.2 Scientific committee and advisory committee

This study uses the opinion of a scientific committee and an advisory committee, made up of professionals with experience in the care of these patients, as well as in carrying out scientific studies on Ax-SpA.

The scientific committee was in charge of evaluating and validating the study's assumptions and results, as well as the current healthcare approach to Ax-SpA in Spain. Specifically, its functions were:

- Advise the project during its implementation.
- Review and validate the patient questionnaire.
- Agree on the current approach of the patients.
- Validate the final results.

The scientific committee was composed of the following experts:

- Eduardo Collantes Estevez. Rheumatologist at the Hospital Reina Sofía and professor at the University of Cordoba / GRESSER.
- Marco Garrido Cumbreña. Lecturer and researcher with the Health & Territory Research (HTR) Group at the University of Seville.
- Jordi Gratacós Masmitjà. Rheumatologist at the Hospital de Sabadell Parc Taulí / GRESSER.
- Álvaro Hidalgo Vega. Lecturer and researcher at the University of Castilla-La Mancha.
- Fernando León Vázquez. Primary care doctor at Health Centre San Juan de la Cruz in Pozuelo de Alarcón.
- Victoria Navarro Compán. Rheumatologist at the University Hospital La Paz / GRESSER.
- Pedro Plazuelo Ramos. President of CEADE.
- Pedro Zarco Montejo. Rheumatologist at the Alcorcón Foundation Hospital / GRESSER.

The scientific committee met in Madrid on three occasions on 25 January 2016, 14 July 2016 and 30 November 2016 to advise, resolve doubts and assess the results obtained by the work team.

In addition to the scientific committee, an advisory committee was also established whose role was to resolve doubts on specific issues. Communication was mainly by email and teleconferences. The composition of the advisory committee was as follows:

- Laura Cano García. Nurse.
- Raúl Ferrando Piqueres. Pharmacist.
- Inmaculada Mayoral Contreras. Primary care doctor.
- Elena Sonsoles Rodríguez López. Physiotherapist.
- Carlos Jesús Delgado Domínguez. Psychologist.
- Susana Anguera Pleite. Psychologist.

## 3.3 Survey of patients with Axial Spondylarthritis

### 3.3.1 Questionnaire design

The questionnaire for the survey of patients with Ax-SpA was based on the opinion of experts on the treatment and management of these patients, as well as on the review of the scientific literature. The questionnaire was developed by the Health & Territory Research (HTR) Group of the University of Seville and the Max Weber Institute. The questionnaire was then reviewed by CEADE and SER during the period from January to May 2016. The criteria used to develop the questionnaire were as follows:

- Ease to understanding for all patients (regardless of their age and educational level).
- Completion time (as short as possible).
- Information grouped into chapters (to facilitate completion of the questionnaire)
- Combination of closed questions (quantitative data) and open-ended questions (qualitative information).

- Interdisciplinary perspective (rheumatology, general medicine, public health, health economics, psychology, physical therapy, health geography, statistics and the patients themselves).
- Balance between medical terminology and informal language.

The questionnaire was validated with patients during April 2016. This validation was performed through a number of personal interviews with a group of 17 people with Ax-SpA belonging to different age groups and educational levels. Of these, 10 were members of the Ankylosing Spondylitis Association of Seville and 7 members of the Fuenlabrada Spondylitis Sufferers Association (Madrid). During these interviews, both the completion time and the difficulties generated by the process were evaluated and the most complex terms were identified. A new version was then drafted incorporating all these comments.

The questionnaire was agreed between January and May 2016 by more than 25 specialists and patients including: members of the University of Seville, the Max Weber Institute, the Spanish Coordinator of Spondyloarthritis Associations, the Spanish Rheumatology Society, the University of Castilla-La Mancha and the scientific committee. These most notably include rheumatologists, primary care doctors, pharmacists, physiotherapists, health economists and health geographers.

The final questionnaire contained a total of 116 items, in addition to 4 open questions, encompassing the following areas:

- Socio-demographic characteristics: year of birth, sex, level of education, marital status, income level, municipality of residence and autonomous region.
- Anthropometric characteristics: height and weight.
- Diagnostic delay: date of first symptoms and diagnosis with Ax-SpA.
- Healthcare resource use: outpatient visits, hospitalisations, accident and emergency visits, medical tests related to Ax-SpA.
- Comorbidity.
- Drug treatment for Ax-SpA: Biologics, NSAIDs and DMARDs.
- Data concerning employment: employment status, occupation, number of working hours per week.
- Loss of productivity at work: problems related to work (in complying with working hours, reduction in working hours, etc.), temporary and permanent sick leave or early retirement due to Ax-SpA.
- Disability benefits.
- Limitations: social and personal in everyday life.
- Physical activity.
- Bad habits: smoking or alcohol.

### 3.3.2 Implementation of the survey

The survey was conducted between 1 May and 15 August 2016 (4 months), a total of 838 people with Ax-SpA agreed to complete the questionnaire. After validation and debugging of the information there were a total of 680 individuals with Ax-SpA who made up the total valid sample.



### 3.4 Supplementary instruments

Two specific rating scales were used in addition to the questionnaire designed for this study. These were the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Goldberg's General Health Questionnaire (GHQ-12) consisting of:

*BASDAI:* This is a self-administered questionnaire that evaluates disease activity in patients with Ax-SpA. It includes six questions relating to the following symptoms: fatigue, pain in the spinal column, inflammation/pain in joints other than the neck, back and hips, level of discomfort in areas painful to the touch and lastly the level of stiffness in the morning. The questions are evaluated using an analogue scale ranging from 0 (no activity) to 10 (maximum activity) (1). This instrument has been proven to have good properties and applicability to daily practice (2).

*GHQ-12:* This questionnaire evaluates the severity of mental health problems in recent weeks, either using a Likert-type four-point scale (0-1-2-3) or it can be transformed into a dichotomous score (0-0-1-1), called the GHQ score. The scoring method (0-0-1-1) was used in this study in order to eliminate any bias resulting from the tendency of the respondents to choose answers 1 and 4 or 2 and 3. The cut off point validated for the Spanish version of the questionnaire was 3, implying that individuals with a score of 3 or more may have a psychiatric disorder. The GHQ-12 was found to be highly reliable in the different studies, obtaining Cronbach's alpha coefficients ranging from 0.82 to 0.86 (3). A recent study carried out in Spain describes a Cronbach's alpha coefficient of 0.76 (4).

GHQ 12 was used with the permission of GL Assessment Ltd and BASDAI with the permission of the Mapi Research Trust

### 3.5 Statistical analysis

More than 80 socio-demographic and clinical variables were examined, which were analysed statistically and graphically represented. In addition, three new indicators were calculated to assess the degree of overall stiffness in the spine, the overall degree of limitations and the extent to which beneficial activities are undertaken:

*Overall stiffness index:* to assess the degree of stiffness experienced by patients in the spinal column, distinguishing between the cervical, dorsal and lumbar areas. This degree of stiffness was evaluated through a scale of responses going from least to most affected (without limitation, mild limitation, moderate limitation and significant limitation), with the result obtained by adding together the responses for the degree of stiffness in each of the areas of the spine without weighting.

*Overall limitation index:* which was generated by adding together without weighting the degree of limitation in 18 activities of daily life (dressing, bathing, showering, tying shoe laces, 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, going to the doctor, doing physical exercise, having sex) resulting in values between 0 and 54. Thus, a value between 0 and 18 implies low limitation, between 18 and 36 medium limitation and between 36 and 54 high limitation. This distribution is the result of assigning 0 to no limitation, 1 to low limitation, 2 medium limitation and 3 high limitation for each of the 18 different daily activities.

*Undertaking beneficial activities:* this indicator is binary and is generated by listing a series of physical activities considered beneficial for the patient such as pilates, yoga, walking, swimming, aquatic therapy, water aerobics, and meditation.

The distribution of drug treatments was calculated on the basis of the different possible treatment combinations, distinguishing between patients taking a single drug (biologic, NSAID or DMARD) and those that combine more than one (eg. biologic plus NSAID) or all three types simultaneously.

The 2017 Atlas used several statistical tests in order to measure the relationship between the different variables. Different tests were used depending on the nature of the variable (qualitative or quantitative) and the sample distribution (parametric or non-parametric). The Kolmogorov-Smirnov test was used to test the normality of all quantitative variables. For those variables whose distribution did not fulfil certain assumptions such as normality and homoscedasticity, non-parametric tests were applied such as:

- Mann-Whitney U test for independent samples (2 groups). This test is based on comparative analysis across ranges and it is used when the data are ordinal but normality cannot be assumed.
- Kruskal-Wallis H test for independent samples (> 2 groups). This test is based on comparative analysis across ranges and it is used when the data are ordinal as a non-parametric alternative to the ANOVA model when normality cannot be assumed.
- Pearson  $\chi^2$  test to verify whether there is a relationship between two categorical variables using a contingency table when the data are not paired.
- Spearman's rank correlation coefficient was used to measure the Association or relationship of monotony between pairs of quantitative variables. It is particularly suitable when some of the variables are ordinal (not cardinal).

The Pearson correlation coefficient was used for cardinal quantitative variables to measure the linear relationship between two variables.

Finally the data obtained for the 2017 Atlas was compared with the results of other studies of AS and SpA at both the national and international level (over 180 references) and with the health and lifestyle habits of the general population. This was achieved using data derived from different statistical sources such as the European Health Survey in Spain (EESE) 2014, the Spanish National Health Survey 2011/12 and the Sports Habits in Spain Survey 2015.

### 3.6 Qualitative analysis

The survey questionnaire for patients with Ax-SpA included the following open questions:

- Describe your fears in relation to Ax-SpA.
- Describe your hopes in relation to Ax-SpA.
- Describe your personal goals in relation to your treatment (to decrease pain, to increase mobility, be cured, to prevent structural damage, etc.).
- Have you ever spoken to your doctor about your personal goals in relation to your treatment?

The qualitative answers were homogenised, standardised, and grouped into several areas, including the frequency of each type of response. This process allowed the qualitative questions to be converted into quantitative questions making it numerically possible to count percentages of answers and thus assess patients' priorities in relation to their hopes and fears in general, as well as their objectives with respect to their treatment.

## 3.7 Societal burden methodology for ankylosing spondylitis

### 3.7.1 Perspective and time horizon

Cost studies can be carried out from four different perspectives, depending on which agent assumes the costs: the societal perspective, that of the payer or healthcare funder, that of the provider and that of the patient. Given the significant economic impact of AS that falls on different actors in society in general, limiting the perspective to that of the national health system (NHS) or the patient would disregard significant societal costs. The ideal situation for decision makers is to understand the burden of AS from a societal perspective. This includes the sum total of all the costs, regardless of who has assumed them and this, in turn, can facilitate the comparison of the economic burden of AS with that of other chronic diseases.

Therefore, the costs have been estimated from a societal perspective. In addition, a conservative perspective has been used at all times, opting to underestimate costs in case of doubt or lack of information on the use of resources by patients with AS.

A time horizon of one year was established to estimate the burden on prevalent patients, this was achieved by assigning a cost to the use of resources in the 12 months prior to the survey. However, the cost assigned to diagnosis spans a longer period of time and represents the total cost of all the resources consumed up until the accurate diagnosis, regardless of the time taken to achieve this.

The use of resources related to spondyloarthritis can vary depending on the disease type and the symptoms of the patients. Our sample is not representative of all these diseases, since it includes a disproportionate number of patients with AS, which represents an advanced and severe form within the spectrum of axial spondyloarthritis. In order to avoid this bias, the scientific committee agreed that the calculation of the disease's economic and societal impact be restricted to those patients with ankylosing spondylitis (578 patients) leaving aside other subtypes.

### 3.7.2 Costs

The disease burden studies considered three main types of disease-related costs: 1) direct, 2) indirect, and 3) intangible.

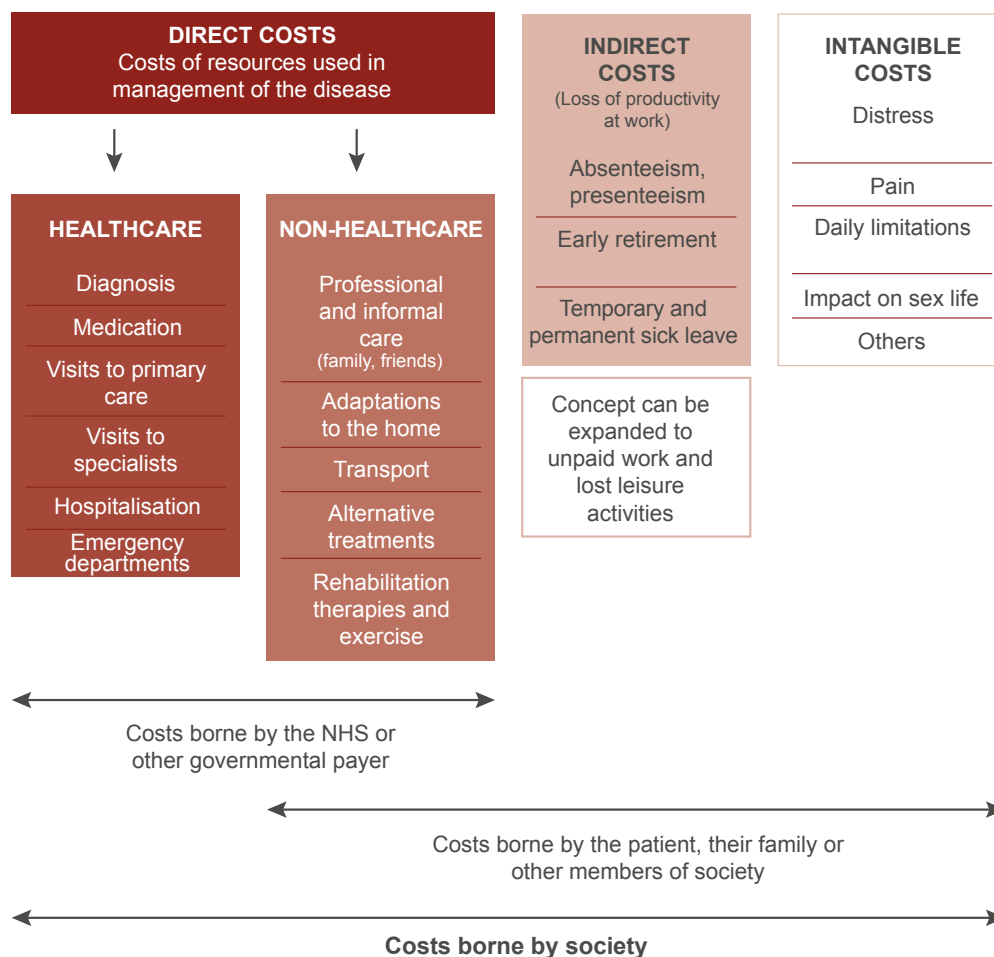
The direct costs can be divided between healthcare and non-healthcare. The direct healthcare costs include all the costs relating to the resources used in the management of the disease, such as diagnosis, medical visits, and pharmacological and non-pharmacological treatment. The direct non-healthcare costs relate to the monetary value of activities which are not directly related to the management of the disease, although they are costs that occur as a result of the disease. These can include transporting the patient to medical centres, adaptations to housing which are a result of a patient's disability, and the help a patient receives at home either from professional (paid) caregivers or family members (unpaid) to perform their daily activities.

On the other hand, the indirect costs include the loss of productivity in terms of absenteeism, presenteeism, temporary or permanent sick leave, early retirement, and premature mortality. They also include those costs resulting from the disability generated by the disease or those that are a consequence of the time spent on consultations, diagnostic tests, treatment and rehabilitation sessions.

Lastly, the intangible costs include the impact on a patient's quality of life and the emotional and psychological burden resulting from the disease.

Figure 1 shows the components of the societal economic burden of AS. The direct healthcare costs include the cost of visiting the primary care doctor or nurse, visits to a specialist (rheumatologist, orthopaedic surgeon, internal medicine specialist), visits to other health professionals (psychologist, physical therapist, etc.), diagnostic and medical tests, hospitalisations, emergency care and the drugs taken by the patient. The direct non-healthcare costs include transporting patients to health centres, adaptations to housing, care received at home from professional carers, care received from family members or friends (called informal care), alternative treatments (for example, acupuncture and homoeopathy), rehabilitation therapies or physical exercise, all resulting from constraints imposed by AS on the patient's activities of daily living. The indirect costs include the monetary cost represented by the productivity losses already referred to in the chapter on work. Lastly, the intangible costs are those associated with a patient's physical and emotional suffering and loss of quality of life.

**Figure 1.** Components of the economic and societal burden of AS.



Source: Own elaboration

The evaluation of the direct costs is obtained directly from retrospective or prospective information on the use of patients' resources multiplied by the costs and unit prices of these resources. The indirect costs or loss of productivity are generally estimated as equivalent to the wage income of a patient and require data on absenteeism, presenteeism, and early retirement (what is known as a human capital method). Lastly, for intangible costs to be included in the assessment of the overall burden of the disease, it is necessary to assess AS's impact, especially in the functionality and the quality of life of a patient, in monetary terms. Although the intangible costs of chronic degenerative diseases tend to be highly relevant, they are very difficult to estimate in monetary terms in practice, so they are often ignored in disease burden studies.

Depending on each country's health system, these three large costs (direct, indirect and intangible) may fall in part or in their entirety on the national health system, other institutional payers, or on the patients and their families. The agents assuming the various cost items are indicated by the lower arrows in Figure 1.

This classification of costs allows them to be grouped into: direct healthcare, direct non-healthcare and indirect. The intangible costs were impossible to quantify.

The direct healthcare costs include those funded both by the NHS as well as those funded privately by the patient or their family. The direct non-healthcare costs included in this analysis are funded entirely by the patient.

All costs are expressed in 2015 euros. To do this all the costs of resources used were updated by applying, in each case, the corresponding inflation rate, in the following manner:

- For direct non-drug healthcare costs<sup>1</sup>, the interannual increase in the CPI for medicine was used (5).

For direct non-healthcare costs the interannual increase in the general CPI was used (6). The calculation of the direct healthcare and non-healthcare costs was performed by multiplying the resources used for each patient by the unit price of each resource (all unit prices can be found in the Appendix). These prices are taken from different sources:

- The prices for visits, tests and emergencies were obtained from the official rates of the public prices in the gazettes for each of the autonomous regions. Due to the wide variability in prices that exists between the different regions, the median of the rates was used, previously updated to 2015 euros (7-27).
- The price of hospitalisation was obtained from the statistical portal of the Ministry of Health, Social Services and Equality. The price used was that provided in the International Classification of Diseases (ICD) under ICD-9-CM 720.0 relating to "ankylosing spondylitis" (28).
- Drug prices were obtained from the General Council of Official Colleges of Pharmacists medications database (29).
- For the calculation of the costs of administering biological drugs the cost per minute of a day hospital was obtained from the scientific literature (30).
- The costs for alternative treatments were based on market prices in 2015.
- The cost of rehabilitation therapies and physical exercise was provided by the patient.

---

<sup>1</sup> Pharmacological costs are updated in 2015 euros.

The quantification of indirect costs can be approached from two different perspectives: the Human Capital approach (31) and the Frictional Costs approach. According to the former the loss of daily productivity can be measured in monetary terms, from the salary which a patient fails to earn during all the time they are not working. In the second approach, only the productivity losses are considered up until the time the sick person is replaced in the workplace. This analysis calculated the indirect costs following the Human Capital approach, the most commonly used approach in disease burden studies. Therefore, a cost was charged for the working days lost or the wages not earned. To achieve this, an average salary was assigned according to gender and level of employment, in the case of workers and patients on temporary sick leave. The average salary according to gender and the average hours worked per year were used for all other situations involving loss of productivity. Wage data was extracted from the National Statistics Institute (INE) (32,33).

### 3.7.2.1 Diagnostic costs

Although this cost is included in the direct healthcare costs, it has been analysed separately due to the fact that the diagnosis is only made once in a patient's lifetime, so it cannot be included in the calculation of a patient's average annual health care cost.

The diagnostic costs (DG) include the following variables:

- visits to clinicians who diagnosed the illness,
- visits to the professionals consulted before the diagnosis of AS, and
- the diagnostic tests undertaken for diagnosing a patient.

### 3.7.2.2 Direct healthcare costs

The direct healthcare costs (DHC) include the following variables:

- Medical visits related to AS: cost of visits to the main specialists dealing with AS, as well as to other professionals reported by the patients, consulted in relation to the disease, carried out in the past 12 months.
- Medical tests related to AS: cost of the main tests related to AS, as well as of others indicated by patients, also linked to the disease, performed in the last 12 months.
- Emergencies: cost of outpatient emergencies, home emergencies, hospital and emergency health transport, linked to the AS, performed in the last 12 months.
- Hospital admissions: cost of hospital admissions related to AS occurring in the last 12 months
- Medication: pharmacological and administration cost of the medication related to AS in the last 12 months, which includes anti-inflammatories, antirheumatics and biologics. The cost was assembled as follows:
  - Pharmacological costs:
    - Anti-inflammatories and antirheumatics. The following factors were taken into account:
      - The daily doses recommended in the summary of product characteristics of each drug (34). If this was not specified in the summary of product characteristics the daily doses recommended by the World Health Organization (WHO) were used (35).
      - The cost per milligram (29).
      - The administration time indicated for each patient.

- **Biologics.** The following factors were taken into account:
  - The dose:
    - The doses recommended in the summary of product characteristics for each biological medicine (34).
    - For patients who reported less than one year of treatment with certolizumab pegol, infliximab, the biosimilars of infliximab and/or secukinumab, the induction period of each drug was considered (34).
    - For all patients who reported receiving treatment with certolizumab pegol, golimumab, infliximab and/or the biosimilars of infliximab, the doses were calculated taking into account the weight of each patient (34). In these cases the optimisation of vials was not taken into account, as it was considered that the remains of the vials would be discarded.
  - The cost per milligram (29).
  - The administration time indicated for each patient.
- **Cost of administration.** This cost applies only to biological drugs, since they are administered parenterally. The cost was assembled taking into account the following factors:
  - Infliximab and the biosimilars of infliximab are administered intravenously. A cost of €62.4 was obtained from a study measuring the mean day hospital time for each infliximab administration (178.29 minutes) as well as the cost per minute (€0.35 updated to 2015 euros) (30).
  - Adalimumab, certolizumab pegol, etanercept, golimumab and secukinumab are administered subcutaneously. The first administration is performed by the nursing staff, who in turn train the patient for later self-administration. Therefore, the cost of a nursing visit was charged.

In order to enrich the information analysed, all the above costs have been broken down in terms of publicly financed expenditures funded by the NHS and those financed privately by the patient (through health insurance or private consultations).

### 3.7.2.3 Direct non-healthcare costs

The direct non-healthcare costs (DNHC) include the following variables:

- Alternative treatments for AS in the last 12 months, such as acupuncture and homoeopathy.
- Expenditure on rehabilitation therapies or physical exercise for the treatment of AS, indicated in monetary form directly by patients.

The survey does not include information on costs related to the transportation of patients to attend consultations, tests, emergencies and other health services. Therefore, this cost is not reflected in our results. Likewise, the survey does not include information on the professional and informal care received by patients, nor on the adaptations patients may have made to their homes as a result of their physical limitations. Previous studies have shown that patients with advanced AS can incur significant out-of-pocket costs to cover informal care and adaptations to their homes (36). Therefore, as described below (see "Scenario Analysis"), an estimate of the cost relative to informal care and adaptations to homes was made, taking data from the literature.



#### 3.7.2.4 Indirect costs

Indirect costs (IC) are an economic valuation of the loss of wealth that disease entails for society. Only the labour productivity losses of the patient were included in this study. This cost is derived from the days of absenteeism due to medical visits, sick leave, hospitalisation days, etc. linked to AS in active people. It also includes labour productivity losses due to early retirement or difficulties in finding employment because of the disease.

#### 3.7.2.5 Total costs

The total cost (TC) includes the sum of direct healthcare costs, direct non-healthcare costs and labour productivity losses. The cost per patient per year refers to the average cost that a patient with SA represents for Spanish society (both for the health system and for society in general) over a period of one year. The total annual cost refers to the cost that AS represents for Spain in one year.

The annual total costs per patient were analysed according to the patient's severity (BASDAI scale) and the patient's sex. In addition, the correlation was analysed between each of the large cost items and the patient's health-related quality of life as measured by the BASDAI scale and the GHQ-12 mental health questionnaire.

### 3.7.3 Sensitivity analysis

In practice, because of agreements between hospitals and suppliers, the actual cost of biological treatments may differ from the official market prices. Additionally, in clinical practice, the use of vials by a hospital can be optimised by seeing a number of patients receiving the drug on the same day, thereby allowing the hospital to take full advantage of the vials. For this reason, a sensitivity analysis was performed focusing on the estimation of the costs for biologics (treatment and administration), trying to approximate the reality of clinical practice, in accordance with the criteria set by the 2017 Atlas scientific committee. To this end:

- The pharmacological cost has been reduced by 30%,
- Vial optimisation has been applied, and
- In patients who have been treated for more than one year, the drug administration time is optimised in accordance with the following criteria: 50% of the half-life of the drug (for example, one week is increased to 10 days).

### 3.7.4 Scenario analysis

Two variables were used for this analysis:

- Informal care As mentioned above, this variable was not included in the patients' questionnaire, so data from scientific literature were used, including the percentage of patients needing informal care and the annual informal care hours they require (36). The cost substitution method was used to calculate this cost, this involves assigning a cost to the time dedicated to informal care equivalent to the cost a patient would have incurred had they had to hire a professional caregiver for the same time. The cost per hour for a home help has been assigned in this study (37).
- Investment in adaptations. As mentioned above, this variable was not included in the patient questionnaire, so a cost reported in a previous study was used for the average per patient investment in adaptations (36).

The inclusion of these two cost items allows the estimation of direct non-healthcare costs and total costs, as well as allowing a re-estimate of the distribution according to cost type.



## References

- 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*. December 1994;21(12):2286-91.
- Haywood KL, M. Garratt A, Jordan K, Dziedzic K, Dawes PT. Disease-specific, patient-assessed measures of health outcome in ankylosing spondylitis: reliability, validity and responsiveness. *Rheumatology*. 2002;41(11):1295-302.
- Goldberg D, Williams P. A user's guide to the General Health Questionnaire. NFER-NELSON, editor. UK; 1988.
- Lobo A, Muñoz P. Validated Spanish language versions. In: Goldberg D, Williams P, editors. GHQ (General Health Questionnaire). Guide for users of different versions. Masson, editor. Barcelona, Spain; 2010.
- Spanish National Statistics Institute Consumer Price Index for medicines from 2006 to 2015. Base 2011.
- Spanish National Statistics Institute Consumer Price Index 2006 to 2015. Base 2011.
- Aragon Resolution of 1 January 2011 by the Directorate-General of the Health Consortium, approving the rates applied within the consortium to third parties obliged to pay or to users without the right to healthcare 2011.
- Aragon Resolution of 30 July 2012 by the Directorate-General of the Aragón Health Service, on the revision of rates applied for the provision of healthcare services to third parties obliged to pay or to users without the right to healthcare 2012.
- Asturias. Decree 120/2013, of 27 December, updating the fixed amount public prices. BOPA no. 301, 31 December 2013. 2013.
- Balearic Islands. Resolution of the Directorate-General of the Health Service modifying Appendix I of the Ministry of Health and Consumer Affairs Order 22 December 2006. BOIB no. 89, 1 July 2014. 2014.
- Canary Islands. Resolution of 30 March 2015 by the Director, which modifies the public prices for healthcare services provided in Decree 81/2009, of 16 June, which establishes the public prices for healthcare services. 2015.
- Cantabria. Order SAN/12/2011, of 20 April, fixing the public prices for the Healthcare Services provided by the Cantabrian Health Service. BOC no. 85, 5 May 2011. 2011.
- Castile - La Mancha. Order 17/11/2014, of the Ministry of Health and Social Affairs, which establishes public prices for healthcare and services provided by the network of health centres dependent on the Healthcare Service. 2014.
- Castile - La Mancha. Resolution 06/08/2013, of the Directorate-General on the economic conditions applicable in 2013 for certain healthcare services through external means, within the scope of management of Sescam. 2013.
- Castile-Leon. Decree 83/2013, of 26 December, updating the public prices for the region of Castilla y León and the rate for administrative actions related to agricultural activities. BOCYL no. 249, 30 December 2013. 2013.
- Catalonia. Order SLT/30/2013, of 20 February, approving the public prices for the Catalan Health Service. DOGC no. 6323, 26 February 2013. 2013.
- Ceuta and Melilla. Resolution of 19 July 2013, of the National Institute of Healthcare Management, revising the healthcare prices applied by the health centres of the National Institute of Healthcare Management in Ceuta and Melilla. 2013.
- Valencian Region. Legislative Decree 1/2005, of 25 February, by the Council of the Autonomous Government, approving the revised text for the Government's Rates Act. Year 2014. DOCV no. 4971, 22 March 2005. 2014.
- Extremadura. Resolution of 17 February 2015, of the Minister, publishing the updated rates of taxes and public prices for the Autonomous region of Extremadura, pursuant to C. Law on General Budgets 2015.
- Galicia. Decree 56/2014, of 30 April, establishing the rates for healthcare services provided in dependent centres of the Galician Health Service and public health foundations. DOG no. 96, 21 May 2014. 2014.
- Galicia. Decree 392/2009, of 1 October, establishing the rates for healthcare services provided by the dependent centres of the Galician Health Service and public health foundations. DOG no. 199, 9 October 2009. 2009.
- La Rioja. Order 17/2014, of 16 November 2014, of the Ministry of Public Administration and Finance, establishing and regulating the public prices for healthcare services provided to individuals in the centres of the Rioja Health Service. 2014.

23. Region of Madrid. Order 731/2013, of 6 September, of the Minister of Health, laying down the public prices for the provision of healthcare services and activities by the network of centres of the Region of Madrid. BOCM no. 2013.
24. Murcia. Order of 3 February 2015 of the Ministry of Economy and Finance, publishing the rates of fees and public prices applicable in 2015. BORM no. 33, 10 February 2015. 2015.
25. Navarra. Resolution 882/2010, of 3 May, from the Directorate-General of the Navarro Health Service-Osasunbidea, updating the rates for providing services in the centres and welfare establishments of the Health Service-Osasunbidea 2010.
26. Basque country. Agreement of 23 February 2015, of the Council of Administration of the Osakidetza-Basque Health Service Public Entity, approving the rates for the provision of healthcare and educational services to third parties obligated to pay during 2015.
27. Andalucía. Order of 18 November 2015, which modifies the order of 14 October 2005, laying down the public prices for healthcare services provided by the centres of the Andalusian Public Health System. BOJA. 2015.
28. Ministry of Health, Social Services and Equality Institute of Healthcare Information. Hospital discharges register – CMBD. CIE9: 428. Diagnosis to the last digit. 2014.
29. General Council of Official Colleges of Pharmacists. Botplusweb.portalfarma.com. BOT Plus 2. Medicines Database
30. Hidalgo A., Cabello P.A., Peña L.M., Ivanova A., Sanz A., Aragón B. Estimation of the cost of intravenous administration of biological medicines in NHS day hospitals. XXXIII Jornadas de Economía de la Salud; 2013.
31. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Healthcare Programmes. Oxford University Press, 2015. 461 p.
32. Spanish National Statistics Institute Average number of weekly effective hours worked by the entire employed population (whether they worked during the week or not) by professional status, sex and occupation (main occupation). Active Population Survey 2015T3. 2015.
33. Spanish National Statistics Institute National results and by AR: Earnings per normal working hour by sex and occupation (2013). Annual survey of wage structure. Series 2008-2013. 2013.
34. AEMPS - Online Medications Information Centre (CIMA) - Main search engine.
35. WHO Collaborating Centre for Drug Statistics Methodology. Norwegian Institute of Public Health. ATC/DDD Index 2016.
36. Kobelt G, Sobocki P, Mulero J, Gratacos J, Pocovi A, Collantes-Estevez E. The Burden of Ankylosing Spondylitis in Spain. Value Health. 2008;11(3):408-15.
37. Spain. Royal Decree 1106/2014, of 26 December, establishing the national minimum wage for 2015. BOE no. 313, 27 December 2014.

## 4. LEGISLATION AND PLANNING WITH REFERENCE TO SPONDYLOARTHRITIS

### 4.1 Planning in rheumatology

SpA is scarcely addressed in Spanish health-related legislation and planning. National protocols and strategies barely refer to the major problems faced by patients with SpA such as: the absence of epidemiological information on the disease, delays in diagnosis, the availability and access to the most innovative drug treatments or the coverage of non-pharmacological treatments such as physical therapy or continued rehabilitation.

SpA is given scant attention in public planning at the national level. Specifically, the only document of relevance is the Strategy on Rheumatic and Musculoskeletal Diseases (RMSD) from the Ministry of Health, Social Services and Equality (2013) (1). However, the strategy does not present data on the prevalence, or labour costs of AS at the state level. In fact, the data provided come from a variety of scientific studies (2-4). The strategy on RMSD establishes 5 lines of action for training and others for improvement in healthcare, the management of healthcare information and research. These actions are aimed at reducing the deterioration in performance status and improving the quality of life of patients with RMSD. For SpA the strategy sets an objective of identifying sufferers of this family of diseases in Spain in order to reduce the progression to disability through early intervention. It recommends that this identification is carried out through the INE's Survey of Disability, Personal Autonomy and Dependency Situations.

At the autonomous regions (AR) level there are differences in the planning and specific strategies aimed at improving the management and treatment of rheumatic diseases. At the time of preparing the 2017 Atlas, the Master Plan on Rheumatic and Musculoskeletal Diseases (2010) from the Health Department of Catalonia (5) and the Strategic Rheumatology Plan (2012) (6) from the Region of Madrid were the only specific plans in rheumatology existing at the autonomous region level.

The objective of the Catalan Master Plan is the establishment of a care model for rheumatic diseases through actions aimed at their prevention, increasing the problem-solving capacity of primary healthcare and improving the efficiency of the diagnostic and therapeutic process.

With respect to SpA, the chapter in the Master Plan presenting an analysis of the situation states that, in the diagnosis of lower back pain, it is necessary to consider that 5% of cases are produced by potentially serious diseases such as SpA. Likewise, SpA is included within the fourth strategic line addressing the care of chronic arthritis. This strategic line describes the clinical and demographic characteristics associated with the diseases that make up chronic arthritis and recommends a reduction in the time to diagnosis in the Catalan health system from an average of 9-17 months to only three months.

The objectives of the Region of Madrid's Strategic Rheumatology Plan (2012) aim for the provision of quality healthcare through the empowerment of the patients, an improvement in the primary healthcare process and the development and use of the most efficient management technologies. These objectives are to be pursued through five strategic lines aimed at improvements in care, research and hospital management.

The plan's section on Internal Analysis provides the results of field work carried out in the Region of Madrid in 2011 by rheumatologists to understand the clinical, demographic and health characteristics of patients with rheumatic diseases. This study indicates that in the Region of Madrid 90% of AS patients received treatment with NSAIDs, 31.42% with conventional DMARDs and 31.42% with biologics (N: 70).

The Strategic Rheumatology Plan's section analysing the external environment also includes information on AS. This section indicates that the majority of rheumatology units have primary healthcare systems with differentiated access for patients with potentially more serious diseases such as spondyloarthritis. This section also describes the research projects on which rheumatologists in the region of Madrid have collaborated, these include the ESPIDEP Project on the early detection of spondyloarthritis.

The group of ARs with specific planning relating to rheumatology includes Andalusia, although this is at an early stage. At the time of writing, the regional government's Rheumatic and Musculoskeletal Diseases Care Plan (2016-2020) (7) was in the process of being approved. This plan aims to develop new mechanisms to enhance the quality, effectiveness and safety of healthcare for rheumatic diseases.

Another planning document addressing SpA is the Valencian Health Department Declaration of the Biological Medicines used in Rheumatology as Medicines with a High Healthcare and/or Economic Impact (MAISE) and Establishment of their Use (2014) (8). This resolution establishes a series of guidelines and clinical criteria for the use of biological drugs in rheumatology by the Valencian Health Department. The objectives established by the resolution are to standardise the decision making criteria for the use of biologics in the treatment of rheumatic diseases and the optimisation of healthcare activities.

Appendix I of the resolution sets out specific recommendations for the use of biologics in patients with SpA. This section contains more information about the characteristics of the disease such as: family aggregation, similar pathogenic mechanisms, the association with HLA-B27 and the association with infections, commonly those of the gastrointestinal tract. It also establishes the clinical criteria enabling both early identification and the definition of pain through 5 criteria and the establishment of a medical history which includes the family history, the personal one and the results of the first assessment. It also recommends that a basic radiographic analysis is carried out as well as the use of specific clinical instruments such as the BASDAI and BASFI.

Lastly, the Strategy for the Care of Patients with Chronic Diseases from the Region of Madrid Ministry of Health (2013) (9) indicates the need to start hospital units focused on chronic diseases, which would include a unit aimed at patients with SpA.

## 4.2 Planning in rare diseases

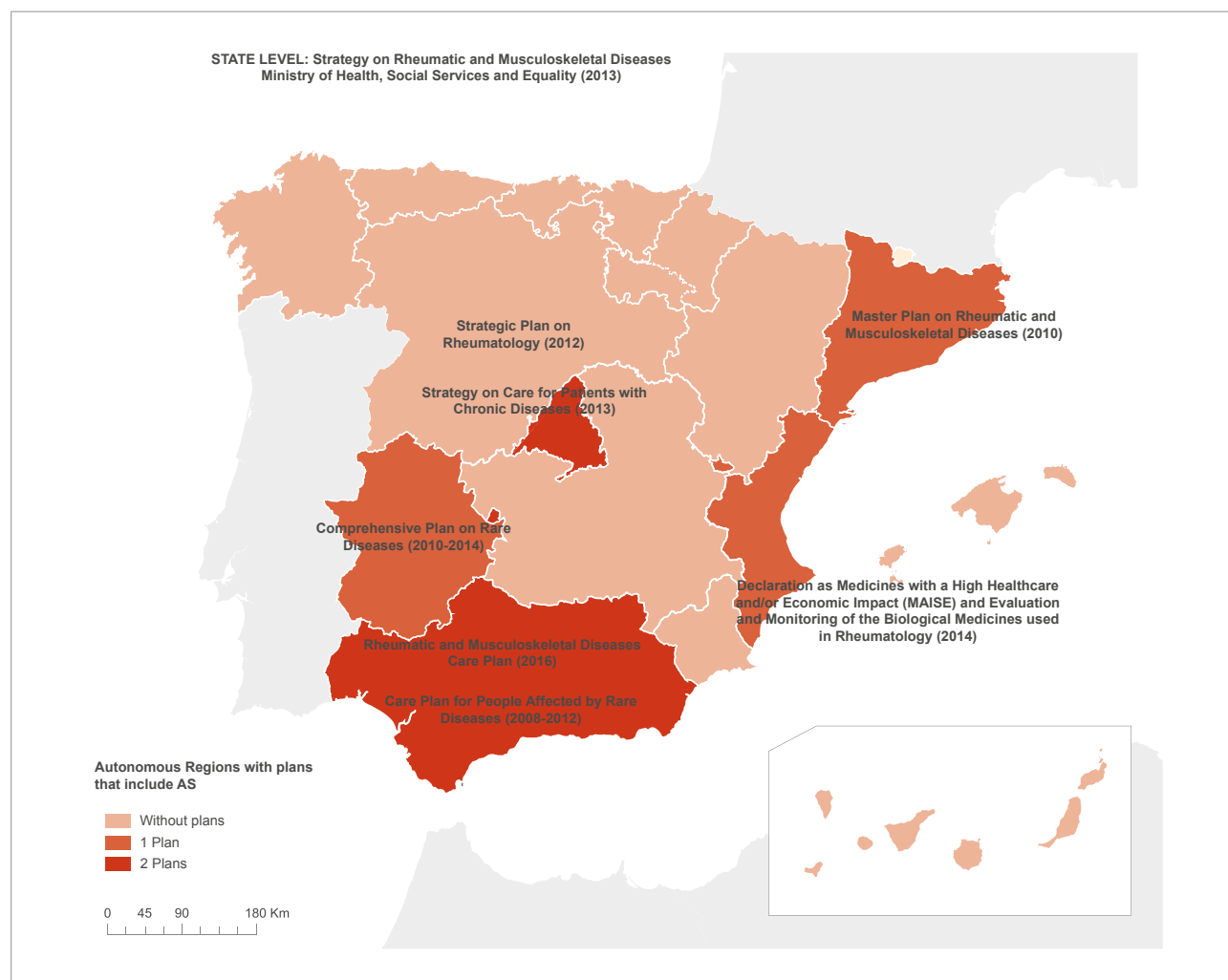
Another group of plans at the autonomous region level that address SpA are the rare diseases planning instruments. The European Union defines rare diseases as those that have a prevalence of less than 5 cases per 10,000 inhabitants, equivalent to 6-8% of the European population. This translates into an estimated 29 million affected in the EU-27 and 3 million in Spain.

Specifically, the two autonomous regions that are the most advanced in regional planning for rare diseases are Andalusia and Extremadura. In 2007, the Andalusian Ministry of Health produced its Care Plan for People Affected by Rare Diseases 2008-2012 (10). In 2010 the Extremadura Ministry of Health produced its Comprehensive Plan on Rare Diseases in Extremadura 2010-2014 (11). Both plans include AS, but within the high-intensity group.

The Andalusian Rare Diseases Plan shows an annual average by gender for each of the diseases categorised as rare (1999-2004). Specifically, in the case of AS the Andalusian plan shows an average annual number of cases of 196.7 men and 45.8 women. For its part, the Extremaduran rare diseases plan estimated the prevalence of this disease in this region as 16.87/100,000 inhabitants (2010), placing AS as the second most prevalent rare disease of all those considered in this plan.

Finally, it should be noted that the inclusion of SpA within the planning for rare diseases involves sharing a common strategy for action, protocols and initiatives within a large set of very different diseases, which leads to the disappearance of specificity. Map 1 illustrates the existence or absence of planning related to SpA by AR in Spain.

**Map 1.** Planning that includes SpA in different regions



Source: Own elaboration

### 4.3 Guidelines for health professionals and training programmes that cover SpA

In relation to the training of the specialists responsible for the diagnosis and monitoring of the disease, the main legal provision is currently the Training Programme for Rheumatology (2009) from the Ministry of Health and Social Policy (Order SAS/2855/2009) (12). This programme is aimed at new rheumatologists and it breaks down the knowledge they need to acquire. Specifically, the training for diagnosis and management of Ax-SpA is located in Chapter VI, which refers to inflammatory spondylarthropathies and Chapter VII refers to childhood rheumatic diseases.

Another group of documents for the training of healthcare workers specialising in the treatment, monitoring and management of Ax-SpA are the guides for healthcare professionals. The most important guides within this group are Espoguía 2009 (13) and Espoguía 2015 (14) produced by the GRESSER group within the Spanish Rheumatology Society (SER). Espoguía 2009 called the Guide to Clinical Practice in the Management of Patients with Spondyloarthritis aims to reduce the variability in the management of SpA and improve the quality of care. It offers advanced practical recommendations for the integrated monitoring of SpA by the doctors and healthcare specialists involved in this clinical phase.

Espoguía 2015 called the Guide to Clinical Practice in the Treatment of Axial Spondyloarthritis and Psoriatic Arthritis (PsA) is aimed at the healthcare professionals involved in the management and treatment of Ax-SpA and psoriatic arthritis. This document establishes recommendations based on the available scientific evidence to help in the management of adult patients and in order to improve the healthcare and quality of life of people with Ax-SpA and PsA.

At the time of writing, Espoguía 2015 offered the most specific guidance in relation to the training of healthcare professionals in the diagnosis and management of Ax-SpA. Therefore, this document's specific objectives are listed here:

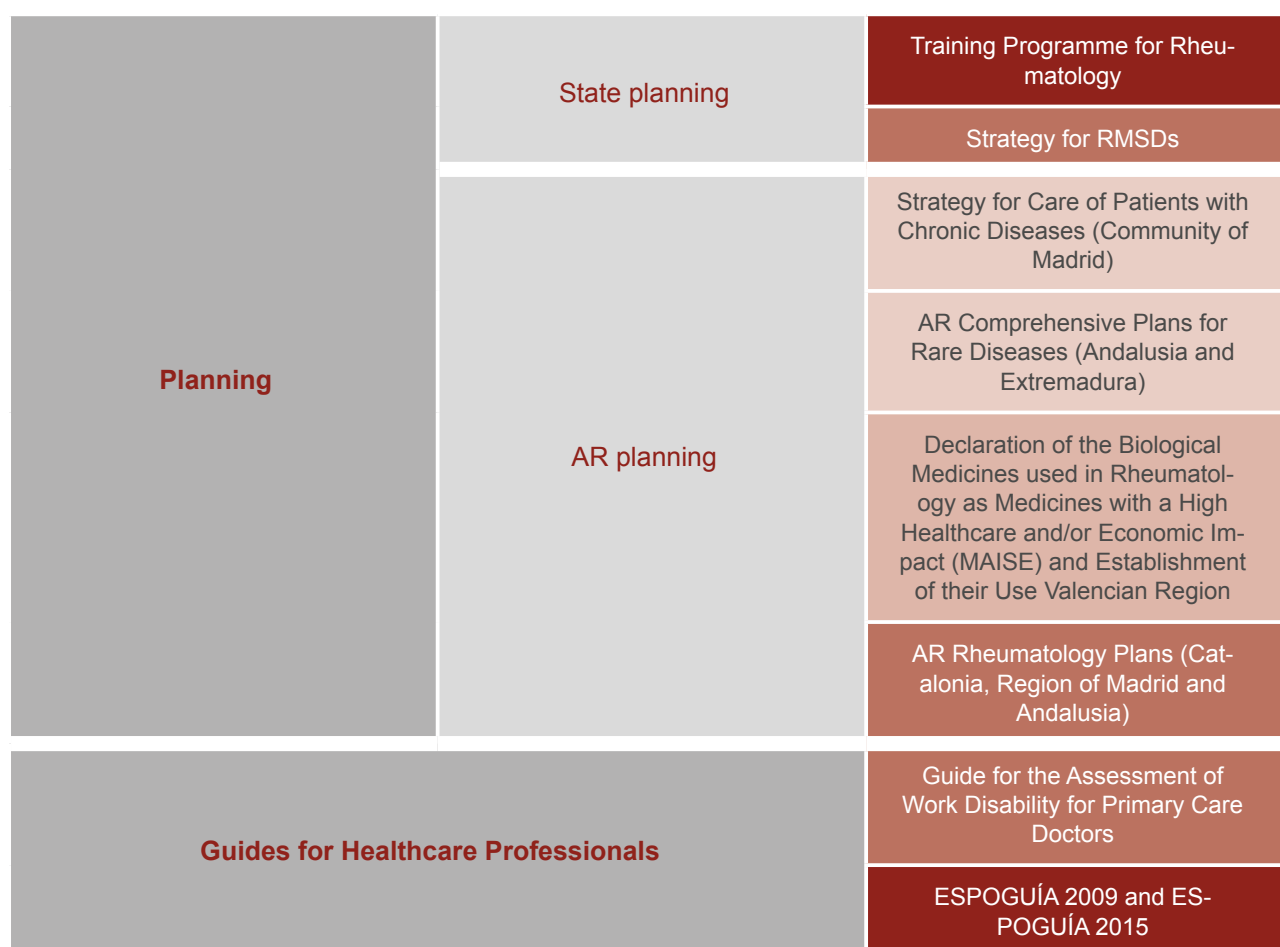
- To improve the health skills of the professionals involved in the care of people with Ax-SpA or PsA.
- To evaluate the pharmacological and non-pharmacological therapeutic proposals for Ax-SpA or PsA.
- To reduce the variability in clinical practice in the therapeutic management of Ax-SpA or PsA.
- To increase the knowledge of the professional participants in the care process through scientific research and evidence.
- To standardise the healthcare of patients with Ax-SpA and PsA.
- To foster collaboration between the professionals from different specialities involved in the management of patients.
- To improve training in the recognition of the characteristics of Ax-SpA and PsA among those affected and their families.

Another guide for healthcare professionals which gathers information on Ax-SpA is the Guide for the Assessment of Work Disability for Primary Care Doctors (2nd Edition, 2015) from the National School of Occupational Medicine and the National Institute of Social Security (INSS) (15). This document, although aimed at the assessment of disability by primary care doctors, contains a list of factors, recommendations and concomitant diseases relating to SpA.

This assessment guide for primary care doctors provides information on common criteria for a set of diseases, complementary tests, clinical conditions and methods for identification, treatment, contingency assessment, etc. It is specifically for the early diagnosis of SpA and it contains information on the symptoms associated with SpA organised into chapters describing sets of diseases such as the infectious diseases, those relating to the respiratory or digestive systems and osteoarticular diseases, among others.

Below there is a diagram providing information about SpA, ranking its importance with a colour ramp where the darker reddish tones show the existence of a greater number of references relating to SpA.

**Figure 1.** Planning and guides for healthcare professionals with reference to SpA



Source: Own elaboration

- Planning for rheumatic diseases and specifically SpA is poor in the autonomous regions, only three have adopted or drafted specific rheumatology plans.



## References

1. Ministry of Health, Social Services and Equality. Strategy on rheumatic and musculoskeletal diseases for the National Health System [Internet]. Madrid, 2013 Available on: <http://www.sespas.es/adminweb/uploads/docs/Estrategia ERYMEs.pdf>
2. Dawson J, Linsell L, Zondervan K, Rose P, Randall T, Carr A, et al. Epidemiology of hip and knee pain and its impact on overall health status in older adults. *Rheumatology*. 6 January 2004;43(4):497-504.
3. Kobelt G, Sobocki P, Mulero J, Gratacos J, Pocovi A, Collantes-Estevez E. The burden of ankylosing spondylitis in Spain. *Value Heal*. 2008;11(3):408-15.
4. Boonen A, Brinkhuizen T, Landewé R, van der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. *Ann Rheum Dis*. 2009;69(6):1123-8.
5. Catalanian Regional Government. Department of Health. Master Plan on Rheumatic and Musculoskeletal Diseases [Internet]. Department. Barcelona; 2010. 97 p. Available on: [http://salutweb.gencat.cat/web/.content/home/ambits\\_tematicos/linies\\_dactuacio/salut\\_i\\_qualitat/plans\\_directors\\_2008-2010/malalties\\_reumatiques\\_i\\_de\\_laparell\\_locomotor/que\\_es/enllasos/locomotor131010.pdf%0A](http://salutweb.gencat.cat/web/.content/home/ambits_tematicos/linies_dactuacio/salut_i_qualitat/plans_directors_2008-2010/malalties_reumatiques_i_de_laparell_locomotor/que_es/enllasos/locomotor131010.pdf%0A)
6. Department of Health. Strategic Plan on Rheumatology. Madrid, 2012
7. Andalusia Regional Government. Resolution of 14 December 2015, of the General Secretariat of Public Health and Consumer Affairs, appointing the Director of the Andalusia Musculoskeletal and Rheumatological Diseases Plan. BOJA unnumbered 245 of 2 [Internet]. Available on: <http://www.juntadeandalucia.es/boja/2015/245/2>
8. Department of Health. Valencian Region. Valencian Health Department Declaration of the Biological Medicines used in Rheumatology as Medicines with a High Healthcare and/or Economic Impact (MAISE) and Establishment of their Use [Internet]. Valencia; 2014. Available on: <http://www.san.gva.es/documents/152919/3080994/RESOLUCION++SAS+-DECLARACION+MAISE+BIOLOGICOS+REUMATOLOGIA+VERSION+3+-04042014.pdf>
9. Ministry of Health of the Region of Madrid. Strategy for the Care of Patients with Chronic Diseases [Internet]. Madrid, 2013 Available on: <http://www.madrid.org/bvirtual/BVCM017570.pdf>
10. González-Meneses López A, Benavides Vilchez J, Fernández de la Mota E, Fernández López R, García García A, García Roldán P, et al. Care Plan for People Affected by Rare Diseases 2008-2012 [Internet]. Andalusia Regional Government. Seville; 2008. 124 p. Available on: <http://www.juntadeandalucia.es/export/drupaljda/PlanAndaluzEnfermedadesRaras2008-2012.pdf>
11. Aranguez Ruiz A, Cordero Torres R, Cordón Arroyo AM, Cortés Mancha M, De la Osa Sánchez AB, Deira Lorenzo JL, et al. Comprehensive Plan for Rare Diseases in Extremadura 2010-2014 [Internet]. Ministry of Health. Mérida; 2010. 168 p. Available on: <http://www.saludextremadura.com/documents/19231/41137/enfermedadesraras2010.pdf>
12. Ministry of Health and Social Policy. Order SAS/2855/2009, of 9 October, approving and publishing the Training Programme for Rheumatology. [Internet]. 2010. Available on: <http://www.boe.es/boe/dias/2009/10/26/pdfs/BOE-A-2009-16994.pdf>
13. Spanish Society of Neurology ESPOGUIA working group. Clinical practice guidelines on the management of patients with spondyloarthritis. ESPOGUIA [Internet]. Madrid, 2009 Available on: [http://www.ser.es/wp-content/uploads/2016/03/Espoguía-completa\\_1\\_def-1.pdf](http://www.ser.es/wp-content/uploads/2016/03/Espoguía-completa_1_def-1.pdf)
14. Spanish Society of Neurology ESPOGUIA working group. Clinical practice guidelines for the treatment of axial spondyloarthritis and psoriatic arthritis [Internet]. Madrid, 2015 Available on: [http://www.ser.es/wp-content/uploads/2016/04/GPC\\_-Tratamiento\\_EspAax\\_APs\\_DEF.pdf](http://www.ser.es/wp-content/uploads/2016/04/GPC_-Tratamiento_EspAax_APs_DEF.pdf)
15. Terradillos García MJ, Aguado Benedí MJ, García Puerto M, Sainz González J, Cabello Heranz MJ. Guide for the evaluation of temporary incapacity for work for primary care doctors (2nd edition) [Internet]. Madrid, 2015 Available on: <http://gesdoc.isciii.es/gesdoccontroller?action=download&id=15/01/2016-440fa7054c>

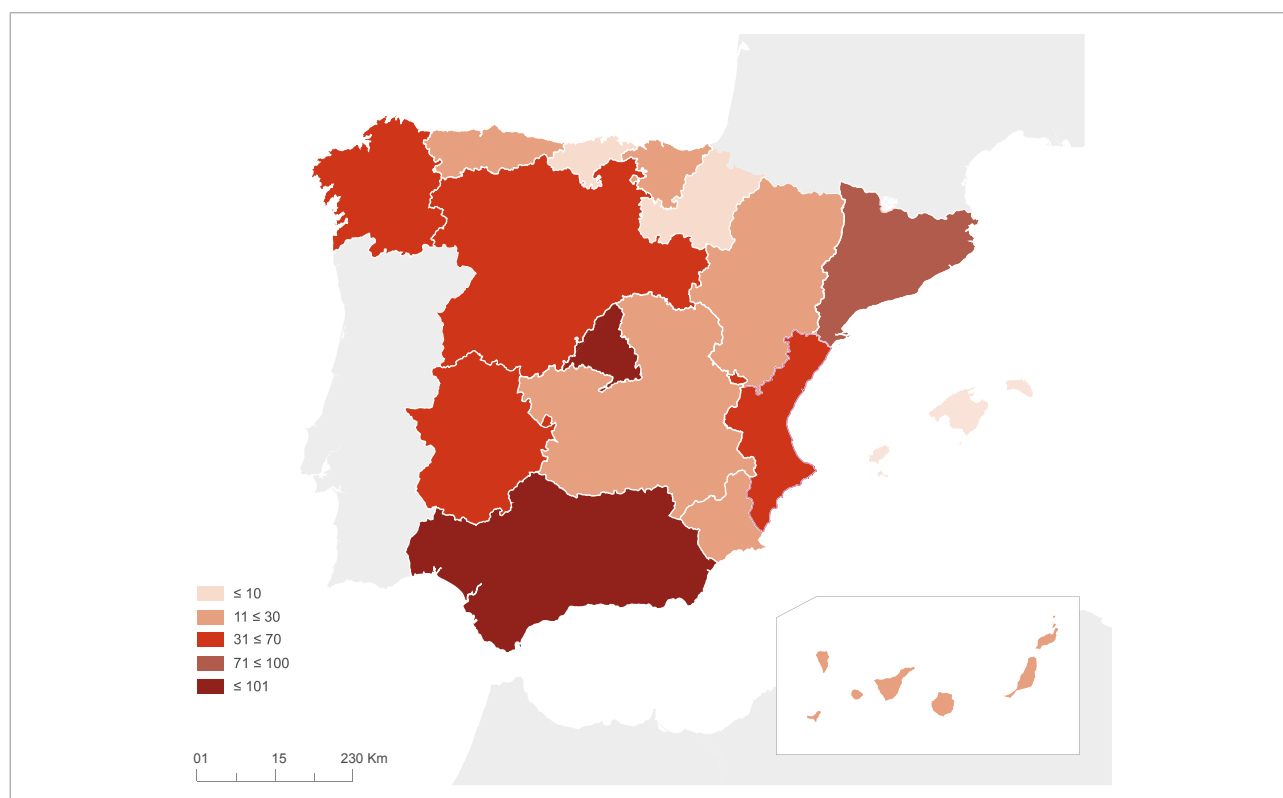


## 5. SAMPLE PROFILE

In the 2017 Atlas survey, 85% of patients suffered from ankylosing spondylitis, 6.8% from peripheral spondyloarthritis, 5.1% from non-radiographic axial spondyloarthritis and 3.1% suffered from axial spondyloarthritis. Axial spondyloarthritis mostly affects the spine and sacroiliac joints, while peripheral spondyloarthritis predominantly affects the peripheral joints. Axial spondyloarthritis includes ankylosing spondylitis and non-radiographic axial spondyloarthritis. Non-radiographic axial spondyloarthritis presents signs and symptoms similar to those of ankylosing spondylitis, which include chronic pain and functional loss, but without radiographic signs indicating damage to the bone structure (1).

The ARs with the highest number of responses in the survey of patients with Ax-SpA were Andalusia, the Region of Madrid, Catalonia, Extremadura, Valencia, Galicia and Castilla y León which is related to the greater demographic weight of these territories.

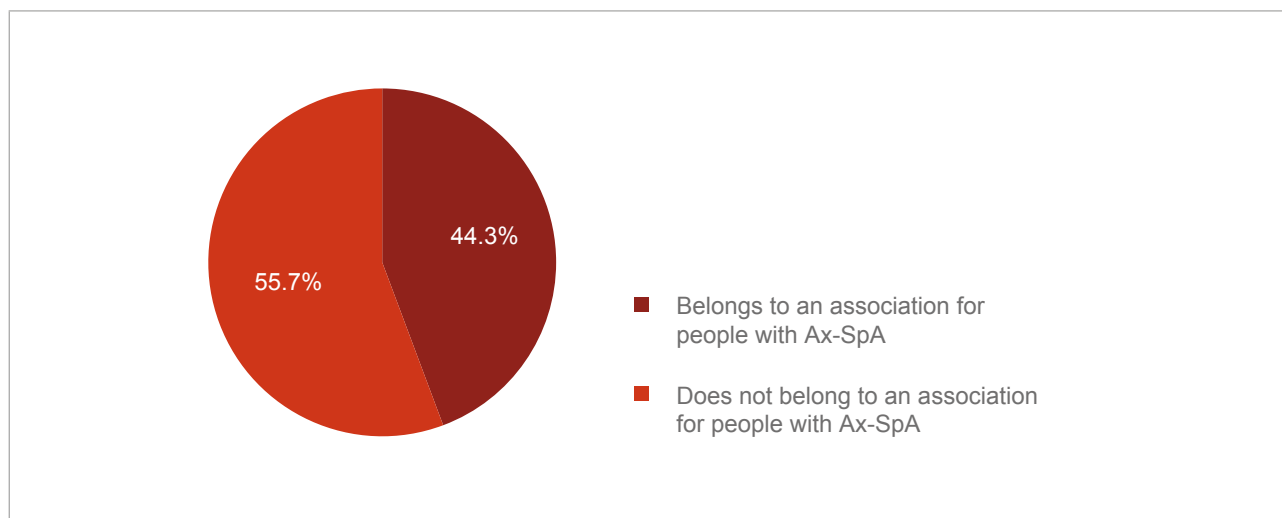
**Map 1.** Distribution of people taking part in the survey with Ax-SpA in different ARs (N: 680)



Source: 2017 Atlas patient survey

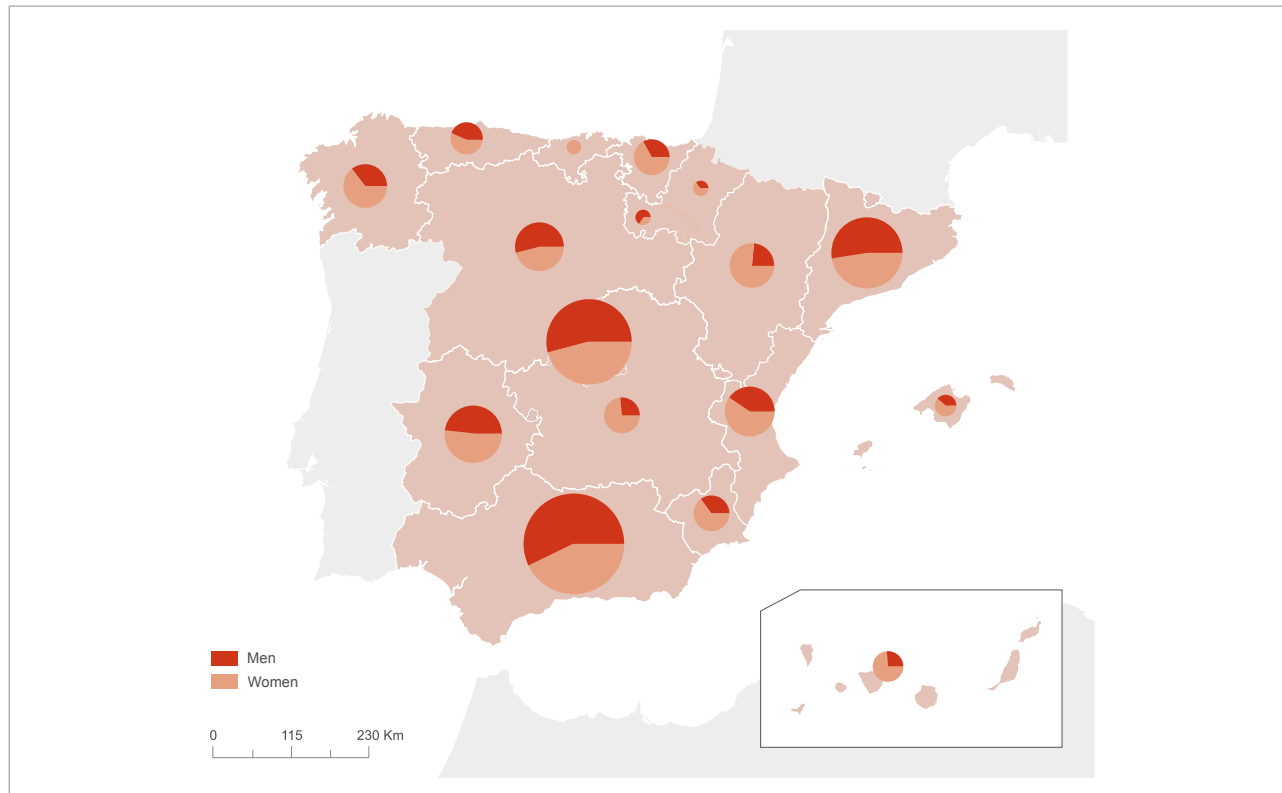
Of the patients who participated in this study, 44.3% belonged to associations for patients with SpA, which could be related to the fact that this survey was promoted by CEADE and other patient associations in Spain.

Membership of an association by a patient has a number of advantages that can better help them cope with the disease. Different studies (2-4) have identified the following advantages: access to more information about the disease through courses or exchanges of experiences with other members of the association, access to health professionals such as physiotherapists, sports activities and social events, as well as advice on medical and legal issues.

**Figure 1.** Membership of associations among patients with Ax-SpA (N: 680)

Source: 2017 Atlas patient survey

Among those surveyed, women with Ax-SpA accounted for slightly more than half of the people who participated (52.5%), although in the most populated ARs (Andalusia, Catalonia and the Region of Madrid) the percentage of men was higher than women (see Map 2).

**Map 2.** Distribution of individuals surveyed with Ax-SpA by sex in different regions (N: 680)

Source: 2017 Atlas patient survey

The patients surveyed were between 18 and 78 years old and had a mean age of 45.7 years. This mean age is similar to that of other studies for patients with SpA (5,6).

**Table 1.** Age of participants in the survey.

	N	Range	Minimum	Maximum	Mean	Standard deviation	Variance
Age	680	60.0	18.0	78.0	45.66	10.83	117.40

Source: 2017 Atlas patient survey

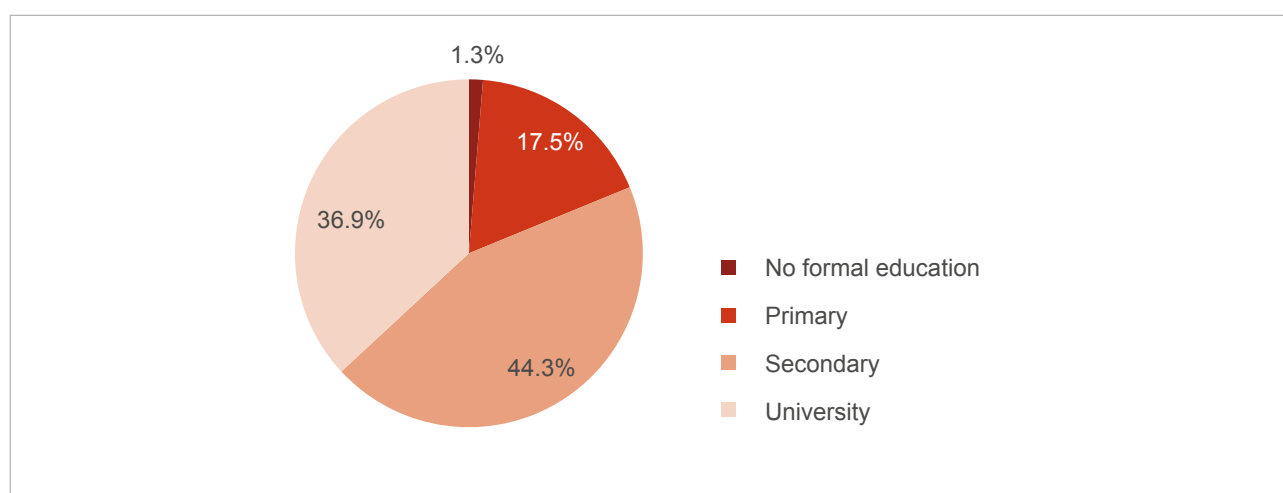
Table 2 shows that only 4.4% of the patients surveyed are of retirement age, only 8% are under 31 years of age and 87.5% are between 32 and 64 years of age.

**Table 2.** Distribution of Ax-SpA patients by age group.

Age	Frequency	Percentage
16 to 31	55	8.1
32 to 47	350	51.5
48 to 64	245	36.0
≥65	30	4.4
Total	680	100

Source: 2017 Atlas patient survey

In relation to the educational level of the respondents, 36.9% had been to university, 44.3% had secondary school level education, 17.5% primary and 1.3% had not attended formal education. These data differ from studies such as that by Casals- Sánchez et al. (7) for patients with SpA, which showed the following distribution: 26.9% with higher education, 28.2% with secondary education, 40.2% with primary education and 4.7% with no formal education (N: 316).

**Figure 2.** Distribution of Ax-SpA patients by educational level (N: 680)

Source: 2017 Atlas patient survey

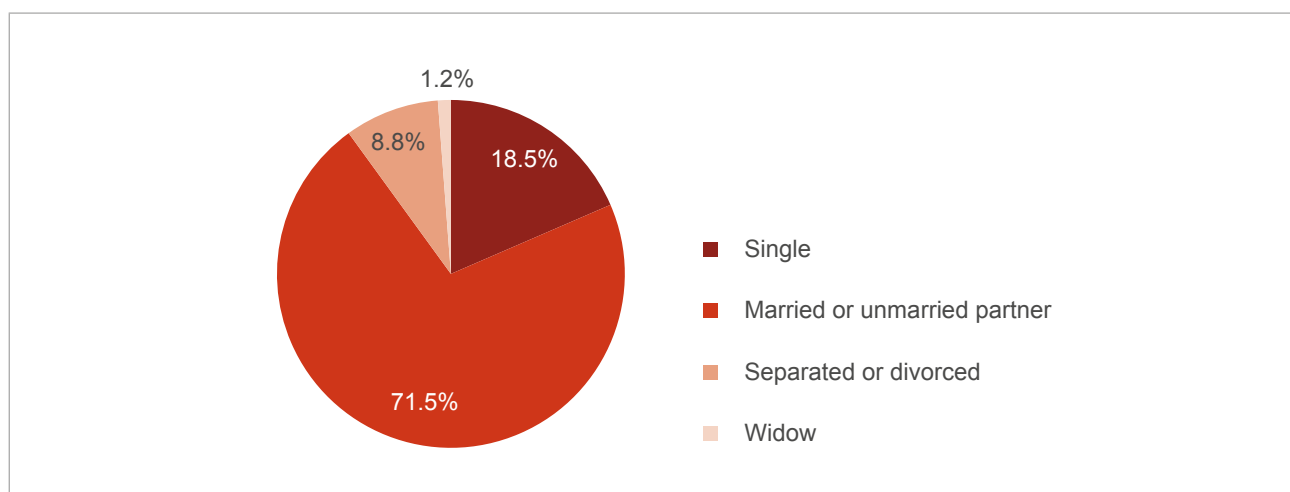
In relation to income level, 60.7% of respondents reported monthly income of between €1,000 and €3,000, while 25.8% of patients received less than €1,000 a month. Table 3 below shows the income intervals and the percentage of respondents for each interval.

**Table 3.** Percentage distribution of Ax-SpA patients by income level (N: 422)

Net monthly income	Percentage
No income	2.4%
≤ €500	6.4%
€501 to ≤ €1,000	17.1%
€1,001 to ≤ €2,000	39.8%
€2,001 to ≤ €3,000	20.9%
> €3,000	13.5%

Source: 2017 Atlas patient survey

In relation to marital status, 71.5% of the patients stated they were married or with a common-law partner, 18.5% single, 8.8% separated or divorced, and 1.2% were widowed. On the other hand, 82.5% of the patients reported having a partner, with the average number of children per person being 1.4. This distribution by civil status is similar to that found in the study by Casals-Sánchez et al. (7) for a population with Ax-SpA, with 79.6% married, 17.2% single, 2.2% separated and 1% widowed (N: 413).

**Figure 3.** Percentage distribution of patients with Ax-SpA according to marital status (N: 680)

Source: 2017 Atlas patient survey

- The majority of the patients surveyed had ankylosing spondylitis, i.e. a form of the disease with irreversible structural damage.
- A total of 44.3% of the respondents belonged to a patient association, 36.9% had university level education and 71.5% were married or with a common-law partner.

## References

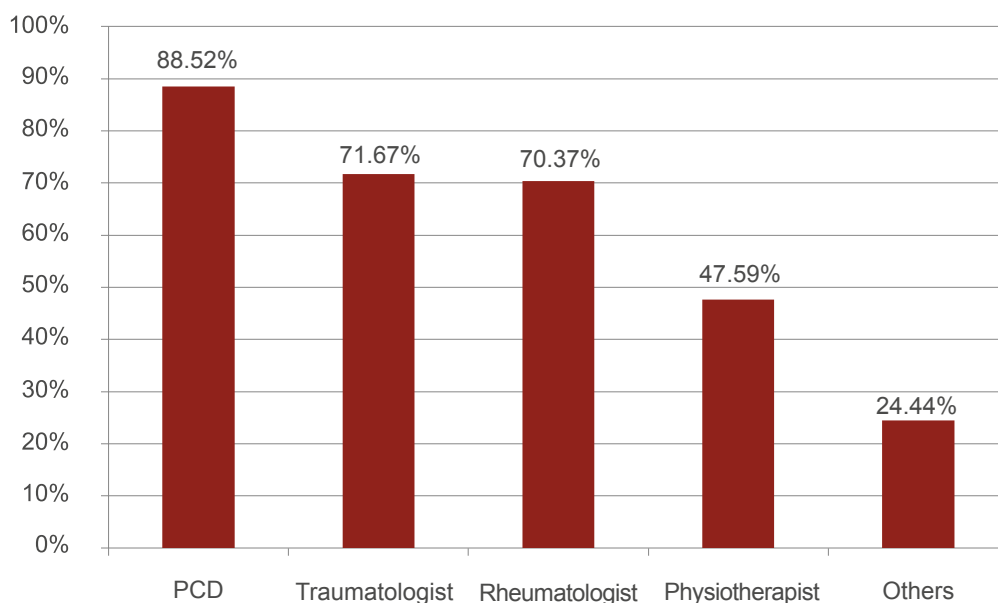
1. Kiltz U, Baraliakos X, Karakostas P, Igelmann M, Kalthoff L, Klink C, et al. Do patients with non-radiographic axial spondyloarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res.* 2012;64(9):1415-22.
2. Feldtkeller E, Lind-Albrecht G, Rudwaleit M. Core set of recommendations for patients with ankylosing spondylitis concerning behaviour and environmental adaptations. *Rheumatol Int.* 2013;33(9):2343-9.
3. Barlow JH, Macey SJ, Struthers G. Psychosocial factors and self-help in ankylosing spondylitis patients. *Clin Rheumatol.* 1992;11(2):220-5.
4. Song IH, Brenneis C, Hammel L, Feldtkeller E, Listing J, Sieper J, et al. Ankylosing spondylitis self-help organisations - do members differ from non-members? *Joint Bone Spine.* 2015;
5. Ariza R. Regisponser. *Reumatol Clínica.* July 2005;1:S7-11.
6. Miranda García MD, Font Ugalde P, Muñoz Gomariz E, Collantes Estévez E, Zarco Montejo P, González Fernández C, et al. National Register of Patients with Spondyloarthritis (REGISPONSER). Descriptive analysis of 2,367 Spanish patients included. *Reumatol Clin Supl.* 2008;4(Suppl. 4):48-55
7. Casals-Sánchez JL, García De Yébenes Prous MJ, Descalzo Gallego M ángel, Barrio Olmos JM, Carmo-na Ortells L, Hernández García C. Characteristics of the patients with spondyloarthritis monitored in rheumatology units in Spain. EmAR II study. *Reumatol Clin.* 2012;8(3):107-13.

## 6. DIAGNOSIS

### 6.1 Personnel involved

The results of the patient survey provided information on the healthcare specialists who are involved in the diagnostic process. Figure 1 shows the percentage of medical specialists that patients visited before being diagnosed with Ax-SpA. The specialist that the greatest number of patients consulted was a primary care doctor, followed by a traumatologist and rheumatologist. It should be taken into account that a patient could have visited more than one medical specialist before being diagnosed.

**Figure 1.** Medical specialist consulted by patients with Ax-SpA before being diagnosed (N: 540)



Source: 2017 Atlas patient survey

In terms of the average number of visits to medical specialists before being diagnosed, patients reported having made more visits to primary care doctors, physiotherapists and traumatologists than visits to rheumatologists.

**Table 1.** Visits to each medical specialist by patients before being diagnosed

Specialist	Total visits	Mean	Standard deviation	Median	Max	Min
Primary care doctor	1,249	2.6	2.17	2	15	1
Traumatologist	1,174	3.0	2.83	2	29	1
Physiotherapist	862	3.4	3.02	3	20	1
Rheumatologist	743	2.0	1.72	1	20	1
Others	485	3.7	3.02	3	15	1

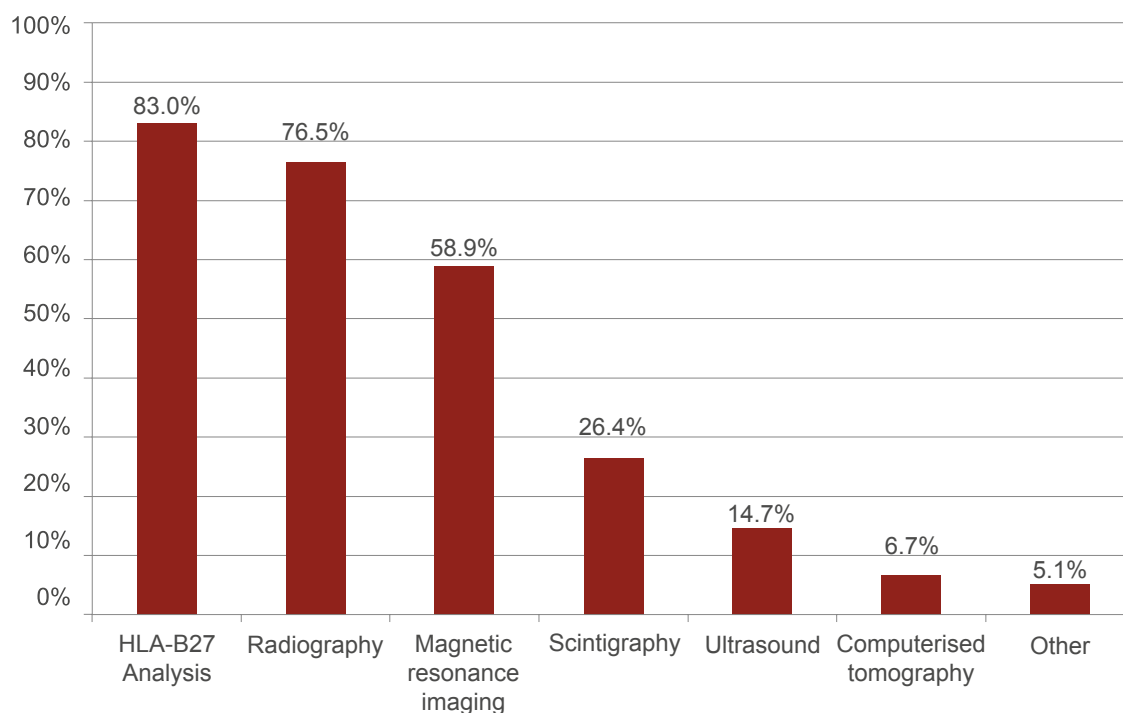
Source: 2017 Atlas patient survey

This high number of visits made by patients to different medical specialists before being diagnosed could be one of the keys that would explain the diagnostic delay. It also represents an increase in healthcare costs. In an ideal scenario, a patient would visit their primary care doctor who, after making the appropriate examinations and investigations of the symptoms, would refer them to the rheumatology unit. However, the complexity of the diagnosis and the strong association of symptoms with other diseases give rise to erroneous referrals to other specialists such as traumatologists, physiotherapists or other specialities. Improvement in communication and collaboration with other specialists such as the primary care doctor, traumatologist, physiotherapist, ophthalmologist or gastroenterologist would also help reduce the current diagnostic times.

## 6.2 Diagnostic tests

The results of the survey show that, according to patients, the most commonly used diagnostic test was the HLA-B27 genetic test, followed by X-ray and MRI. Of the patients who underwent HLA-B27, 77.1% were positive and 22.9% negative (N = 507). These values are similar to those derived from other studies in patients with Ax-SpA (1-3)

**Figure 2.** Most commonly used diagnostic tests



Source: 2017 Atlas patient survey

## 6.3 Diagnostic delay

The delay in diagnosing Ax-SpA is one of the main problems yet to be resolved (4-6). According to Rojas-Vargas et al. (7) the mean delay in the diagnosis of Ax-SpA was 6.5 years. According to data from the National Spondyloarthritis Register (REGISPONSER), of the 2,367 patients interviewed classified as suffering from

SpA, only 25.3% were diagnosed before the first year and 20.6% exceeded 10 years. Patients with Ax-SpA had an even greater delay in diagnosis (8).

The results of the 2017 Atlas survey confirm this diagnostic delay, as, on average, patients reported having suffered the first symptoms (pain, inflammation, stiffness) associated with the disease at 24.4 years of age, while the mean age at which they were diagnosed was 32.9 years. This means that the average diagnostic delay from the appearance of the first symptoms until the diagnosis of the disease was 8.5 years.

**Table 2.** Mean age at first symptoms, at diagnosis and diagnostic delay

	Mean	Standard deviation	Median	Max	Min
<b>Age at first associated symptoms (N: 555)</b>	24.4	8.8	24	53	3
<b>Age at diagnosis (N: 556)</b>	32.9	9.6	32	67	11
<b>Diagnostic delay in years (N: 550)</b>	8.53	7.66	6	48	0

Source: 2017 Atlas patient survey

Only 25% of the respondents had been diagnosed in less than 2 years, while 50% took more than 6 years and 25% more than 12 years. Therefore, it can be stated that for 75% of the patients the diagnostic delay was greater than 6 years.

**Table 3.** Diagnostic delay in years by percentiles (N: 552)

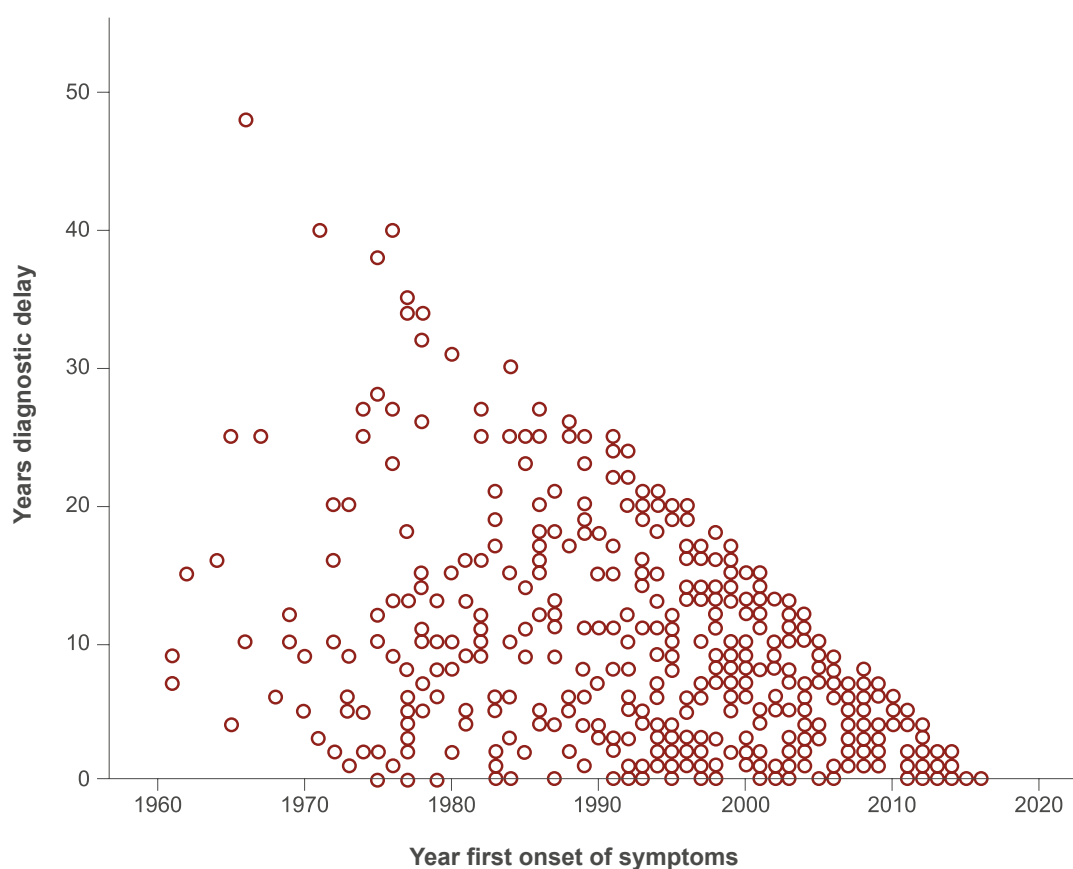
Percentiles	Years
25	2
50	6
75	12

Source: 2017 Atlas patient survey

It is essential to determine whether the new diagnostic criteria and better training of primary care doctors in the diagnosis of Ax-SpA has resulted in a reduction in the diagnostic delay for the disease. For this reason, a possible correlation was evaluated between the pairs of values for the year of onset of the first symptoms and the years of diagnostic delay for the 550 patients who answered both questions in the questionnaire (year of appearance of the first symptoms and years of diagnostic delay). The scatter plot in Figure 3 shows a clear trend towards lower diagnostic delay in the most recently diagnosed individuals, which is supported by the linear correlation analysis.



**Figure 3.** Scatter diagram for value pairs for year of appearance of the first symptoms and years of diagnostic delay (N: 550)



Source: 2017 Atlas patient survey

The linear correlation test shows that the more current the year of onset of the first symptoms of the disease, the lower the diagnostic delay (significance of 0.00 and correlation of -0.429). In other words, in the last few years Ax-SpA is being diagnosed earlier, with a significant decrease in the diagnostic delay.

It is interesting to analyse whether the average diagnostic delay varies according to a patient's educational level. Table 4 shows a large difference between patients who received no formal education and those who received a formal education, although there are no significant differences between the different educational levels considered (primary, secondary and university).

**Table 4.** Mean diagnostic delay of Ax-SpA in relation to patient educational level

Educational Level	Diagnostic delay in years
No formal education	24.8
Primary	8.7
Secondary	8.2
University	8.3

Source: 2017 Atlas patient survey

The difference in the diagnostic delay between those with formal education and those without could be important, although the small number of patients without formal education included in the sample (9 people, equivalent to 1.3%) makes it impossible to draw conclusions.

## 6.4 Importance of other medical specialities

As the survey results show, on many occasions, primary care doctors often erroneously refer patients with back pain arising from an inflammatory disease to traumatology units when they really should be referred to rheumatology. Therefore, it is necessary to emphasise that to reduce diagnostic times a correct referral is necessary and for this the role of the primary care doctor is fundamental.

The study “Recognising and Diagnosing Ankylosing Spondylitis Reliably (RADAR)” showed how the application of a simple rheumatology referral strategy, based on the identification of inflammatory lower back pain, can accelerate the diagnosis of Ax-SpA and the prescription of a suitable treatment (9).

This diagnostic delay causes a loss in the quality of care and family doctors need training in the early detection of Ax-SpA, simple detection criteria and easy access to specialist rheumatology units for suspected cases. For this reason, the GRESSER group, with the support of the SER Research Unit, developed an initial Joint Spondyloarthropathies Management and Research Programme, which was called the ESPeranza Programme (2009-2015) (10).

Among the main objectives of the ESPeranza Programme were the reduction in variability in clinical practice, reduction in diagnostic time, improvements in the training of primary care doctors and specialists and stimulation of research. The ESPeranza programme applies the following referral criteria for primary healthcare:

- Age < 45 years
- Evolution >3 months and < 24 months for any of:
  - Inflammatory lower back pain, defined as lower back pain and at least 2 of the following:
    - Insidious onset
    - Morning spinal stiffness >30 minutes
    - Improvement with activity and not with rest
    - Asymmetric arthritis, preferably in lower limbs, or
  - Rachialgia or arthralgia and any of the following concomitant diseases:
    - Psoriasis
    - Inflammatory bowel disease
    - Anterior uveitis
    - Family history of any of the above
    - Radiographic sacroiliitis
    - HLA B27 +

During the 6 years in which the programme was in force, more than 1,800 primary care doctors were trained in the diagnosis of AS, 25 care units were created for patients with SpA and 1,179 patients suspected of suffering from the disease were referred to rheumatology. However, it is not known whether the primary care doctor at the outpatient centres that participated in the ESPeranza programme have continued to use the same techniques for correct referral.

In order to evaluate its possible efficacy, the following table shows how people who began to suffer the first symptoms before 2009, the year the ESPeranza programme was implemented, suffered a mean diagnostic delay of 9.5 years, whereas for those whose first symptoms began after 2009 the average diagnostic delay was 2.5 years.

**Table 5.** Mean diagnostic delay for Ax-SpA patients in relation to the year of onset of the first symptoms ( $\leq 2008$  and  $\geq 2009$ )

Year first symptoms appeared	Mean	N	Standard deviation
$\leq 2008$	9.48	475	7.79
$\geq 2009$	2.52	75	2.07
Total	8.53	550	7.66

Source: 2017 Atlas patient survey

The Mann-Whitney mean difference test was performed in order to confirm that these differences between the means obtained for those with first symptoms  $\leq 2008$  and those where the first symptoms started  $\geq 2009$  were significant ( $p < 0.001$ ). The results show that there is a significant difference in means for the populations of patients with symptoms before and after the ESPeranza programme ( $\leq 2008$  and  $\geq 2009$ ).

This seems to prove the effectiveness of the new diagnostic criteria and improvements in the training of primary care doctors in reducing the diagnostic delay of the disease.

- Before being diagnosed, patients with Ax-SpA made more visits to physical therapists and orthopaedic surgeons than to rheumatologists, which may indicate incorrect referrals.
- Patients reported having suffered the first symptoms associated with the disease at age 24 on average, with diagnosis at age 33 on average.
- The diagnostic delay in the patients surveyed was almost 9 years on average, with it exceeding 6 years in 75% of patients.
- Ax-SpA is being diagnosed earlier nowadays with a significant reduction in diagnostic delay. Therefore, while before 2009 the mean diagnostic delay was 9.5 years, after 2009 it has decreased to 2.5 years.

## References

1. Lee T-J, Park B-H, Kim JW, Shin K, Lee EB, Song Y-W. Cost-of-illness and quality of life in patients with ankylosing spondylitis at a tertiary hospital in Korea. *J Korean Med Sci.* 2014;29(2):190-7.
2. Younes M, Jalled A, Aydi Z, Zrour S, Korbaa W, Ben Salah Z, et al. Socioeconomic impact of ankylosing spondylitis in Tunisia. *Jt Bone Spine.* 2010;77(1):41-6.
3. Zhang S, Li Y, Xu X, Feng X, Yang D, Lin G. Effect of cigarette smoking and alcohol consumption on disease activity and physical functioning in ankylosing spondylitis: a cross-sectional study. *Int J Clin Exp Med.* 2015;8(8):13919-27.
4. Khan MA. Ankylosing spondylitis: introductory comments on its diagnosis and treatment. *Ann Rheum Dis.* December 2002;61 Suppl 3(suppl 3):iii3-7.
5. Bandinelli F, Salvadorini G, Sedie AD, Riente L, Bombardieri S, Matucci-Cerinic M. Impact of gender, work, and clinical presentation on diagnostic delay in Italian patients with primary ankylosing spondylitis. *Clin Rheumatol.* 2015;35:473-8.
6. Deodhar A, Mittal M, Reilly P, Bao Y, Manthena S, Anderson J, et al. Ankylosing spondylitis diagnosis in US patients with back pain: identifying providers involved and factors associated with rheumatology referral delay. *Clinical Rheumatology.* 2016;1-8.
7. Rojas-Vargas M, Munoz-Gomariz E, Escudero A, Font P, Zarco P, Almodovar R, et al. First signs and symptoms of spondyloarthritis--data from an inception cohort with a disease course of two years or less (REGISPONSER-Early). *Rheumatology.* 30 January 2009;48(4):404-9.
8. Miranda García MD, Font Ugalde P, Muñoz Gomariz E, Collantes Estévez E, Zarco Montejo P, González Fernández C, et al. National Register of Patients with Spondyloarthritis (REGISPONSER). Descriptive analysis of 2,367 Spanish patients included. *Reumatol Clin Supl.* 2008;4(Suppl. 4):48-55
9. Juanola X, Fernandez-Sueiro JL, Torre-Alonso JC, Miguelez R, Munoz-Fernandez S, Ballina J, et al. Comparison of 2 referral strategies for the diagnosis of axial spondyloarthritis in Spain. The RADAR study. *Reumatol Clin.* 2013;9(6):348-52.
10. Spanish Society of Rheumatology ESPOGUIA working group. Clinical practice guidelines on the management of patients with spondyloarthritis. ESPOGUIA [Internet]. Madrid, 2009 Available on: [http://www.ser.es/wp-content/uploads/2016/03/Espoguia-completa\\_1\\_def-1.pdf](http://www.ser.es/wp-content/uploads/2016/03/Espoguia-completa_1_def-1.pdf)

## 7. PHYSICAL HEALTH, LIMITATIONS, COMORBIDITY AND DISABILITY

### 7.1 Disease activity (BASDAI)

As shown in Table 1, of the 442 people who completed the BASDAI scale, the average was 5.5 which implies that the average disease activity was high (exceeding 4 which is the cut-off point between a high BASDAI score and a low one, according to the rheumatological standards) (1-3).

**Table 1.** Level of BASDAI disease activity in the last week (N: 442)

<b>Mean</b>	5.49
<b>Median</b>	5.72
<b>Standard deviation</b>	2.17

Source: 2017 Atlas patient survey

The division of the BASDAI scale into high (for those patients with a score equal to or greater than 4) and low (for patients with a score less than 4), allows us to assess the distribution of patients according to their BASDAI score. The main conclusion is that 76.7% of the patients had a high BASDAI score, that is, a high degree of disease activity.

**Table 2.** Level of BASDAI disease activity in the last week (N: 442)

<b>BASDAI</b>	<b>Frequency</b>	<b>Percentage</b>
Low (>4)	103	23.3
High (≥4)	339	76.7
Total	442	100

Source: 2017 Atlas patient survey

On average, women have a higher BASDAI score than men, with statistically significant difference at all levels ( $p = 0.00$ ).

**Table 3.** Disease activity level in the last week assessed using the BASDAI score for the different sexes (N: 442)

<b>Sex</b>	<b>Mean BASDAI</b>	<b>N</b>
Men	5.10	222
Women	5.88	220
Total	5.49	442

Source: 2017 Atlas patient survey

While the general trend is that disease activity (BASDAI) is lower in older people, it should be mentioned that the highest level of disease activity is concentrated between 32 and 47 years of age. It should be noted that the period between 32 and 47 years of age coincides with the stage of high levels of professional activity, causing further loss in productivity. This mean difference by age groups is statistically significant ( $p = 0.03$ ).

**Table 4.** Disease activity level in the last week assessed using the BASDAI score by age group (N: 442)

	Mean BASDAI	N
<b>16-31</b>	5.54	39
<b>32-47</b>	5.72	230
<b>48-64</b>	5.26	159
<b>≥65</b>	4.01	14
<b>Total</b>	5.49	442

Source: 2017 Atlas patient survey

## 7.2 Stiffness by spinal column areas

According to the international group of experts in the Assessment in SpondyloArthritis International Society (ASAS), spinal stiffness is defined by the severity and duration on waking and this is included in the BASDAI scale. As stiffness is a common symptom in Ax-SpA, the aim of one of the survey questions was to assess the degree of stiffness experienced by patients in the spinal column. Table 5 shows how lumbar stiffness affects a majority of Ax-SpA patients, with 63% of the patients with moderate or significant stiffness, a higher percentage than found in the other two areas of the spine (cervical 45.1% and dorsal 42.1%). In fact, Ax-SpA tends to mainly affect the sacroiliac joint that is located in the lumbar area, where the spine meets the pelvis.

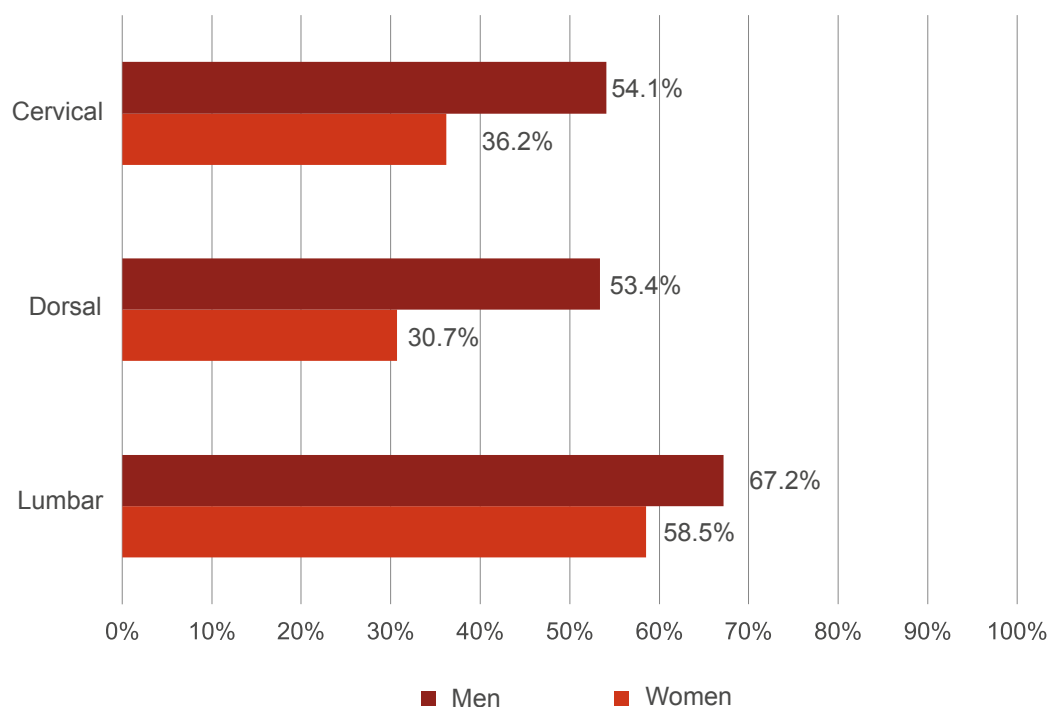
On comparing these data with those from the European Health Survey in Spain, it can be seen that only 19.22% of the general population expressed some degree of lumbar stiffness, compared to 85.8% of the patients with Ax-SpA. In addition, 16.52% of the general population reports having some degree of neck stiffness (4), compared with 76.7% of patients with Ax-SpA.

**Table 5.** Degree of stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA (N: 506-532)

	Cervical stiffness		Dorsal stiffness		Lumbar stiffness	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
<b>No limitation</b>	121	23.3	133	26.3	75	14.1
<b>Mild limitation</b>	164	31.6	160	31.6	123	23.1
<b>Moderate limitation</b>	135	26	137	27.1	180	33.8
<b>Significant limitation</b>	99	19.1	76	15	154	28.9
<b>Total</b>	519	100	506	100	532	100

Source: 2017 Atlas patient survey

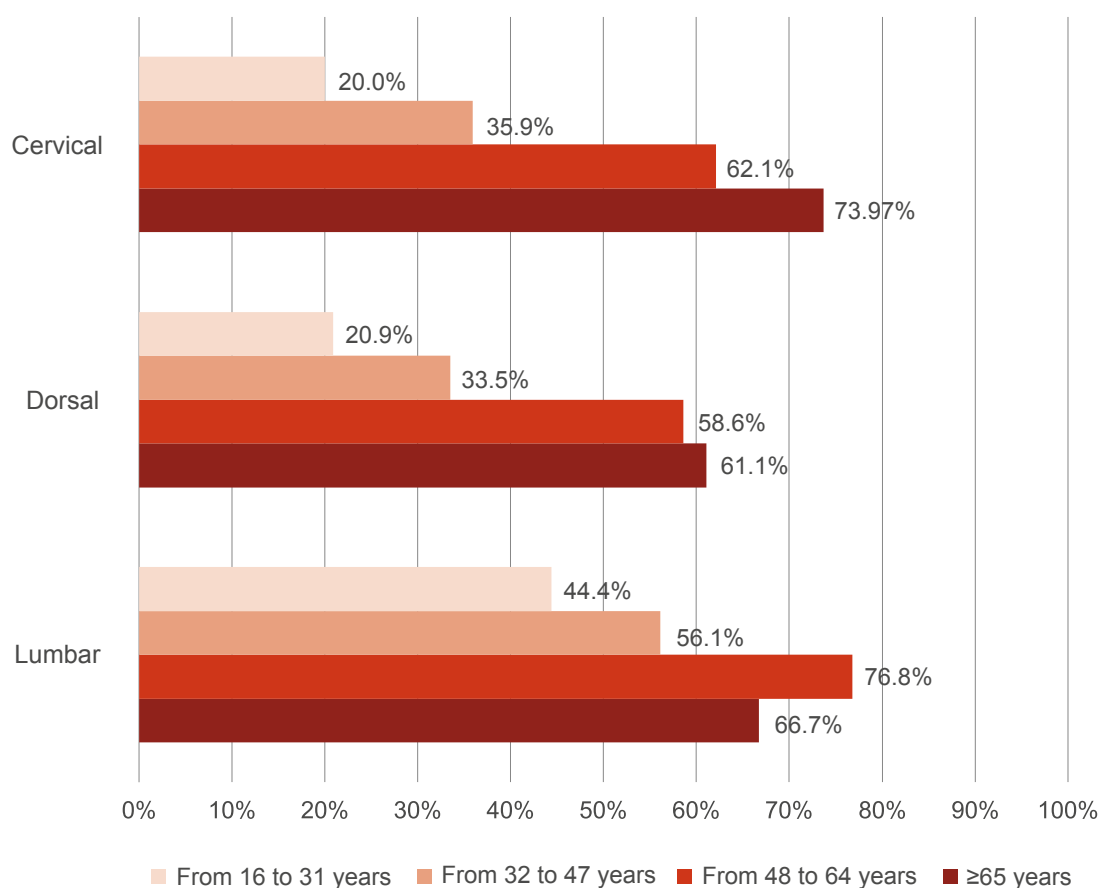
As for differences between the sexes, the percentage of men with moderate and significant stiffness in the three areas of the spine (cervical, dorsal and lumbar) is greater than for women, and this difference is greater in the case of dorsal stiffness (see Figure 1).

**Figure 1.** Degree of significant/moderate stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA by sex (N: 506-532)

Source: 2017 Atlas patient survey

In terms of age, the percentage of older people ( $\geq 64$  years) with moderate and significant stiffness in the three areas of the spine (cervical, dorsal and lumbar) is greater than for younger people. As shown in Figure 2, increasing age increases the degree of stiffness (both cervical, dorsal and lumbar).

**Figure 2.** Degree of significant/moderate stiffness in areas of the spine (cervical, dorsal and lumbar) in patients with Ax-SpA by age group (N: 506-532)



Source: 2017 Atlas patient survey

The overall stiffness index is derived by adding the different degrees of limitation (no limitation, slight limitation, moderate limitation and significant limitation) for each of the three areas of the spine studied (cervical, dorsal and lumbar).

Table 6 confirms that the degree of significant overall stiffness is high in patients over 48 years of age, while a greater percentage of younger patients (16-31) suffer from slight limitation.



**Table 6.** Degree of overall stiffness in patients with Ax-SpA according to age group (N: 494)

		<b>16-31</b>	<b>32-47</b>	<b>48-64</b>	<b>≥65</b>	<b>Total</b>
<b>No limitation</b>	Frequency	8	36	13	0	57
	Percentage	18.6%	13.7%	7.6%	0.0%	11.5%
<b>Slight</b>	Frequency	16	91	24	5	136
	Percentage	37.2%	34.6%	14.0%	29.4%	27.5%
<b>Moderate</b>	Frequency	14	57	34	1	106
	Percentage	32.6%	21.7%	19.9%	5.9%	21.5%
<b>Significant</b>	Frequency	5	79	100	11	195
	Percentage	11.6%	30.0%	58.5%	64.7%	39.5%
<b>Overall</b>	Frequency	43	263	171	17	494
	Percentage	100%	100%	100%	100%	100%

Source: 2017 Atlas patient survey

If we break down the overall stiffness by gender, it can be seen that the percentage of men with moderate and significant overall stiffness is greater (66.7%) than for women (55.1%), this difference is significant at any level ( $p = 0, 00$ ) affirming that there is dependence between sex and the degree of overall stiffness.

**Table 7.** Degree of overall stiffness in patients with Ax-SpA by sex (N: 494)

		<b>Men</b>	<b>Women</b>	<b>Total</b>
<b>No limitation</b>	Frequency	20	37	57
	Percentage	8.0%	15.1%	11.5%
<b>Slight</b>	Frequency	63	73	136
	Percentage	25.3%	29.8%	27.5%
<b>Moderate</b>	Frequency	46	60	106
	Percentage	18.5%	24.5%	21.5%
<b>Significant</b>	Frequency	120	75	195
	Percentage	48.2%	30.6%	39.5%
<b>Total</b>	43	249	245	494
	100%	100%	100%	100%

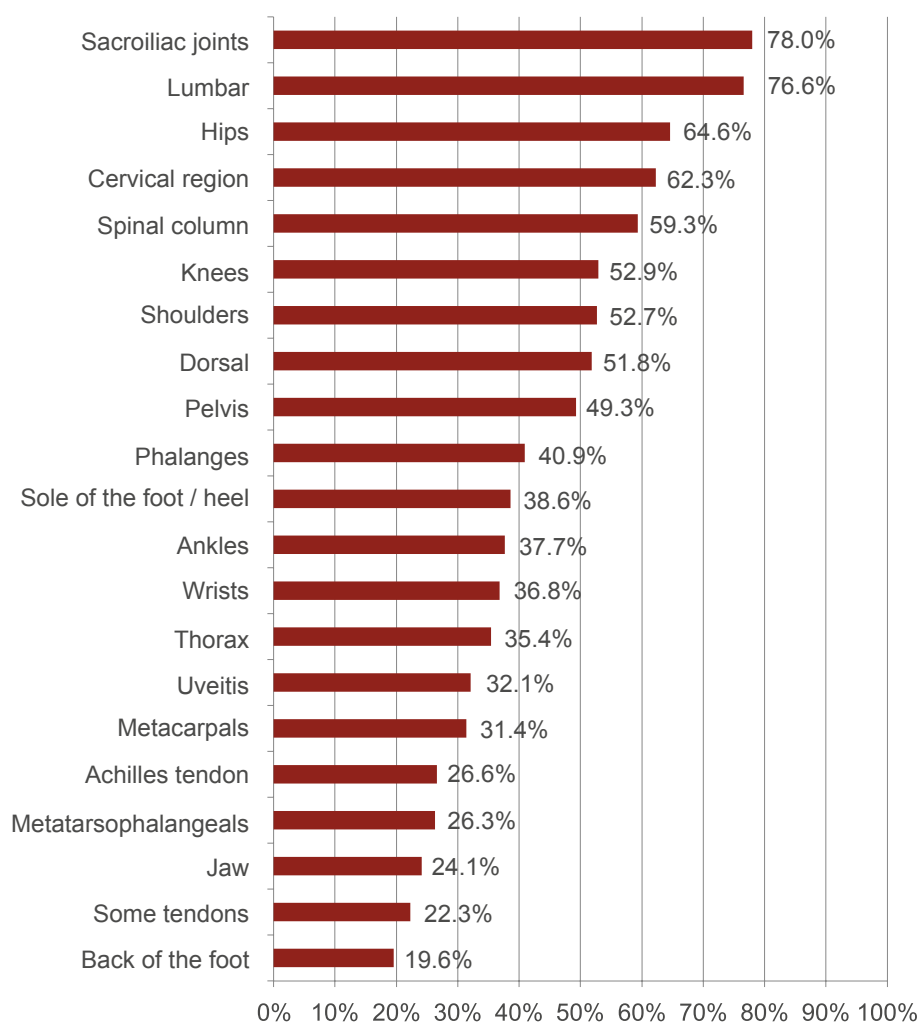
Source: 2017 Atlas patient survey

In order to validate the overall stiffness index, the arithmetic mean of the last two questions of the BASDAI questionnaire were used: “How would you describe the overall degree of morning stiffness that you have had on waking up?” and “How long does your morning stiffness last after waking up?”. Therefore, if the overall stiffness index was a valid indicator its value should be correlated with the average value of these two questions. The Spearman's rank correlation coefficient for this correlation was 0.27 ( $p = 0,00$ ), it is, therefore, possible to affirm that there is a positive and significant correlation and, therefore, it is a valid indicator.

### 7.3 Body area with inflammation

The surveyed patients reported having suffered inflammation in a number of areas of the body, highlighting the sacroiliac joints, the lumbar and cervical regions, the spine, knees, shoulders, dorsal region, pelvis, phalanges, the sole of the foot and heel. A total of 21 areas of the body were identified by the patients, ranging from 78% of patients who had experienced inflammation in the sacroiliac joints to 19.6% of the patients who had felt swelling at the back of the foot. More than 50% of the total surveyed patients declared they had suffered inflammation in 8 areas of the body.

**Figure 3.** Areas of the body where patients with Ax-SpA experienced inflammation (N: 526)



Source: 2017 Atlas patient survey

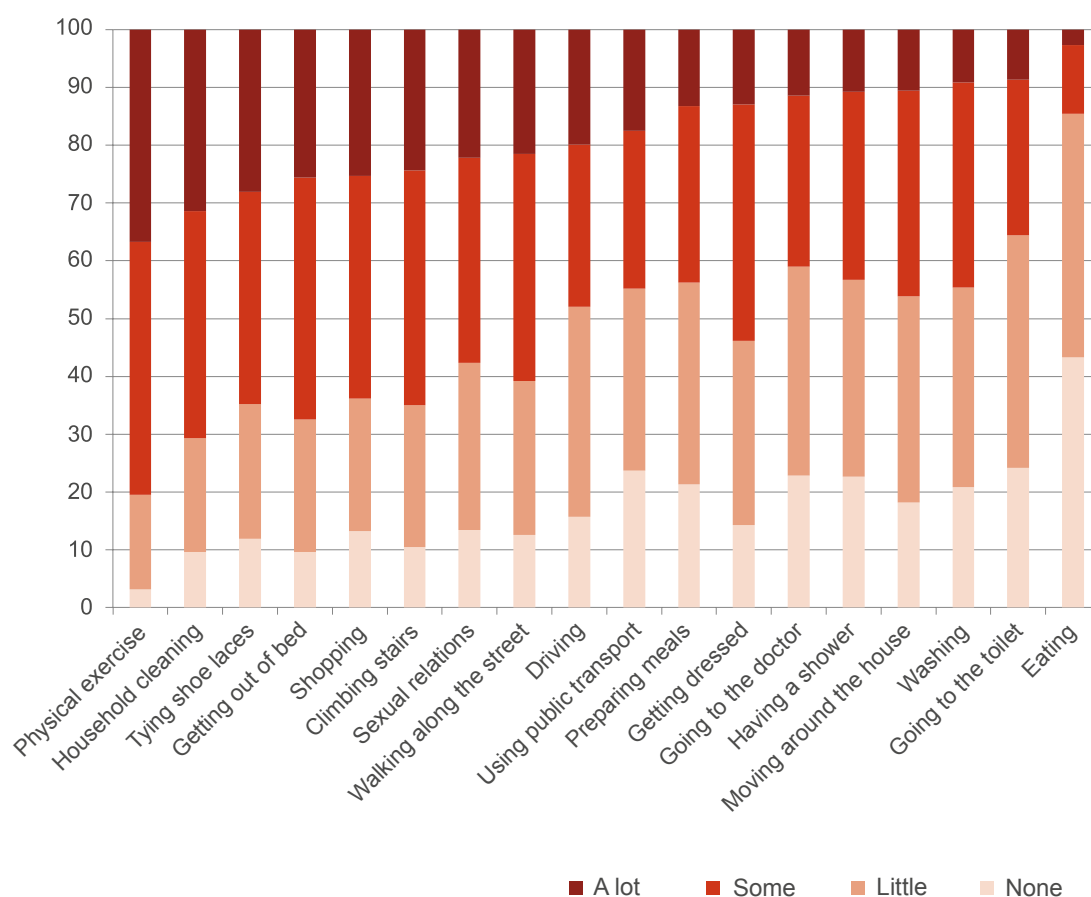
## 7.4 Limitations on activities in daily life

The variety of symptoms that exist in the case of patients with Ax-SpA (chronic pain, stiffness, restrictions on movement, etc.) has a great impact on patients' daily functioning and therefore on their quality of life. It is, therefore, important to adopt an approach that integrates both physical and psychosocial aspects. In addition, the chronic pain associated with Ax-SpA is also responsible for discomfort, disability and suffering which can affect many other areas of everyday life and the quality of life in general (5).

The limitations encountered by patients with Ax-SpA in relation to the areas evaluated by this project are consistent with the results of other similar research. A study carried out by Bagcivan et al. (6) reported that most of the participants found it difficult to perform activities of daily living and fulfil their personal needs because of the physical limitations caused by the pain. Hamilton-West et al. (7) N = 68 reported that pain and fatigue had an adverse effect on social relationships, while causing problems in sexual relations negatively influencing their marriage.

As shown in Figure 4, the main activities in which patients reported to experience some or many limitations during the moments of crisis arising from their Ax-SpA were: physical exercise, household cleaning, getting out of bed and climbing stairs. On the other hand, the activities in which they stated to experience little limitation were eating, going to the toilet, washing, moving around the home and showering.

**Figure 4.** Daily activities in which patients with Ax-SpA manifest some degree of limitation in times of crisis (N: 605)



Source: 2017 Atlas patient survey

By grouping the 18 different daily activities into a single indicator, it was observed that 52.6% of the patients with Ax-SpA suffered some or many limitations, 30.2% few limitations and 17.3% did not suffer any limitations. This contrasts with data for the general population in this regard, where, according to the European Health Survey in Spain only 5.61% of the population had serious limitations, 19.65% had minor limitations and 74.74% did not have any limitations (4). In short, the percentage of people without limitations is 57.5% more in the general population than in the population with Ax-SpA.

An analysis of these limitations by gender shows dependence between sex and the degree of limitation. The percentage of women with a higher degree of limitation is greater than that for men, especially in the case of eating, preparing meals, shopping, domestic cleaning and moving about the home (except for dressing, washing and tying shoe laces). This may reflect a much deeper reality, since almost all of these activities, usually referred to as domestic, have been and, in many cases, still are traditionally performed by women, and it is likely that this division continues to exist among patients with Ax-SpA.

**Table 8.** Descriptive statistics for the index of overall limitation as a result of Ax-SpA in times of crisis (N: 605)

<b>Mean</b>	27.67
<b>Median</b>	28.00
<b>Standard deviation</b>	13.20
<b>Percentiles</b>	
25	18.00
50	28.00
75	37.00

Source: 2017 Atlas patient survey

Table 9 shows that 46.6% of respondents gave a medium degree of limitation and the percentage of those with a high degree of limitation was greater than those with a low degree of limitation.

**Table 9.** Index of overall limitation (low, medium and high) as a result of Ax-SpA in times of crisis (N: 605)

<b>Degree of overall limitation</b>	<b>Frequency</b>	<b>Percentage</b>
Low	152	25.1
Mean	282	46.6
High	171	28.3

Source: 2017 Atlas patient survey

Table 10 shows the varying degrees of medium limitation for the 4 age groups (16-31, 32-47, 48-64 and  $\geq 65$  years of age). The analysis of means corroborates the finding that older people have a lower degree of limitation, whereas younger patients have a higher degree of limitation. This difference of means is statistically significant.

**Table 10.** Index of overall limitation as a result of Ax-SpA by age group in times of crisis (N: 605)

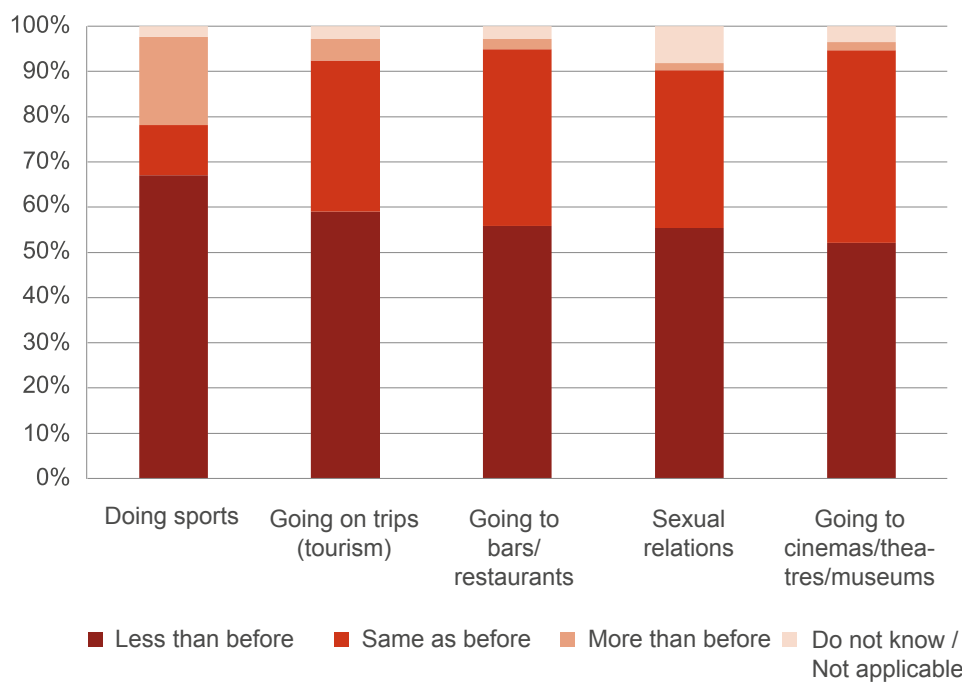
	Mean	N	Standard deviation
<b>16-31</b>	28.88	50	14.33
<b>32-47</b>	29.03	315	12.41
<b>48-64</b>	25.97	216	13.31
<b><math>\geq 65</math></b>	22.71	24	17.24
<b>Total</b>	27.67	605	13.20

Source: 2017 Atlas patient survey

With a view to studying the relationship between limitations and disease activity (measured through the BASDAI score) the mean BASDAI score was calculated for patients grouped according to degrees of limitation (no/few against some/many). The result of the comparative analysis of means is that the average BASDAI score is significantly higher in those who have some/many limitations than for those with no/few limitations (Mann-Whitney test).

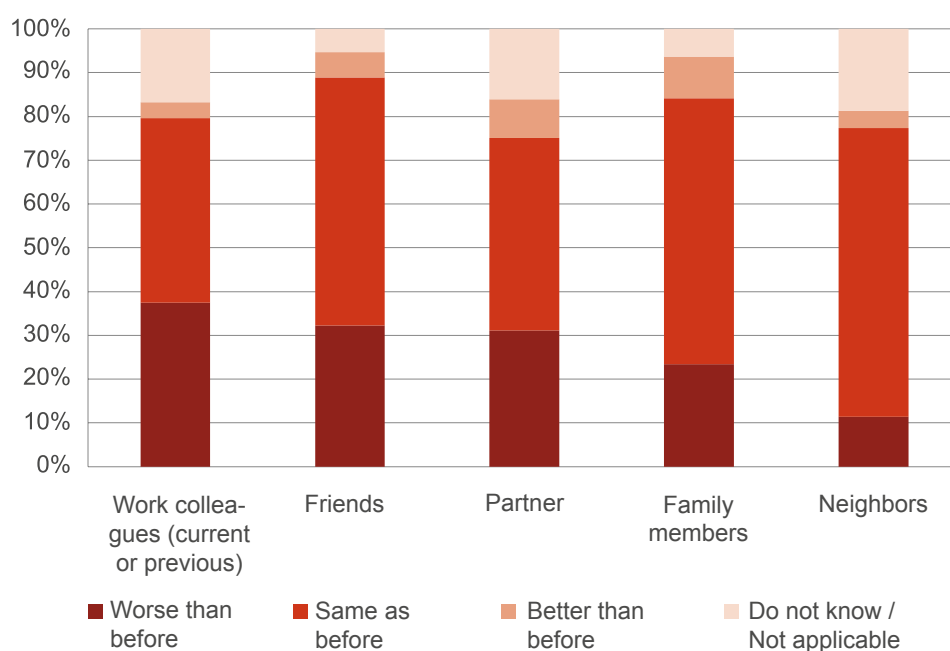
Just as for the stiffness index, in order to validate this index of overall limitation, the arithmetic mean of the two last questions of the BASDAI questionnaire was used: “How would you describe the overall degree of morning stiffness that you have had on waking up?” and “How long does your morning stiffness last after waking up?” Therefore, to corroborate that the index is valid, its correlation with the mean for these questions was verified. With a correlation coefficient of 0.44 ( $p = 0, 00$ ) it is possible to affirm that there is a positive and significant correlation and, therefore, it is a valid indicator in terms of consistency.

The frequency with which people suffering from Ax-SpA perform common leisure activities tends to be reduced as a result of the progressive worsening that the disease causes. Figure 5 shows how playing sports, travelling and going to bars and restaurants were the activities that were most affected as a result of the disease. AS also means a reduction in the frequency of sexual activity, as has been shown in previous studies (8).

**Figure 5.** Frequency of taking part in activities by patients with Ax-SpA (N: 605)

Source: 2017 Atlas patient survey

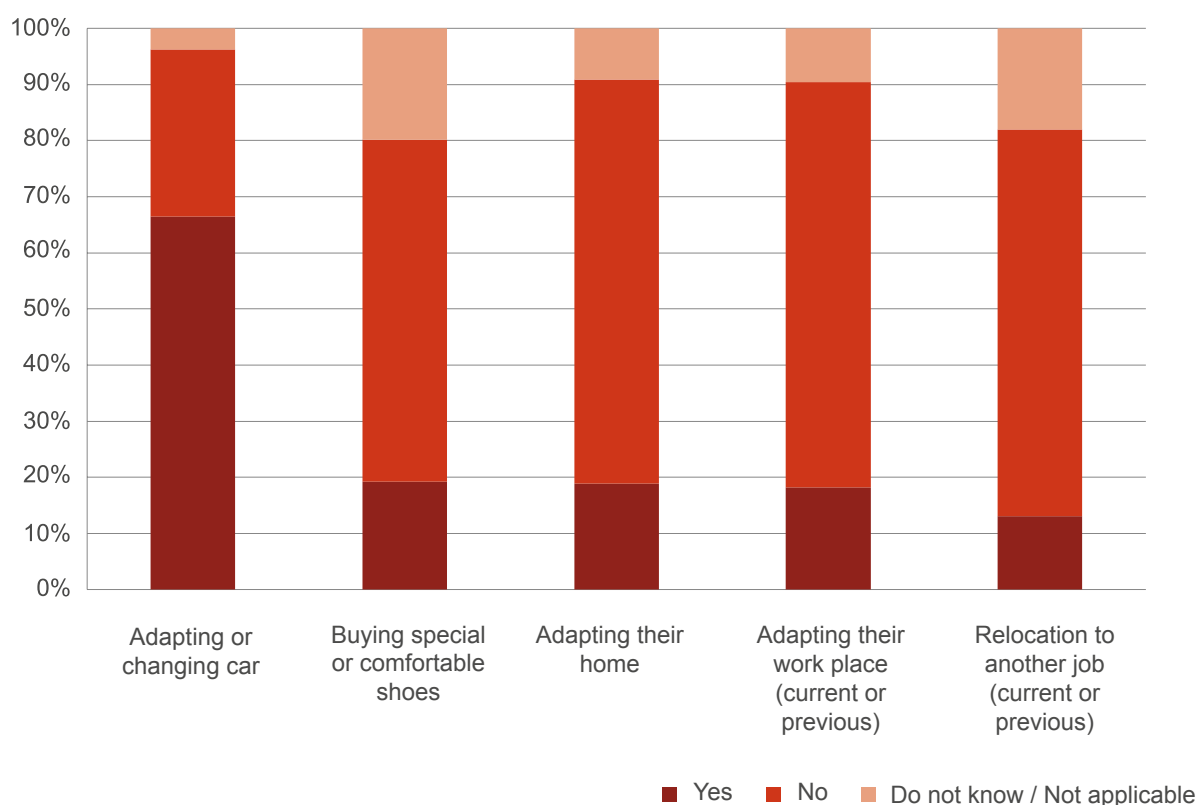
Another aspect analysed in this study was how suffering from Ax-SpA affects different facets of personal relationships. Figure 6 shows that a third of patients stated that relationships at work and with their family and partner had worsened due to suffering from the disease. Relationships with neighbours or friends were less affected. Only a few patients indicated that some of these relationships had improved.

**Figure 6.** Assessment of personal relationships before suffering from Ax-SpA (N: 605)

Source: 2017 Atlas patient survey

The limitations that these patients have in their activities of daily living (restricted movement, reduction in social activity, chronic pain, etc.) means that they have to make a series of adaptations to their environment. This study, therefore, evaluated some of the most important adaptations made by people with Ax-SpA (Figure 7). This assessment indicates that around 65% of the people affected by Ax-SpA had to adapt or change their car, while around 20% had to adapt their workplace, their home or buy special shoes. Relocation to another job was the least frequent change (around 15%).

**Figure 7.** Adaptations made by patients since they suffered from Ax-SpA (N: 605)



Source: 2017 Atlas patient survey

Boonen et al. (9), in their study on limitations in the productivity of patients with Ax-SpA at work, gave the adaptation of the work environment as one of the actions taken by people with Ax-SpA.

As can be seen in this section, people affected by Ax-SpA experience a wide variety of constraints that can affect their daily life. This is why, from a psychosocial and even economic point of view, it is important to evaluate these aspects in order to find what patients' most important needs are when it comes to providing them with resources from a social, economic and even work-related point of view.

## 7.5 Comorbidity declared by patients with Ax-SpA

Comorbidity is common among patients with Ax-SpA. Casals-Sánchez et al. (10) reported that in patients with AS, 17.4% suffered from high blood pressure, 4.7% infections, 4.4% liver disease, 3.5% ischaemic heart disease, 3.3% malignant tumours, 2.1% oral anticoagulation and 1.1% stroke.

In the study by Zarco et al. (11), 19% of AS patients suffered from uveitis, 5.4% psoriasis, 2.1% Crohn's disease and 3.9% inflammatory bowel diseases. In other extra articular manifestations it was considered that between approximately 9% and 20% of AS patients suffer from osteoporosis and between 2% and 7% enthesitis, while 10% suffer from palmoplantar pustulosis and between 1% and 3% dactylitis.

A study using the register from the Taiwanese health system found that the most common comorbidities in a sample of 11,701 AS patients were hypertension (16.4%), stomach ulcer (13.9%) and headache (10.2%) (12).

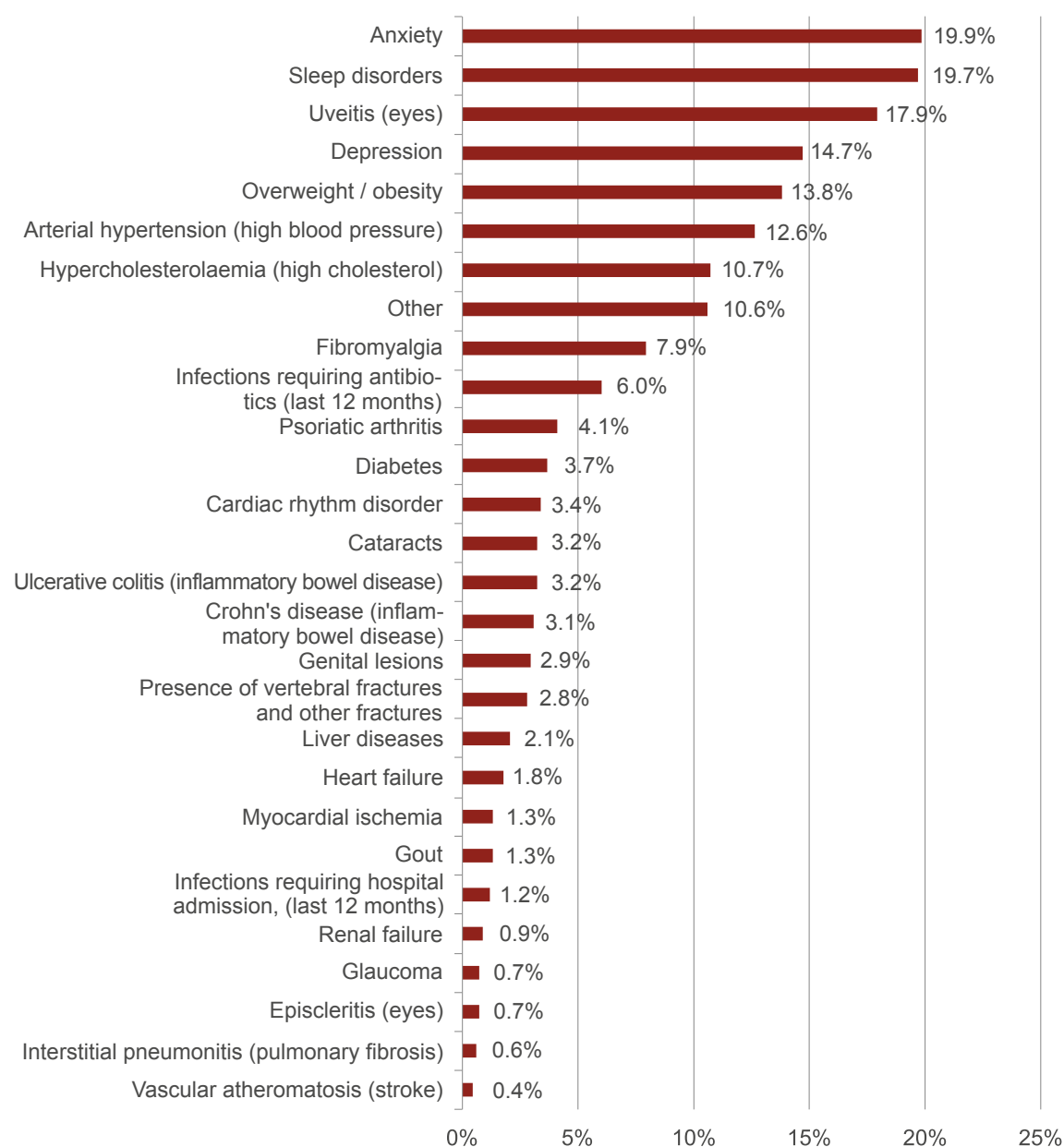
The study by Mass et al. (13) established that obesity was more common in patients with Ax-SpA than in the general population, and this was associated with worse clinical outcomes.

The data obtained in the 2017 Atlas survey show that the most common concomitant diseases reported by the patients were anxiety, sleep disorders, uveitis, depression, overweight/obesity, high blood pressure, hypercholesterolemia, fibromyalgia, severe infections requiring antibiotic therapy and psoriatic arthritis.

Three psychological disorders (anxiety, sleep disorders and depression) are among the four most commonly declared concomitant diseases, according to the data from the 2017 Atlas survey. This finding is consistent with the data from other studies (11,14) carried out on a population with Ax-SpA. The percentage of patients with Ax-SpA with depression (14.7%) is notable as it compares with only 7.4% for the general population (4), which is almost half.

In relation to the condition of obesity/overweight, the 2017 Atlas survey showed lower obesity values than other studies (11,13), with the joint prevalence of overweight and obesity similar to that for the general population (4).



**Figure 8.** Comorbidity reported by patients with Ax-SpA (N: 368)

Source: 2017 Atlas patient survey

## 7.6 Disability in patients with Ax-SpA

Knowledge of the degrees of recognised disability in people with Ax-SpA may help evaluate the impairment caused by the disease. In the 2017 Atlas survey 50.7% of the patients stated that their degree of disability had been evaluated by an evaluation team, of which 86.4% had an officially recognised degree of disability.

In relation to gender, 60.1% of the patients with an officially recognised degree of disability were men, while 51.3% were between 48 and 64 years of age. On the other hand, Table 11 shows the descriptive data for the

degree of disability recognised by patients with Ax-SpA. It can be seen that 50% of patients had a degree of disability equal to or greater than 38% (33% being the threshold for obtaining a certificate of disability). Additionally, the percentiles show that 25% of the patients presented a degree of disability higher than 55% and lower than 33%.

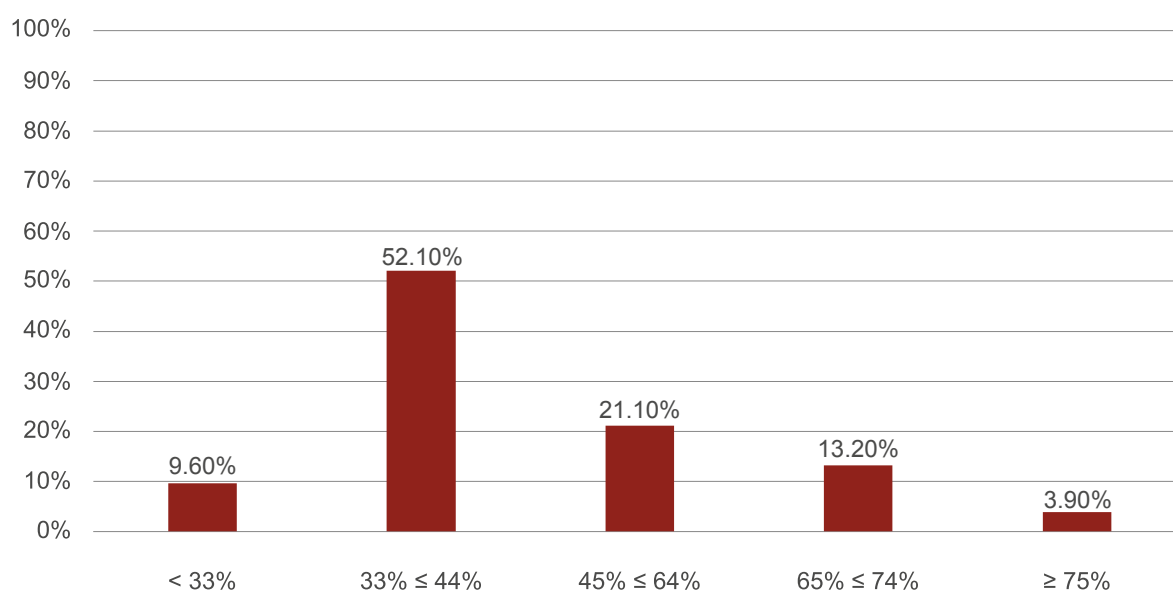
**Table 11.** Descriptive statistics for the degree of disability recognised in patients with Ax-SpA (N: 280)

	Degree of disability
Mean	43.74
Median	38.00
Standard deviation	16.85
Percentiles	
25	33.00
50	38.00
75	54.75

Source: 2017 Atlas patient survey

In relation to grouping in the degree of disability, it is observed that more than 17.1% of patients with Ax-SpA showed a degree of disability equal to or greater than 65%, while in the over-65 age group almost 60% had a degree of disability greater than 65%.

**Figure 9.** Percentage distribution of patients with Ax-SpA by degree of disability (N: 280)



Source: 2017 Atlas patient survey

- ▶ The patients surveyed reported having suffered inflammation in 21 areas of the body, with percentages ranging from 78% for patients with inflammation in the sacroiliac joints to 19.6% with pain in the back of the foot, with more than 50% of patients suffering pain in one or more of 8 specific areas.
- ▶ Ax-SpA causes a number of negative effects such as susceptibility to a large number of concomitant diseases, including anxiety, sleep disorders, uveitis, depression, overweight/obesity, high blood pressure, hypercholesterolemia, fibromyalgia, severe infections requiring antibiotic treatment and psoriatic arthritis.
- ▶ The main activities in which patients stated they experienced the greatest limitations during moments of crisis arising from their Ax-SpA were physical exercise, domestic cleaning, getting out of bed and climbing stairs.
- ▶ The main activities patients have been forced to do less often after suffering from Ax-SpA include practising sport, travelling and going to bars and restaurants.
- ▶ The majority of patients felt that their personal relationships (with neighbours, family and their partner) had not been affected as a result of their Ax-SpA, although there was a greater perception of a worsening in relationships in the work environment and with friends.
- ▶ The adaptation or purchase of a car was the action taken by the majority of patients, followed by the purchase of special or comfortable shoes.
- ▶ Half of the patients evaluated their degree of disability, of these patients 50% rated it as 38% (33% being the minimum threshold for obtaining a certificate of disability). This demonstrates the high level of disability associated with Ax-SpA.
- ▶ There is a correlation between disease activity, body stiffness and the limitations in daily activities and mental health problems in patients with Ax-SpA.

## References

1. Rudwaleit M, Listing J, Brandt J, Braun J, Sieper J. Prediction of a major clinical response (BASDAI 50) to tumour necrosis factor alpha blockers in ankylosing spondylitis. *Ann Rheum Dis*. 2004;63(6):665-70.
2. Chen C-H, Lin K-C, Yu DTY, Yang C, Huang F, Chen H-A, et al. Serum matrix metalloproteinases and tissue inhibitors of metalloproteinases in ankylosing spondylitis: MMP-3 is a reproducibly sensitive and specific biomarker of disease activity. *Rheumatology*. 2006;45(4):414-20.
3. Bodur H, Ataman S, Rezvani A, Buğdayci DS, Cevik R, Birtane M, et al. Quality of life and related variables in patients with ankylosing spondylitis. *Qual Life Res*. 2011;20(4):543-9.
4. Spanish National Statistics Institute (INE) European Survey on Health in Spain (EESE) 2014 [Internet]. 2014 [cited 14 February 2017]. Available on: [https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc\\_Eur\\_Salud\\_en\\_Esp\\_2014.htm](https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc_Eur_Salud_en_Esp_2014.htm)
5. Kotsis K, Voulgari P V, Drosos AA, Carvalho AF, Hyphantis T. Health-related quality of life in patients with ankylosing spondylitis: a comprehensive review. *Expert Rev Pharmacoecon Outcomes Res*. 5 December 2014;14(6):857-72.
6. Bagcivan G, Cinar FI, Cinar M, Oflaz F, Uzun S, Pay S. Living with pain in ankylosing spondylitis: a qualitative study. *Contemp Nurse*. 2015;51(2-3):135-47.
7. Hamilton-West KE, Quine L. Living with Ankylosing Spondylitis: The Patient's Perspective. *J Health Psychol*. 2009;14(6):820-30.
8. Younes M, Jalled A, Aydi Z, Zrour S, Korbaa W, Ben Salah Z, et al. Socioeconomic impact of ankylosing spondylitis in Tunisia. *Jt Bone Spine*. 2010;77(1):41-6.
9. Boonen A, Boone C, Albert A, Mielants H. Understanding limitations in at-work productivity in patients with active ankylosing spondylitis: The role of work-related contextual factors. *J Rheumatol*. 2015;42(1):93-100.
10. Casals-Sánchez JL, García De Yébenes Prous MJ, Descalzo Gallego M ángel, Barrio Olmos JM, Carmo-Ortells L, Hernández García C. Characteristics of the patients with spondyloarthritis monitored in rheumatology units in Spain. EmAR II study. *Reumatol Clin*. 2012;8(3):107-13.
11. Zarco P, González CM, Rodríguez de la Serna A, Peiró E, Mateo I, Linares L, et al. Extra-articular manifestations in patients with spondyloarthritis. Baseline characteristics of the cohort of patients with spondyloarthritis in the AQUILES study. *Reumatol Clin*. 2015;11(2):83-9.
12. Kang J-H, Chen Y-H, Lin H-C. Comorbidity profiles among patients with ankylosing spondylitis: a nationwide population-based study. *Ann Rheum Dis*. June 2010;69(6):1165-8.
13. Maas F, Arends S, van der Veer E, Wink F, Efde M, Bootsma H, et al. Obesity Is Common in Axial Spondyloarthritis and Is Associated with Poor Clinical Outcome. *J Rheumatol*. 2016;43(2):383-7.
14. Meesters JJJ, Petersson IF, Bergman S, Haglund E, Jacobsson LTH, Bremander A. Sociodemographic and disease-related factors are associated with patient-reported anxiety and depression in spondyloarthritis patients in the Swedish SpAScania cohort. *Clin Rheumatol*. 2014;33(11):1649-56.

## 8. PSYCHOLOGICAL HEALTH

Psychological factors are of great importance in adapting to chronic diseases of various kinds and there is no doubt that incorporating a psychological approach into the interdisciplinary therapeutic plan for chronic patients has a clear and large potential to positively influence this adaptation process (1).

Focusing on the field of rheumatic diseases and more specifically on axial spondyloarthritis, it should be emphasised that its varied symptoms (eg loss of mobility, chronic pain, physical exhaustion, etc.) have a great impact on patients' daily functioning. This also affects their quality of life (social, family, work, etc.), resulting in a complex and dynamic interaction of feelings, emotions, motivations, cognitions and behaviours that are often difficult to handle. This, together with the chronicity of the disease, as well as the partial effectiveness of the treatments currently used, has meant that special attention is paid to other factors that are not merely biomedical and which can alleviate or worsen the symptoms associated with these diseases (2). It is on this point that there is increasing evidence on the importance of psychological factors in patients' adjustment to their physical limitations as well as to the chronic pain caused by the disease. It is also worth highlighting that some variables such as anxiety and depression can have a significant impact on a patient's response to treatment for this disease (3).

These variables, such as depression and anxiety, can influence the response to treatment as found in a longitudinal study carried out over a year in patients with ankylosing spondylitis. The study found depression to be a mediating factor between levels of disease activity and functional limitations. This, in turn, suggests that these emotionally affective components can be important in improving the treatment and, therefore, the health of these patients (4).

### 8.1 Psychological health and its relationship with socio-demographic variables

Goldberg's General Health Questionnaire (GHQ-12) was used to assess the risk of poor mental health in the patients with axial spondyloarthritis (Ax-SpA) participating in this study (5). The study participants had an average GHQ score of 5.74 points out of 12, with up to 45% of patients being at risk of suffering from poor mental health. In turn, women and young people had a greater risk of poor mental health as shown in Table 1 (statistically significant differences in means).

In comparison, data for the general population from the Spanish National Health Survey 2011/12 showed an average of only 1.5 points, with the highest scores coming from women, with 1.7 points, and the population over 65 years of age, with 1.8 points (6).

**Table 1.** Mental health problems (GHQ-12) in patients with Ax-SpA by gender and age group

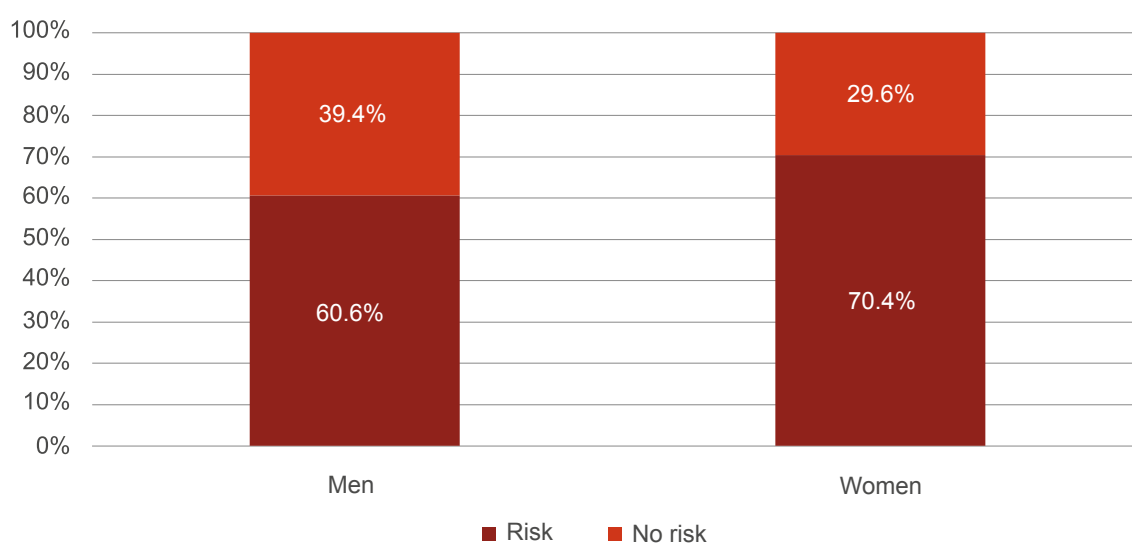
	Mean	N	Standard deviation
Men	5.30	241	4.52
Women	6.19	233	4.41
Age group			
16-31	7.00	40	4.13
32-47	6.26	250	4.47
48-64	4.90	168	4.46
≥65	3.13	16	3.52
Total	5.74	474	4.48

Source: 2017 Atlas patient survey

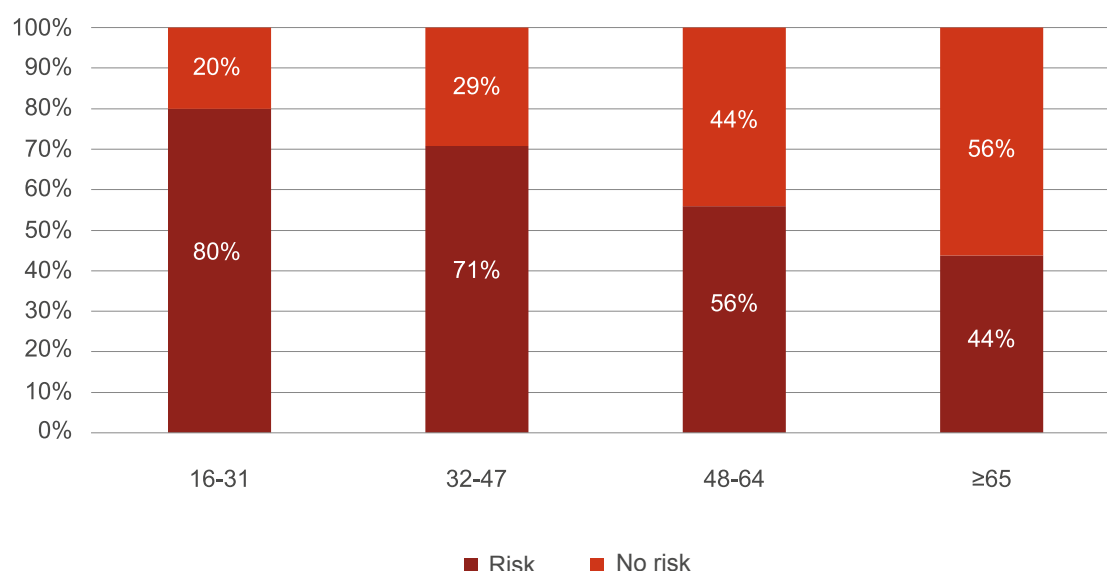
The GHQ scoring scale (0-0-1-1) was used in the 2017 Atlas to assess mental health risk. A result of 3 points or more on this scale indicates a risk of suffering from a psychiatric disorder.

Figure 1 shows that 70.4% of women and 60.6% of men are at risk of suffering from poor mental health. The Chi-square test indicates that there is a dependence between sex and the risk of poor mental health.

By age group, it is clear that younger patients have a greater percentage risk of suffering from poor mental health. In addition, the Chi-square test establishes dependence between these two variables at any level of significance.

**Figure 1.** Mental health problems (GHQ-12) in patients with Ax-SpA by gender

Source: 2017 Atlas patient survey

**Figure 2.** Mental health problems (GHQ-12) in patients with Ax-SpA by age group

Source: 2017 Atlas patient survey

## 8.2 Psychological health, disease activity and limitations in daily life

Pearson's correlation coefficient was used to determine whether there was a relationship between mental health (GHQ-12) and the degree of disease activity (BASDAI). The result is a linear correlation coefficient value of 0.514, with a maximum significance level ( $p = 0.00$ ), which indicates a moderate linear correlation between both variables. This indicates that high levels of disease activity (BASDAI index score) are accompanied by poorer mental health (measured by GHQ-12).

Likewise, the degree of correlation between the risk of suffering from poor mental health (GHQ-12) and the different degrees of cervical, dorsal and lumbar stiffness was evaluated using Spearman's rank correlation coefficient. A weak positive correlation (Spearman's rank correlation coefficient equal to 0.158) was found at acceptable significance levels for lumbar stiffness. That is, a greater degree of stiffness may lead to an increased risk of suffering from poor mental health.

Analysis of the relationship between the risk of poor mental health and disease activity showed that patients with poor mental health have a higher BASDAI score.

**Table 2.** Relationship between poor mental health (GHQ-12) and disease activity (BASDAI) in patients with Ax-SpA

Poor mental health	Mean BASDAI	N	Standard deviation
Yes	6.20	291	1.815
No	4.10	151	2.126
Total	5.49	442	2.169

Source: 2017 Atlas patient survey

On the other hand, it is obvious and undeniable that the limitations in daily activities are one of the components that can lead a patient with Ax-SpA to suffer a decrease in their levels of mental health. Using Spearman's rank correlation coefficient gave positive linear correlations with moderate-low degrees of statistical significance for all the limitations. Therefore, it is possible to affirm that any limitation in daily life has negative repercussions on the mental health of patients with Ax-SpA. In addition, higher levels of limitation in domestic activities such as cooking and domestic cleaning are the ones that are most related to poor mental health (Spearman's rank correlation coefficients equal to 0.366 and 0.398, respectively). As was the case with the BASDAI score, although to a lesser extent, there is a moderate-low linear correlation (Spearman's rank correlation coefficient equal to 0.362) between GHQ-12 and the degree of overall limitation. This indicates that higher levels of limitation are accompanied by high levels of GHQ-12 and, therefore, an increased risk of suffering from poor mental health.

### 8.3 Psychological health and comorbidity

The section on comorbidity in patients with Ax-SpA showed that three of the five most common concomitant diseases among the patients who participated in this study were related to psychological disorder such as anxiety, depression and sleep disorders. This finding is in line with the study by Shen et al. (7), which showed that AS can increase the risk of suffering from depression, anxiety and/or sleep disorders. Progressive deterioration, increased pain, and increased daily limitations reduce the patient's quality of life and ability to work. As spinal mobility is progressively lost, difficulties arise in the performance of simple tasks, the consequences of which extend beyond physical difficulties, endangering the patient's emotional and mental state (8).

Table 3 shows results with significant differences in means between patients at risk of poor mental health who suffer from emotional disturbances (depression, anxiety and sleep disorders) and those who do not suffer from them ( $p = 0.00$ ).

**Table 3.** Risk of poor mental health (GHQ-12) in relation to a comorbidity with emotional disturbances (depression, anxiety and sleep disorders) in patients with Ax-SpA

Poor mental health		Depression	Anxiety	Sleep disorders
Yes	Mean	9.06	8.17	7.67
	N	99	134	134
No	Mean	4.86	4.78	4.97
	N	375	340	340

Source: 2017 Atlas patient survey

Sleep disorders are closely linked to the pain and stiffness patients with Ax-SpA experience during sleep. Several studies have shown how the relationship between sleep disorders and AS and SpA can have an impact on a patient's quality of life (8,9).

Finally, according to the data from our study, patients suffering from emotional disorders usually seek psychological and psychiatric care. The results highlight how patients visiting these mental health professionals present higher GHQ-12 levels, which highlights the quality of this indicator.



**Table 4.** Mental health problems (GHQ-12) in relation to visits to psychologists and psychiatrists in patients with Ax-SpA

		Poor mental health
<b>Yes</b>	Mean	8.99
	N	100
<b>No</b>	Mean	4.87
	N	374
<b>Total</b>	Mean	5.74
	N	474

Source: 2017 Atlas patient survey

Psychological or psychiatric care for patients with Ax-SpA lasting more than one year is high (21.1%) when compared to the general population in Spain (4.6%) (10). This data corroborates the percentages shown for emotional alterations (anxiety, sleep disorder and depression) in the comorbidities chapter of this 2017 Atlas.

It is interesting to analyse whether membership of an Ax-SpA association influences the risk of poor mental health in patients. Table 5 shows that the members of an Ax-SpA patients' association have better average mental health than patients who do not belong to an association, this difference is significant at all levels (Mann-Whitney test).

**Table 5.** Mental health problems (GHQ-12) in relation to membership of an SpA association

		Poor mental health
<b>Yes</b>	Mean	4.94
	N	227
<b>No</b>	Mean	6.46
	N	247
<b>Total</b>	Mean	5.74
	N	474

Source: 2017 Atlas patient survey

- ▶ The majority of patients surveyed (70% of women and 60% of the men) have mental health problems.
- ▶ Three psychological disorders (anxiety, sleep disorder and depression) are among the four most commonly described concomitant diseases.
- ▶ Members of associations for patients with Ax-SpA have fewer mental health problems than other patients.

## References

1. de Ridder D, Geenen R, Kuijer R, van Middendorp H. Psychological adjustment to chronic disease. *Lancet*. 2008;372(9634):246–55.
2. Kotsis K, Voulgari P V, Drosos AA, Carvalho AF, Hyphantis T. Health-related quality of life in patients with ankylosing spondylitis: a comprehensive review. *Expert Rev Pharmacoecon Outcomes Res*. 2014 Dec 5;14(6):857-72.
3. Kilic G, Kilic E, Ozgocmen S. Relationship between psychiatric status, self-reported outcome measures, and clinical parameters in axial spondyloarthritis. *Medicine (Baltimore)*. 2014 Dec;93(29):e337.
4. Jang JH, Green CE, Assassi S, Reveille JD, Ward MM, Weisman MH, et al. The contribution of disease activity on functional limitations over time through psychological mediators: a 12-month longitudinal study in patients with ankylosing spondylitis. *Rheumatology*. (50):2087-92.
5. Sánchez López MP, Dresch V. The 12-Item General Health Questionnaire (GHQ-12): Reliability, external validity and factor structure in the Spanish population. *Psicothema*. 2008;20(4):0214–9915.
6. Ministry of Health, Social Services and Equality. Spanish National Health Survey 2011/12 (ENSE 2011/12) [Internet]. 2011 [cited 2017 Feb 14]. Available on: <https://www.msssi.gob.es/estadEstudios/estadisticas/encuestaNacional/encuesta2011.htm>
7. Shen C-C, Hu L-Y, Yang AC, Kuo BI-T, Chiang Y-Y, Tsai S-J. Risk of Psychiatric Disorders following Ankylosing Spondylitis: A Nationwide Population-based Retrospective Cohort Study. *J Rheumatol*. 2016 Mar 1;43(3):625-31
8. Demirci S, Demirci K, Doğru A, İnal EE, Koyuncuoğlu HR, Şahin M. Restless legs syndrome is associated with poor sleep quality and quality of life in patients with ankylosing spondylitis: a questionnaire-based study. *Acta Neurol Belg*. 2016 Sep 12;116(3):329-36.
9. İn E, Turgut T, Gülkesen A, Yolbaş S, Akgöl G, Koca SS. Sleep Quality Is Related to Disease Activity in Patients With Ankylosing Spondylitis. *JCR J Clin Rheumatol*. 2016;22(5):248–52.
10. Spanish National Statistics Institute (INE) European Survey on Health in Spain (ESEE) 2014 [Internet]. 2014 [cited 2017 Feb 14]. Available on: [https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc\\_Eur\\_Salud\\_en\\_Esp\\_2014.htm](https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc_Eur_Salud_en_Esp_2014.htm)

## 9. HEALTHCARE

### 9.1 Visits by speciality

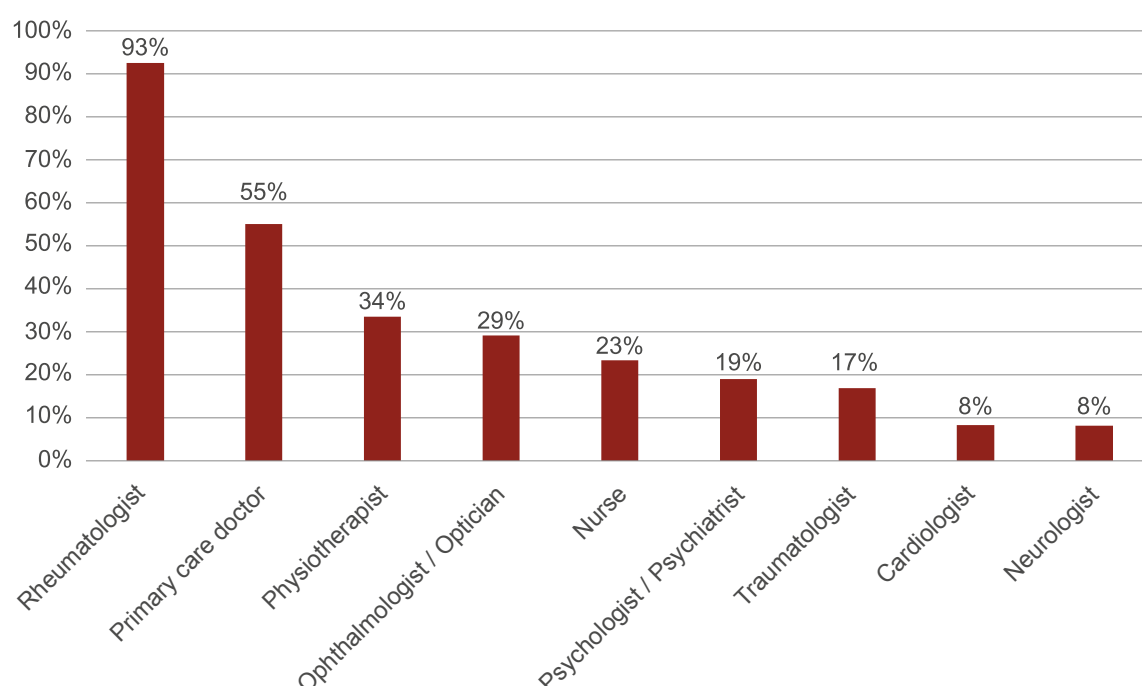
The majority of axial spondyloarthritis (Ax-SpA) patients surveyed for the 2017 Atlas relied on public healthcare (95.5%), 29.3% had private insurance, and 31.8% had been for at least one private consultation in the last 12 months. It is worth noting the high number of patients with double coverage or who have had some type of private consultation during the last 12 months.

There is a large difference between the proportion of patients with Ax-SpA surveyed for the 2017 Atlas with private health coverage and the proportion of the general population (15.6%) (1). This could indicate that patients with Ax-SpA find it necessary to supplement the services offered within the public healthcare service.

The main medical specialists patients reported visiting within the healthcare service were rheumatologists, primary care doctors, physiotherapists, ophthalmologists/optometrist, nurses, psychologists/psychiatrists and traumatologists.

Figure 1 shows that 34% of the patients with Ax-SpA had visited a physiotherapist at least once during the previous year. This percentage is high when compared to the 15.6% for the general population (1).

**Figure 1.** Percentage of patients with Ax-SpA visiting specialists during the last 12 months (N: 552)



Source: 2017 Atlas patient survey

Table 1 shows the number of total visits and the average number of visits a patient has made to each healthcare specialist. If we look at the total number of visits made to healthcare specialists in the last year, we see the importance of physiotherapists and primary care doctors, followed by rheumatologists, although the latter received almost half as many visits per year. The number of visits to psychologists/psychiatrists and nurses is slightly lower than those to rheumatologists. This emphasises that, in addition to rheumatologists, other specialists play an important role in the management of the patients.

**Table 1.** Frequency of visits to medical specialists by patients with Ax-SpA in the last 12 months (N: 552)

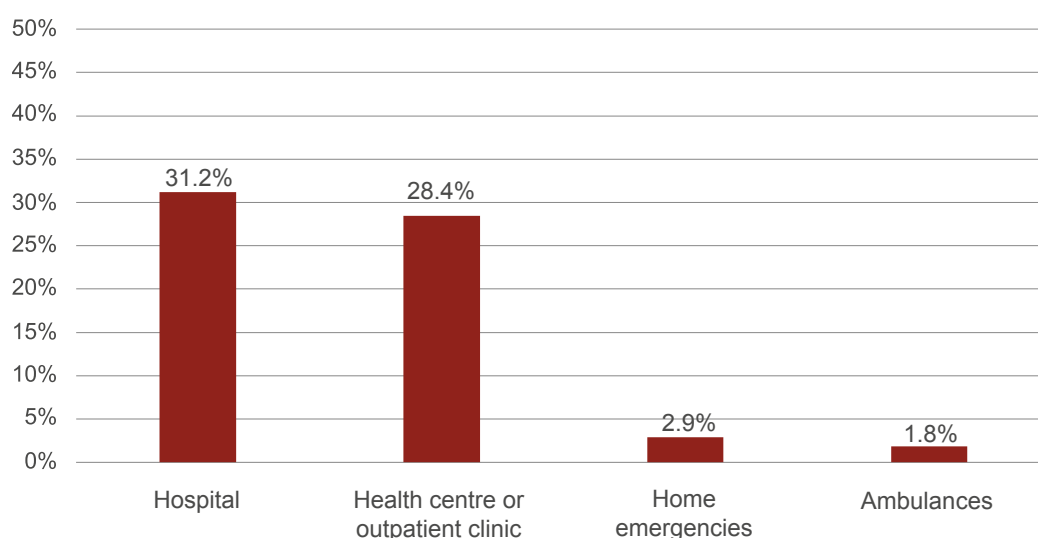
	Total visits	Mean	Median	Standard deviation	Min	Max
Physiotherapist	4,582	20.1	10	28.9	1	240
Primary care doctor	3,545	9.5	5	16.5	1	230
Rheumatologist	2,228	4.4	4	3.9	1	50
Psychologist/Psychiatrist	1,438	11.1	4	20	1	174
Nurse	1,387	8.7	4	14.6	1	100
Ophthalmologist/Optometrist	566	2.9	2	3.3	1	28
Traumatologist	392	3.4	2	4	1	30
Cardiologist	126	2.2	1	2	1	9
Neurologist	123	2.2	2	1.6	1	10

Source: 2017 Atlas patient survey

The data collected for the 2017 Atlas in relation to the median number of visits to rheumatologists over a year agrees with that presented by Jovani et al. (2) for patients with spondyloarthritis (4 visits/year). On the other hand, the mean number of visits to a rheumatologist was higher (4.4 visits/year) than the data collected in the study by Zink et al. (3) for AS patients in Germany (4.2 visits/year). The average number of visits to a physiotherapist per year among patients with Ax-SpA is high, as shown by the 2017 Atlas data (20.1 visits/year), which is corroborated by the study by Boonen et al. (4) for AS patients in The Netherlands (18.3 visits/year).

## 9.2 Resource utilisation

The most used emergency services identified in the survey by patients with Ax-SpA are hospitals with 31.2% and health centres or outpatient clinics with 28.4%, with the latter the service that experienced the largest number of visits with a mean of 5.49 times in the last 12 months (Graph 2 and Table 2).

**Figure 2.** Attendance at emergency departments during the last 12 months (N: 552)

Source: 2017 Atlas patient survey

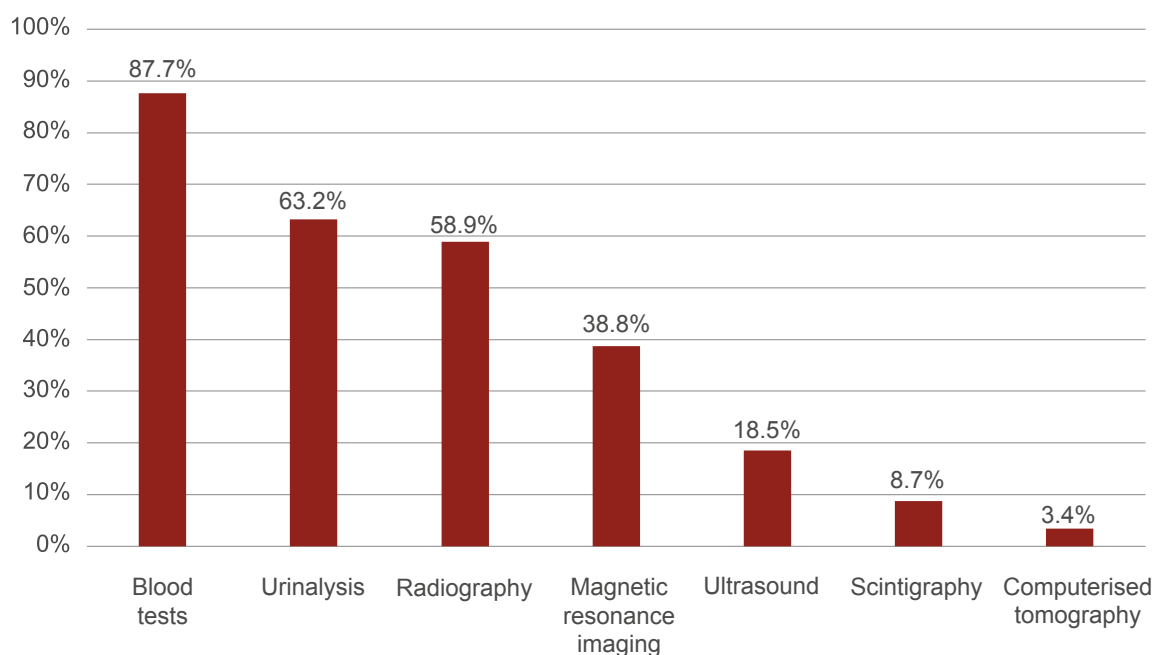
**Table 2.** Attendance at emergency departments during the last 12 months (N: 552)

	Total visits	Mean	Median	Standard deviation	Min	Max
Health centre or outpatient clinic	862	5.49	2.00	11.19	1	80
Hospital	518	3.01	2.00	3.21	1	23
Home emergencies	38	2.38	1.50	1.93	1	7
Ambulances	21	2.10	1.50	1.66	1	6

Source: 2017 Atlas patient survey

A series of tests are performed throughout the year as part of the management and monitoring of patients with Ax-SpA. The 2017 Atlas survey asked about the most common tests carried out as part of healthcare.

In the 2017 Atlas survey 87.7% of the patients had undergone some form of blood tests in the previous year, while more than 63% had undergone a urinalysis and 58.9% at least one x-ray. In addition, 38.8% of patients had undergone magnetic resonance imaging (Figure 3).

**Figure 3.** Monitoring tests performed during the last 12 months (N: 552)

Source: 2017 Atlas patient survey

In general, the population with Ax-SpA presents higher percentages for testing such as: analysis, radiography, ultrasound and MRI than the general population. Specifically, 69.6% of the general population had undergone some analysis, 27.1% radiography, 16.2% ultrasonography and 7.8% magnetic resonance, much lower rates than in the population with Ax-SpA (1).

The analysis of the average number of times that each of the tests is performed shows that blood tests are carried out an average of 4.5 times a year, while radiography and resonance 3.5 and 2.2, respectively (Table 3).

**Table 3.** Frequency of monitoring tests in the last 12 months (N: 552)

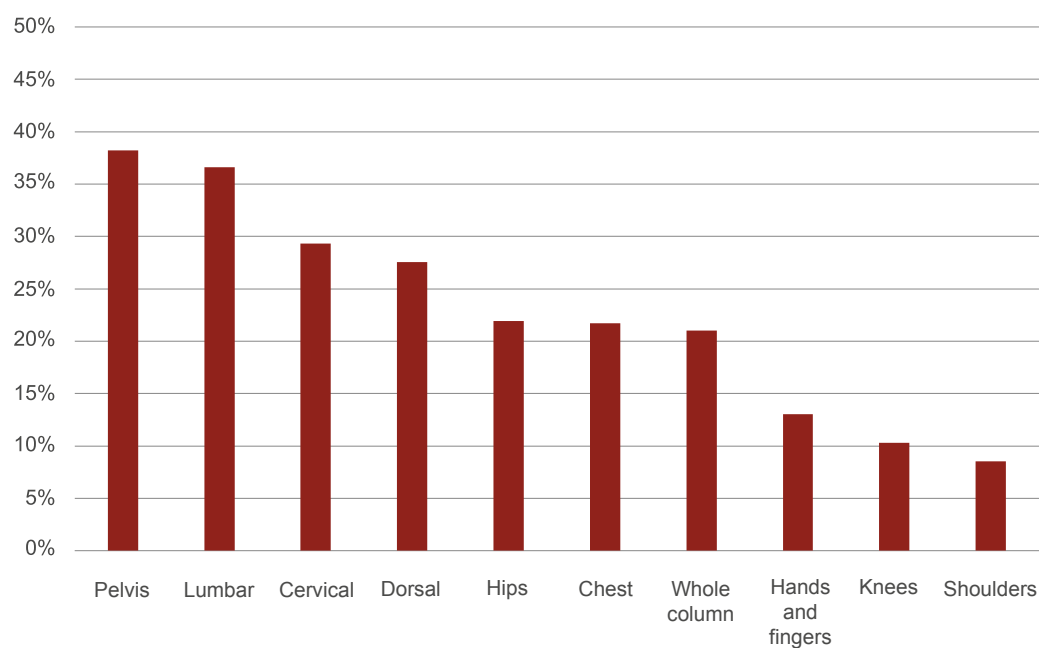
	<b>Total visits</b>	<b>Mean</b>	<b>Median</b>	<b>Standard deviation</b>	<b>Min</b>	<b>Max</b>
<b>Blood tests</b>	2,185	4.51	4.00	4.14	1	35
<b>Urinalysis</b>	1,287	3.69	3.00	3.14	1	30
<b>Radiography</b>	1,135	3.49	2.00	3.72	1	26
<b>Magnetic resonance imaging</b>	478	2.23	2.00	1.83	1	12
<b>Ultrasound</b>	193	1.89	2.00	1.26	1	8
<b>Scintigraphy</b>	73	1.52	1.00	0.74	1	4
<b>Computerised tomography</b>	25	1.32	1.00	0.58	1	3

Source: 2017 Atlas patient survey

## 9.3 Radiology by body regions

One of the most used tests in the monitoring and management of the disease is radiography. This test is performed on different body areas depending on the pain or inflammation experienced by each patient.

In health care, the area of the body most commonly examined using radiography was the pelvis, followed by the lumbar, cervical, and dorsal areas. These same results are consistent with the total number of X-rays performed on each patient in each area (Table 4).

**Figure 4.** Radiography by body region over the last 12 months (N: 552)

Source: 2017 Atlas patient survey

**Table 4.** Radiography by body region over the last 12 months (N: 552)

	Total visits	Mean	Median	Standard deviation	Min	Max
<b>Pelvis</b>	393	1.86	1.00	2.23	1	28
<b>Lumbar</b>	369	1.83	1.00	1.85	1	20
<b>Cervical</b>	286	1.77	1.00	1.36	1	10
<b>Dorsal</b>	257	1.69	1.00	1.32	1	10
<b>Hips</b>	201	1.66	1.00	1.25	1	11
<b>Whole column</b>	193	1.66	1.00	1.40	1	12
<b>Chest</b>	183	1.53	1.00	0.97	1	7
<b>Knees</b>	118	2.07	1.00	1.74	1	10
<b>Hands and fingers</b>	113	1.57	1.00	1.13	1	8
<b>Shoulders</b>	78	1.66	1.00	1.18	1	7

Source: 2017 Atlas patient survey

- The majority of patients with Ax-SpA received public healthcare (95.5%) and 29.3% had private insurance, this percentage is double that for the general population.
- The main medical specialists involved in the management and monitoring of the disease are primary care doctors, rheumatologists, physiotherapists and psychologists/psychiatrists.

## References

1. Spanish National Statistics Institute (INE) European Survey on Health in Spain (EESE) 2014 [Internet]. 2014 [cited 14 February 2017]. Available on: [https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc\\_Eur\\_Salud\\_en\\_Esp\\_2014.htm](https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc_Eur_Salud_en_Esp_2014.htm)
2. Jovani V, Loza E, García de Yébenes MJ, Descalzo MÁ, Barrio JM, Carmona L, et al. Variability in the use of resources in patients with spondyloarthritis in Spain. Preliminary descriptive data from the emAR II study. *Reumatol Clin*. 2012;8(3):114-9.
3. Zink A, Thiele K, Huscher D, Listing J, Sieper J, Krause A, et al. Healthcare and burden of disease in psoriatic arthritis. A comparison with rheumatoid arthritis and ankylosing spondylitis. *J Rheumatol*. 2006;33(1):86-90.
4. Boonen A, van der Heijde D, Landewé R, Guillemin F, Rutten-van Mölken M, Dougados M, et al. Direct costs of ankylosing spondylitis and its determinants: an analysis among three European countries. *Ann Rheum Dis*. 2003;62(8):732-40.

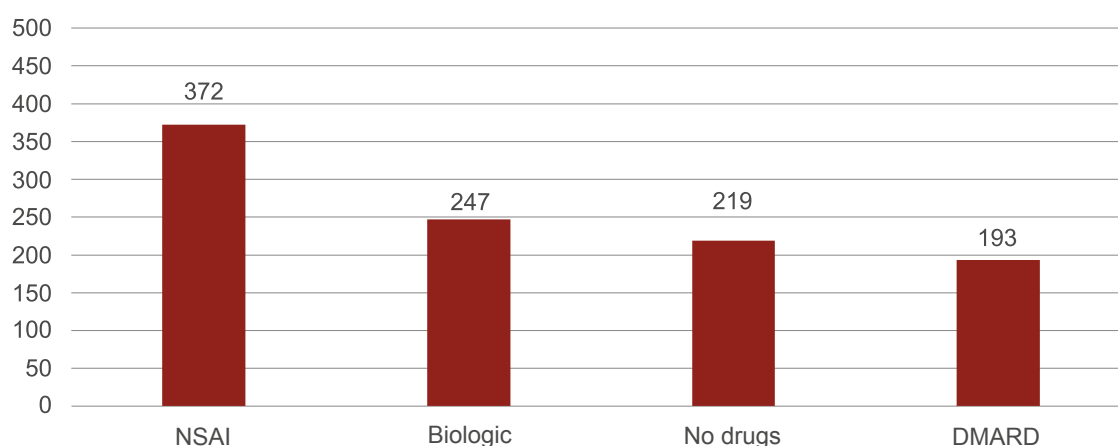


## 10. PHARMACOLOGICAL TREATMENT

### 10.1 Pharmacological therapy

Figure 1 shows the absolute number of patients according to the type of treatment (biological therapy, NSAID or DMARD treatment) and those who were not using any type of drug.

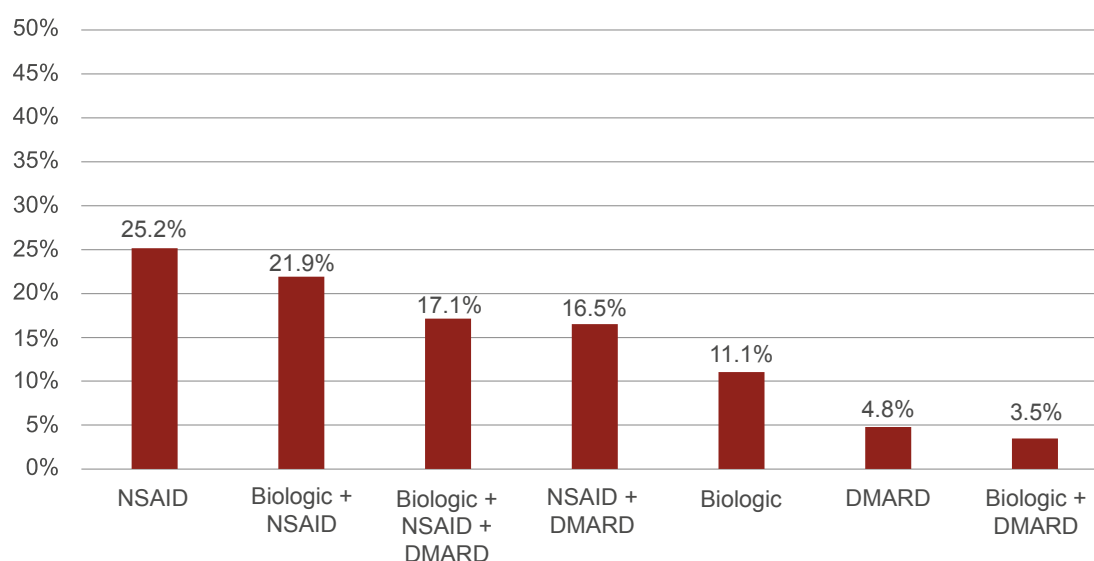
**Figure 1.** Total patients consuming NSAIDs, biologics and DMARDs and those who did not use any drugs.



Source: 2017 Atlas patient survey

Figure 2 shows the distribution of patients according to the different possible combinations of pharmacological treatment, distinguishing between patients using a single drug (biologics, NSAIDs or DMARDs) and those combining more than one (eg. Biologics plus NSAIDs) or those taking all available types. It can be observed that the most common treatment is with NSAIDs, followed by biologics with NSAIDs and biologics with NSAIDs and DMARDs.

**Figure 2.** Percentage of drug use distinguishing between patients taking a single drug (biologics, NSAIDs or DMARDs) and those combining more than one or all those available (N: 461).



Source: 2017 Atlas patient survey

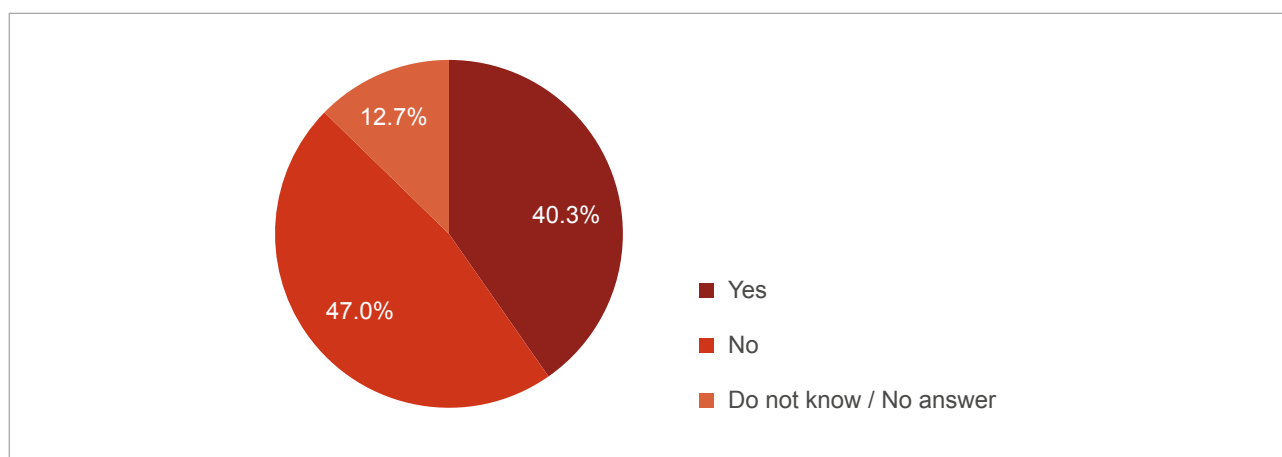
In the study by Collantes et al. (1) 69.0% of patients with AS reported taking NSAIDs, 18.8% DMARDs, 15.6% biologics and 6% glucocorticoids. It is worth noting that approximately 10 years have elapsed since the study, during which time the prescription and consumption of DMARDs has decreased and the number of patients following biological therapies has increased.

## 10.2 Use of anti-inflammatory drugs (NSAIDs)

NSAIDs are drugs that are used to reduce both pain and inflammation and, since 1950, they have been the basis of pharmacological treatment in patients with Ax-SpA. This is because they produce rapid relief from pain and stiffness and facilitate mobility and the performance of physical exercise (2).

More than 40% of the patients surveyed reported experiencing side effects related to NSAID treatment (Figure 3).

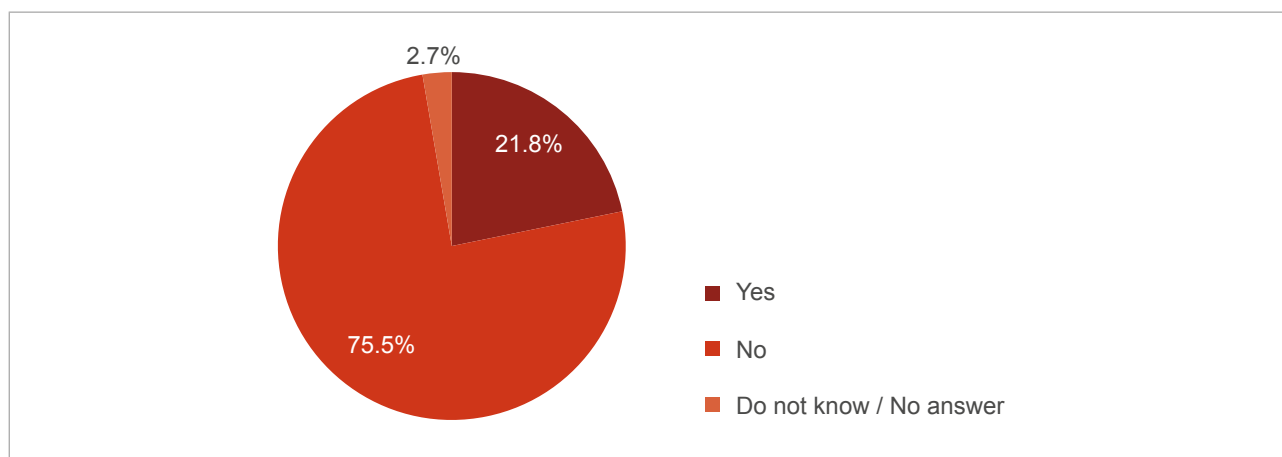
**Figure 3.** Percentage distribution of patients taking NSAIDs in the past 12 months who have experienced side effects from these drugs (N: 372)



Source: 2017 Atlas patient survey

Out of the group of patients who reported taking NSAIDs, 21.8% had stopped taking them (Figure 4).

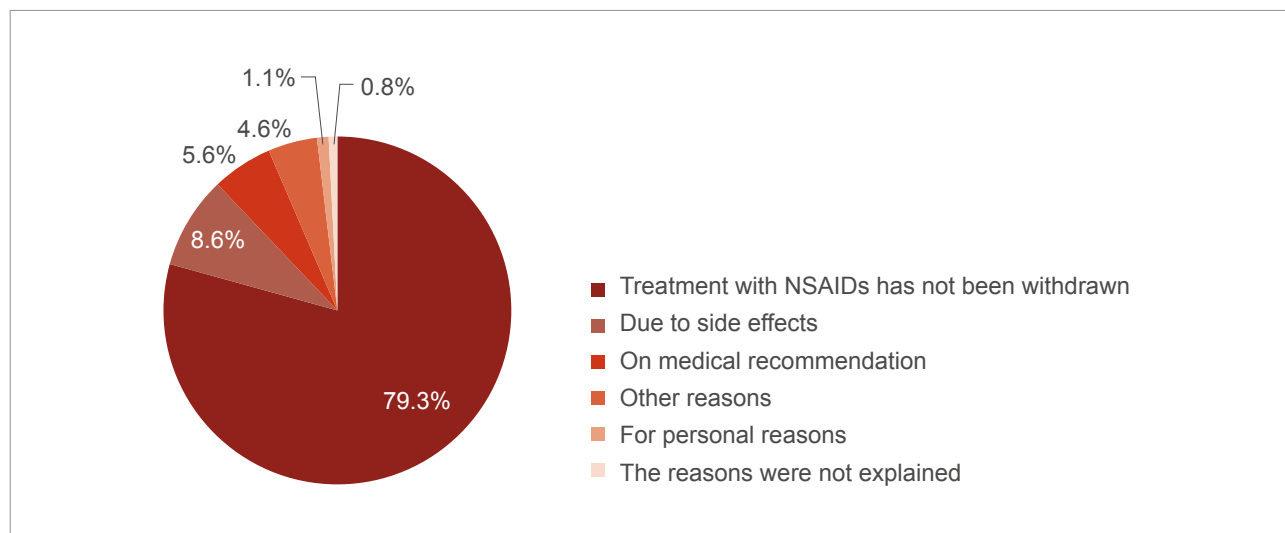
**Figure 4.** Percentage of patients being treated with NSAIDs in the past 12 months who had been withdrawn from treatment (N: 372)



Source: 2017 Atlas patient survey

Among those patients who reported that they had withdrawn from NSAID therapy, the main reasons for withdrawal were due to side effects, medical recommendation and change to biological therapy (Figure 5).

**Figure 5.** Reason NSAID treatment was withdrawn from those taking these drugs in the last 12 months (N: 372)

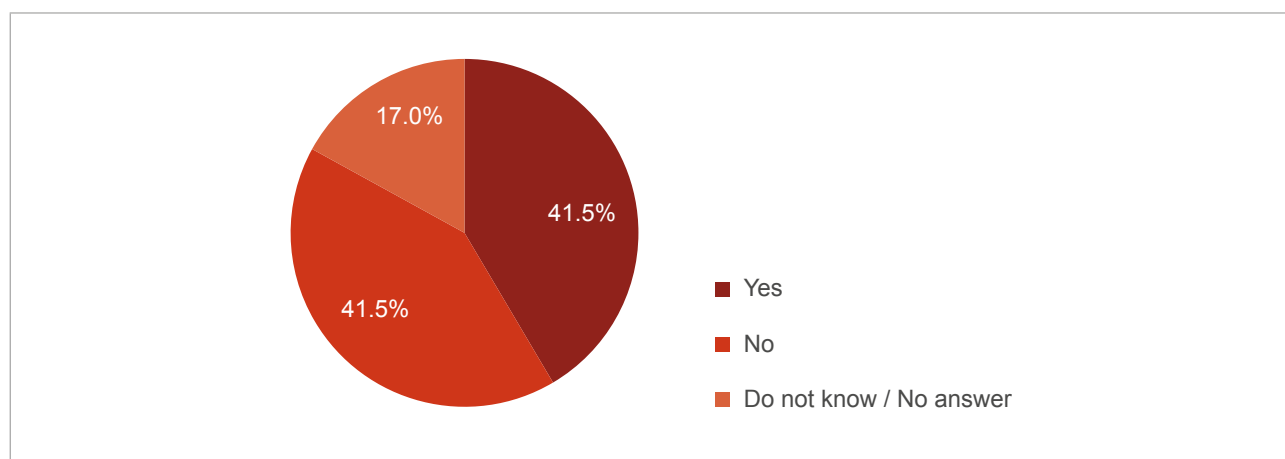


Source: 2017 Atlas patient survey

### 10.3 Consumption of disease modifying antirheumatic drugs (DMARDs)

Of the total number of patients surveyed who had been treated with DMARDs in the last 12 months, a significant percentage had experienced side effects (Figure 6).

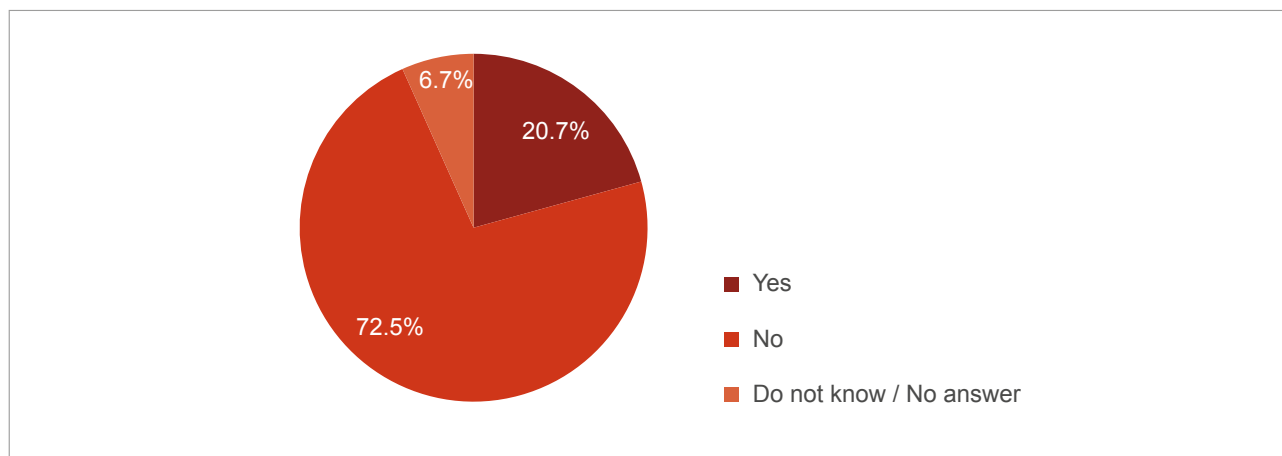
**Figure 6.** Percentage distribution of patients being treated with DMARDs in the last 12 months who had experienced side effects from these drugs (N: 193)



Source: 2017 Atlas patient survey

Of the patients who had been treated with DMARDs, more than 20% had been withdrawn from the treatment (Figure 7).

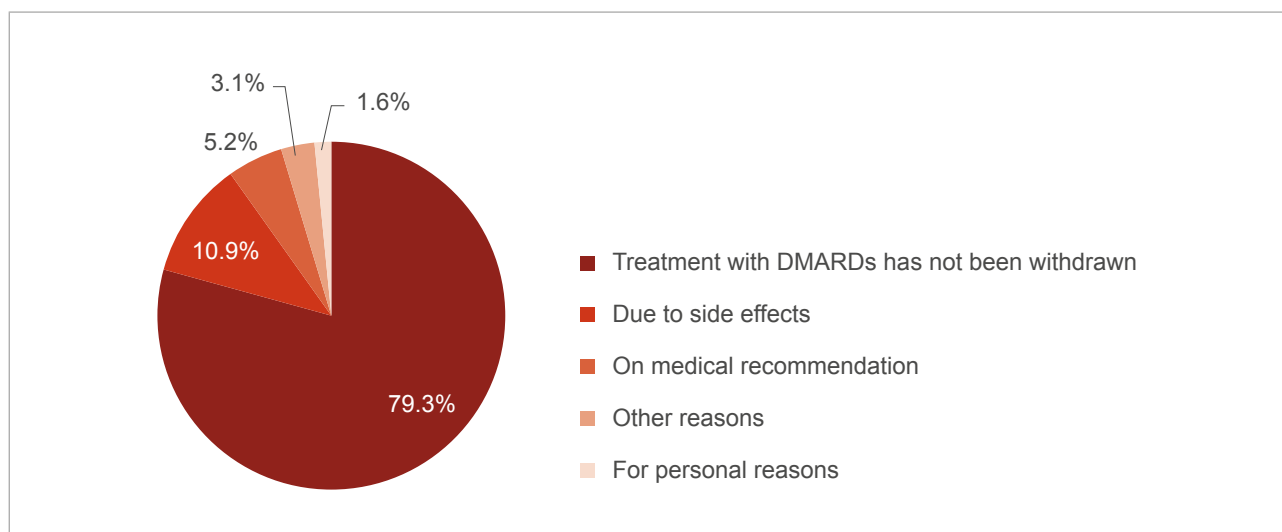
**Figure 7.** Percentage distribution of patients receiving DMARDs in the last 12 months who had been withdrawn from the treatment (N: 193)



Source: 2017 Atlas patient survey

Among the main reasons that led to the withdrawal of treatment with DMARDs were the side effects, medical recommendation and due to a change to biologics (Figure 8).

**Figure 8.** Percentage distribution of patients receiving DMARDs in the last 12 months who had been withdrawn from treatment for various reasons (N: 193)



Source: 2017 Atlas patient survey

## 10.4 Use of biological therapies

Pharmacological treatment for patients with Ax-SpA has been revolutionised in recent years with the introduction of more and more biological treatments (anti-tumour necrosis factor inhibitor therapy and, more recently, interleukin-17A inhibitors). These drugs have shown their efficacy in a large number of patients in controlling the physical impairment caused by the disease and improving their quality of life (3-5).

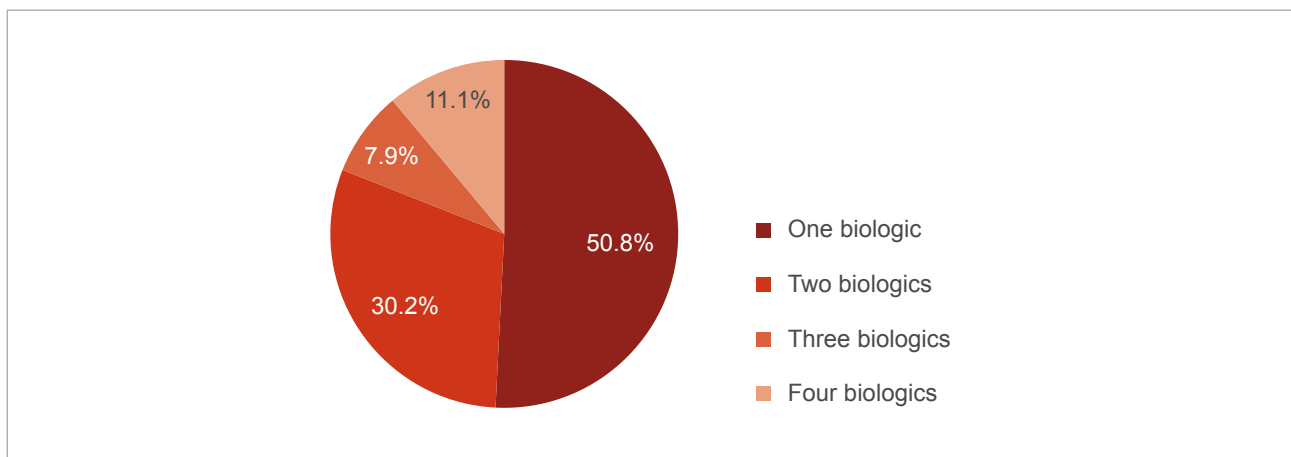
SER has made a series of recommendations based on available evidence relating to AS, a model for Ax-SpA, for which the use of biological therapy is approved in Spain (6).

- Biological therapy is indicated in patients with active SpA and is refractory to conventional therapy.
- Treatment with biological therapy in Ax-SpA is still indicated even if, in spite of suitable conventional treatment, the disease remains active according to the previously indicated criteria.
- The use of biological therapy is not precluded in patients with an extensive radiological condition or absolute limitation of mobility but with activity criteria. In any case, when establishing the definitive indication, the opinion of a rheumatologist or other doctor expert in Ax-SpA and in biological therapy will be considered of utmost relevance.
- Evaluation of whether this treatment is indicated is also considered necessary in patients who meet the ASAS group classification criteria for SpA in both the axial and peripheral forms. The treatment should also be considered for patients when the disease is active and the patient has been refractory to conventional therapy.
- In confirmed cases of AS when the condition is peripheral, sulfasalazine should be used in addition to treatment with NSAIDs, at doses of 2-3 g/day for at least 3 months.
- In cases of enthesitis, dactylitis, monoarthritis or oligoarthritis, local infiltrations with glucocorticoids should also be tested.

Anti-TNF- $\alpha$  drugs have been shown to be effective in patients with SpA by reducing the signs of vertebral inflammation as demonstrated by several studies (7-10). They are effective at any stage of the disease, although the best results are when the disease has not progressed too far (11,12). Its efficacy is also proven in patients who are resistant to NSAIDs and DMARDs, as well as in patients with extra-articular manifestations such as osteoporosis, uveitis and amyloidosis (13-15). On the other hand, recent investigations on the cytokine interleukin-17 (IL-17) showed that it is an important inflammatory mediator acting on monocytes/macrophages, dendritic cells, endothelial cells, osteoblasts, fibroblasts and chondrocytes, among others (3).

More than half of the patients, who declared that they were on biological therapy, had taken only one biologic, although almost half had taken two, three or even four (Figure 9).

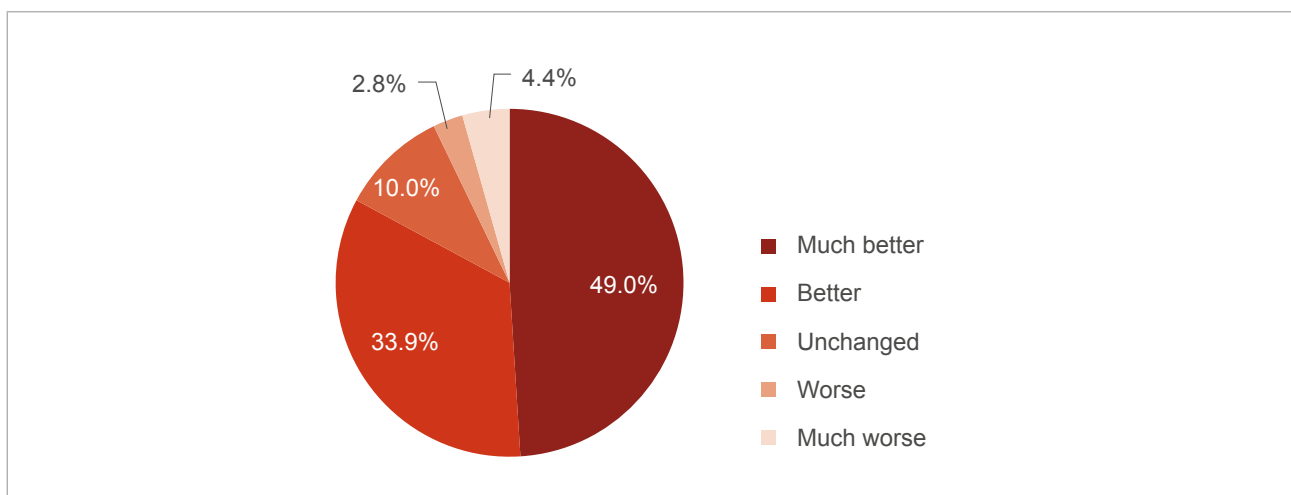
**Figure 9.** Percentage distribution of patients according to the number of different biologics prescribed to date (N: 63)



Source: 2017 Atlas patient survey

In terms of the self-perceived consequences of biological therapies, 82.9% of the patients stated that they felt much better or better than when they did not receive them, 10.0% said they felt the same and only 7.2% said they felt worse or much worse (Figure 10).

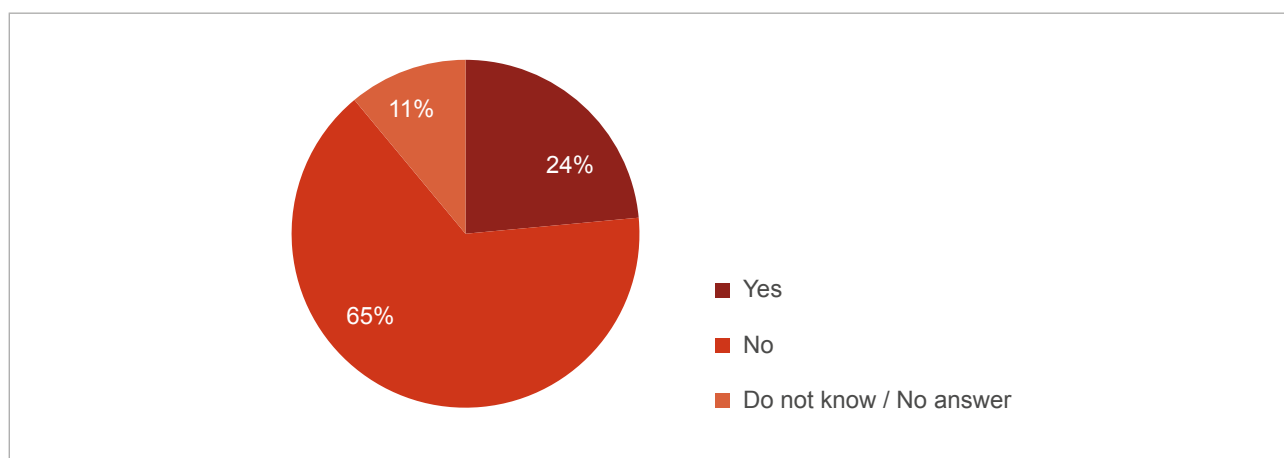
**Figure 10.** Assessment of the difference between taking a biologic drug and not taking it (N: 251)



Source: 2017 Atlas patient survey

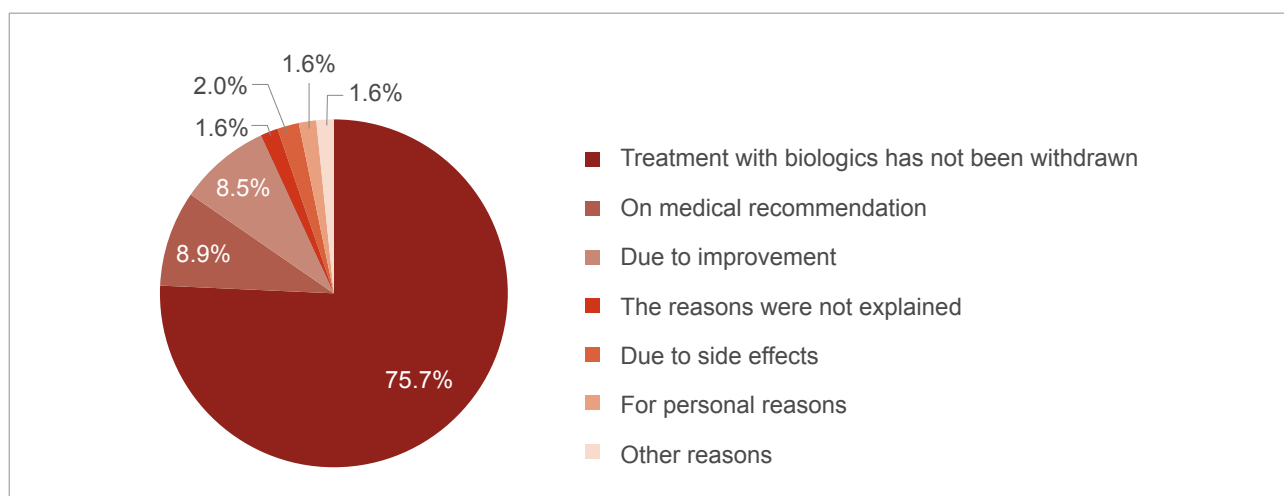
The change in the frequency of biological treatment by lengthening or reducing it occurred in 23.5% of the patients, the main reasons being medical recommendation and improvement in the patient (Figure 11).

**Figure 11.** Patients who have changed consumption frequency in biological treatment in the last 12 months (N: 272)



Source: 2017 Atlas patient survey

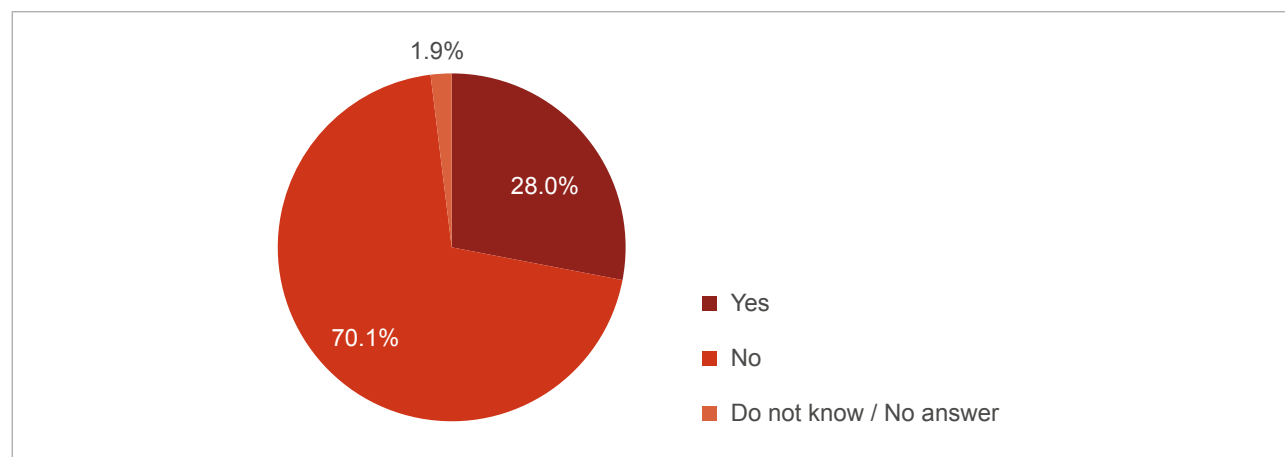
**Figure 12.** Percentage distribution of patients receiving biological treatment in the last 12 months who had their frequency modified for various reasons (N: 247)



Source: 2017 Atlas patient survey

The results show that 28% of the patients reported having changed their biological treatment in the last 12 months (Figure 13).

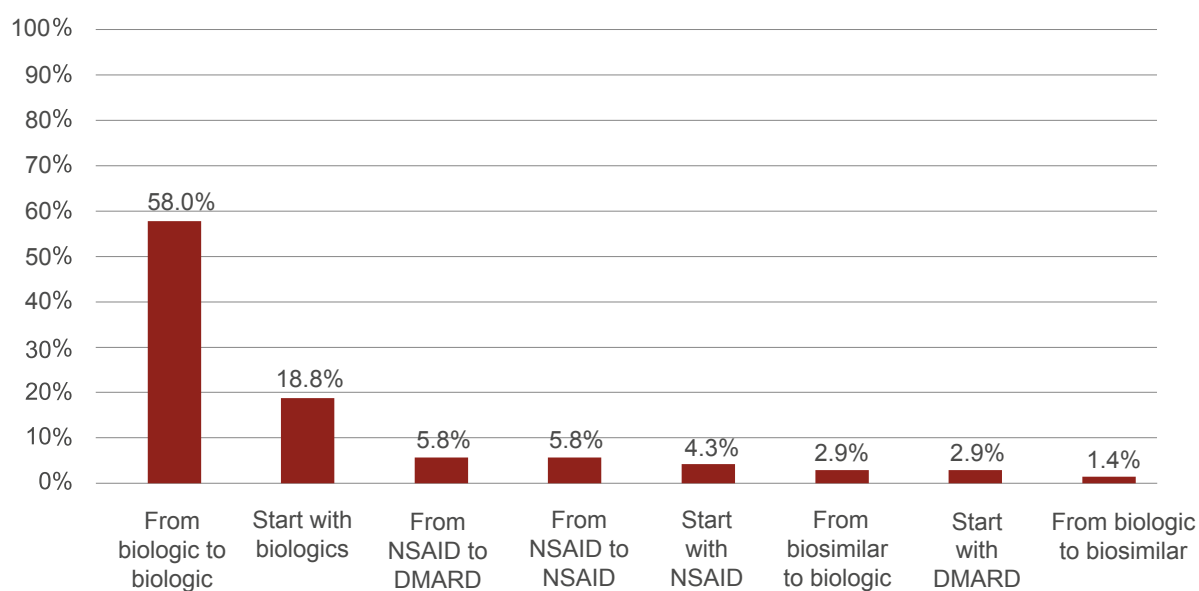
**Figure 13.** Change in biological treatment in the last 12 months (N: 272)



Source: 2017 Atlas patient survey

Among those patients who had changed treatment, most of them moved between different biologics (58%), 18.8% started on biologics, 5.8% changed from NSAIDs to DMARD and an equal percentage changed to a different NSAID. (Figure 14).

**Figure 14.** Patients who changed treatment in the last 12 months, specifying the type of drug (N: 69)



Source: 2017 Atlas patient survey



## 10.5 Effects of pharmacological treatments on quality of life

After treatment with NSAIDs patients rated their improvement in different aspects related to their quality of life using a scale from 0 to 10 in which 0 meant no improvement and 10 greatest improvement. Taking this scale into account and their type of medication, the patients were divided into major improvement ( $\geq 6$ ) and minor improvement ( $\leq 5$ ).

More than half of the patients receiving biological therapy considered that they had achieved a major improvement in their quality of life, compared to less than 30% in the case of NSAIDs and only 21% in the case of DMARDs.

If we distinguish between different aspects of quality of life such as independence, social relations or physical activity, we can observe that patients taking NSAIDs did not think that any of the 7 quality of life aspects they rated had improved by over 30%, which is the level considered to indicate a major improvement. However, for patients taking the biologics the improvement was 51.5%. In the case of biological therapy, it is observed that all activities, except for sports and sexual activity, had a positive score in more than 50% of patients. On the other hand, the performance of leisure and free time activities was considered the aspect where the biological treatment had improved quality of life to the greatest extent (Table 1).

**Table 1.** Major improvement ( $\geq 6$ ) in different aspects related to quality of life in patients treated with biologics (N: 219), NSAIDs (N: 386) and DMARDs (N: 167)

Quality of life	Major improvement Biologics	Major improvement NSAIDs	Major improvement DMARDs
Independence	53.0%	32.1%	22.9%
Leisure and free time	57.4%	31.8%	20.8%
Work related	53.8%	31.7%	22.9%
Social relationships	53.3%	30.0%	23.1%
Sports and physical activity	43.7%	28.4%	17.1%
Mood	55.9%	28.1%	21.5%
Sexual activity	43.2%	26.4%	18.4%
Overall	51.5%	29.8%	21.0%

Source: 2017 Atlas patient survey

In order to more clearly identify the effect of biological and anti-inflammatory therapies, a variable has been created that distinguishes between those taking biological drugs from those taking other types of drugs (NSAIDs and/or NSAIDs without biologics). Table 2 shows how the patients who follow biological therapies present a much larger and statistically significant improvement in each of the areas of daily life for which the associated limitations have been considered.

**Table 2.** Level of average improvement in different aspects related to the quality of life when consuming biologics and other medication

		Work	Mood	Leisure and free time activities	Social relationships	Sports and physical activity	Independence	Sexual	Overall
Biologics	Mean	6.75	6.49	6.31	6.32	5.82	6.53	5.89	5.34
	N	146	184	185	171	169	175	151	199
NSAID without biologic	Mean	5.37	5.18	5.22	4.95	5.19	5.59	5.38	4.59
	N	96	93	109	91	99	93	77	128
Total	Mean	6.2	6.05	5.91	5.84	5.59	6.2	5.71	5.04
	N	242	277	294	262	268	268	228	327
P-value difference between biologics and NSAIDs without biologics		0.00	0.00	0.00	0.00	0.06	0.01	0.14	0.01

Source: 2017 Atlas patient survey

- ▶ A total of 36.3% of the patients were being treated with biologics, 31.5% took NSAIDs and/or DMARDs but without biologics and 32.2% were not taking any type of drug.
- ▶ A total of 51.5% of the patients receiving biological therapy considered that the improvement due to this treatment was major. The figures for NSAIDs was 29.8% and only 21.0% of those who were taking DMARDs considered that they had experienced a major improvement.
- ▶ A total of 83% of patients following biological therapy considered that they were appreciably better than before taking biologics.

## References

1. Collantes E, Zarco P, Muñoz E, Juanola X, Mulero J, Fernández-Sueiro JL, et al. Disease pattern of spondyloarthropathies in Spain: Description of the first national registry (REGISPONSER) - Extended report. *Rheumatology*. 2007;46(8):1309-15.
2. M Dougados, B Dijkmans, M Khan, W Maksymowych, S van der Linden JB. Conventional treatments for ankylosing spondylitis. *Ann Rheum Dis*. 2002;61(3):40-51.
3. Romero-Sánchez C, De A J, Londoño J, Mora A, Bello J, Valle-Oñate R. A new paradigm in spondyloarthritis: Th-17 lymphocytes. *Rev Colomb Reumatol*. 2010;17(1):48-57.
4. Baeten D, Baraliakos X, Braun J, Sieper J, Emery P, van der Heijde D, et al. Anti-interleukin-17A monoclonal antibody secukinumab in treatment of ankylosing spondylitis: a randomised, double-blind, placebo-controlled trial. *Lancet*. November 2013;382(9906):1705-13.
5. Montilla Morales C, Gómez-Castro S, Sánchez M, López R, Hidalgo C, Del Pino-Montes J. New therapeutic targets in psoriatic arthritis. *Reumatol Clin*. 2012;8(SUPPL.1):15-9.
6. Juanola Roura X, Zarco Montejo P, Sanz Sanz J, Muñoz Fernández S, Mulero Mendoza J, Linares Ferrando LF, et al. SER consensus document on the use of biological therapies in ankylosing spondylitis and other spondyloarthritis, except for psoriatic arthritis. *Reumatol Clin*. 2011;7(2):113-23.
7. Baraliakos X, Listing J, Rudwaleit M, Brandt J, Alten R, Burmester G, et al. Safety and efficacy of readministration of infliximab after longterm continuous therapy and withdrawal in patients with ankylosing spondylitis. *J Rheumatol*. 2007;34(3):510-5.
8. Brandt J, Haibel H, Reddig J, Sieper J. Successful Short Term Treatment of Severe Undifferentiated Spondyloarthropathy with the Anti-Tumor Necrosis Factor-  $\alpha$  Monoclonal Antibody Infliximab. *J Rheumatol*. 2002;29(1):4-9.
9. Heiberg MS, Nordvåg B-Y, Mikkelsen K, Rødevand E, Kaufmann C, Mowinckel P, et al. The comparative effectiveness of tumor necrosis factor-blocking agents in patients with rheumatoid arthritis and patients with ankylosing spondylitis: A six-month, longitudinal, observational, multicenter study. *Arthritis Rheum*. 2005;52(8):2506-12.
10. van der Heijde D, Salonen D, Weissman BN, Landewé R, Maksymowych WP, Kupper H, et al. Assessment of radiographic progression in the spines of patients with ankylosing spondylitis treated with adalimumab for up to 2 years. *Arthritis Res Ther*. 2009;11(4):R127.
11. Rudwaleit M, Claudepierre P, Wordsworth P, Cortina EL, Sieper J, Kron M, et al. Effectiveness, safety, and predictors of good clinical response in 1250 patients treated with adalimumab for active ankylosing spondylitis. *J Rheumatol*. 2009;36(4):801-8.
12. Revicki DA, Luo MP, Wordsworth P, Wong RL, Chen N, Davis JC, et al. and Efficacy for Ankylosing Spondylitis (ATLAS) Adalimumab Reduces Pain, Fatigue, and Stiffness in Patients with Ankylosing Spondylitis: Results from the Adalimumab Trial Evaluating Long-Term Safety and Efficacy for Ankylosing Spondylitis (ATLAS). *J Rheumatol*. 2008;35(7).
13. Calin a, Dijkmans B a C, Emery P, Hakala M, Kalden J, Leirisalo-Repo M, et al. Outcomes of a multicentre randomised clinical trial of etanercept to treat ankylosing spondylitis. *Ann Rheum Dis*. 2004;63(12):1594-600.
14. Fernández-Nebro A, Tomero E, Ortiz-Santamaría V, Castro MC, Olivé A, de Haro M, et al. Treatment of rheumatic inflammatory disease in 25 patients with secondary amyloidosis using tumor necrosis factor alpha antagonists. *Am J Med*. 2005;118(5):552-6.
15. Lange U, Teichmann J, Müller-Ladner U, Strunk J. Increase in bone mineral density of patients with rheumatoid arthritis treated with anti-TNF- $\alpha$  antibody: A prospective open-label pilot study. *Rheumatology*. 2005;44(12):1546-8.

## 11. REHABILITATION THERAPIES, PHYSICAL ACTIVITY AND BAD HABITS

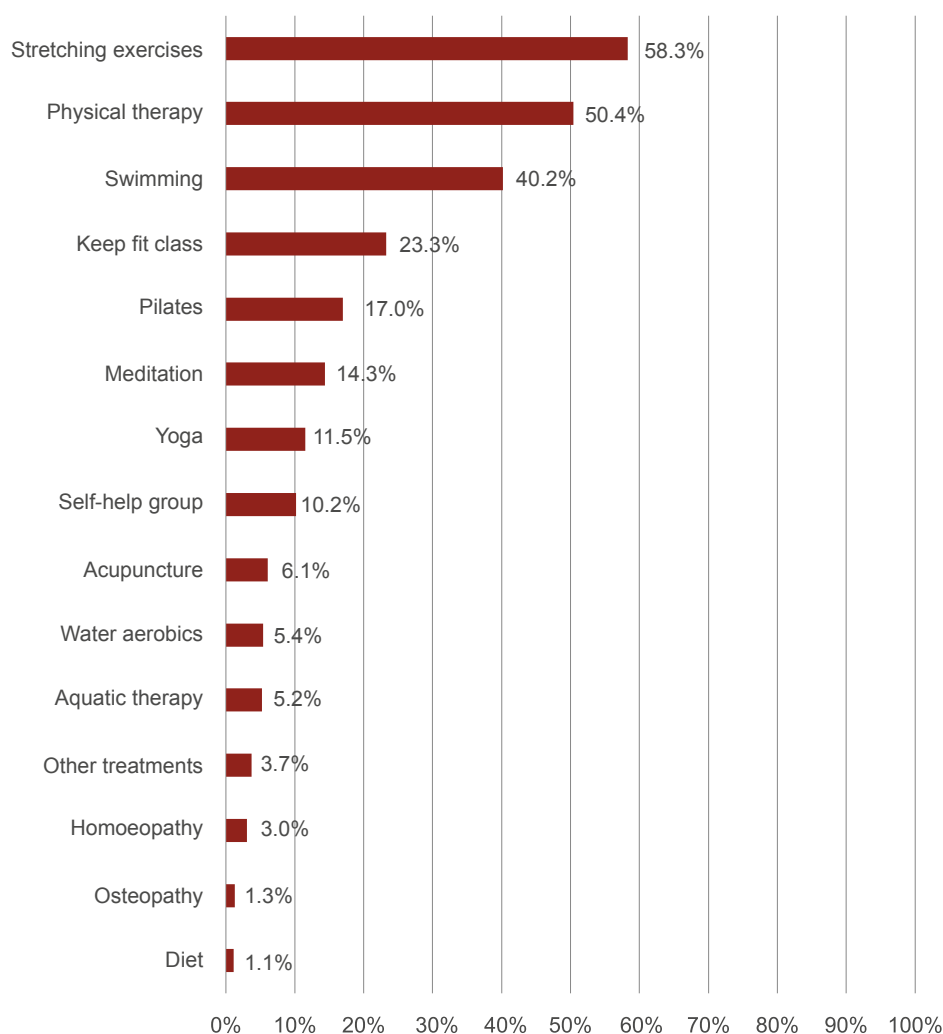
### 11.1 Rehabilitation therapies

It has been shown that regular exercise when suffering from SpA significantly relieves pain, reduces disease activity and fatigue and improves functional status, depression and sleep. In the case of patients with spondylitis receiving treatments with biologics, a direct relationship has been found between exercise and reduced disease activity as assessed by BASDAI score and improvements in joint mobility as assessed by the BASMI scale (1).

Of the non-pharmacological treatments currently used for patients with AS, aerobic strengthening and joint mobility (stretching) exercises or specific exercise programmes such as pilates and swimming have been shown to be effective. In the case of supervised active exercises (in these studies physical therapy is considered to be equivalent to supervised active exercises), studies such as those by Dagfinrud et al. (2) and Hidding et al. (3) have shown that this therapy improved the mobility, physical state and overall functioning of AS patients. In the case of pilates, studies such as those by Altan et al. (4) and Roşu et al. (5) have shown improvements in the functionality, spine mobility, disease activity and thoracic expansion of AS patients. Finally, the study by Karapolat et al. (6) showed the positive effects of swimming on the quality of life and lung function of AS patients.

Figure 1 shows the weekly rehabilitation therapies undertaken by patients with axial spondyloarthritis. This figure includes physical activities or rehabilitation therapies such as physiotherapeutic care, complementary treatments such as homoeopathy or acupuncture and physical activities recommended to enable patients to better cope with the disease, such as water aerobics or aquatic therapy

The data obtained for this indicator show the predominance of activities such as stretching exercises or swimming and treatments such as physical therapy. The percentage of the population with Ax-SpA that uses complementary treatments (acupuncture 6.1% and homoeopathy 3.0%) is much higher than in the general population (0.9% and 1.5%, respectively) (7).

**Figure 1.** Complementary treatments most used by people with Ax-SpA (N: 460)

Source: 2017 Atlas patient survey

For complementary treatments such as aquatic therapy, water aerobics, homoeopathy and acupuncture, Table 1 shows how aquatic therapy is the activity with the highest frequency of mean visits per year. On the other hand, comparing the number of mean acupuncture sessions per year with the study by Torres Ferraz et al. (8) for AS patients in Brazil (2 sessions per year), similar means are observed, even in a sociodemographic context that was different from that in Spain.

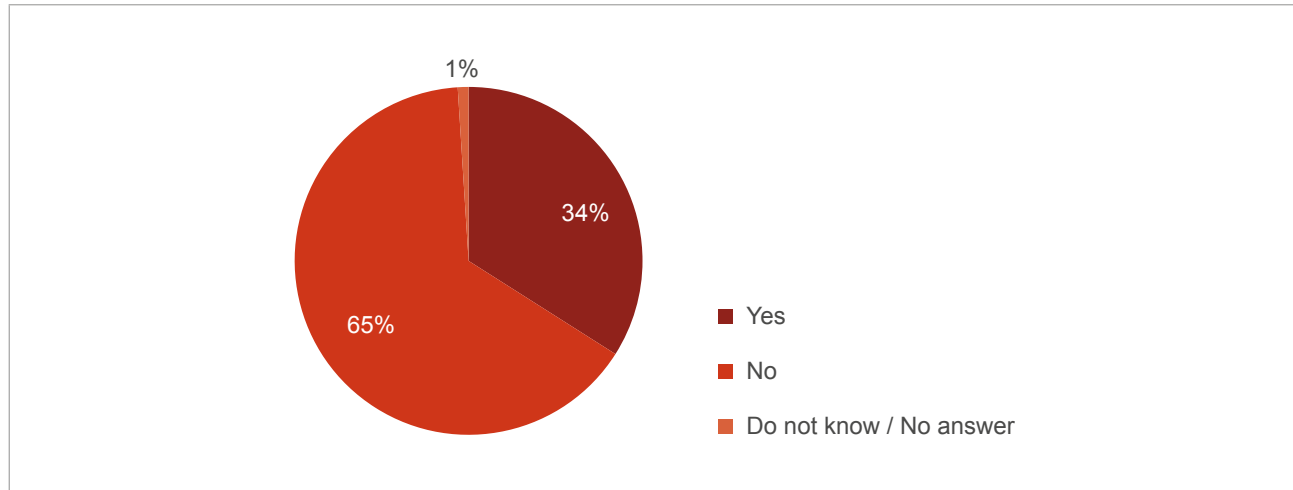
**Table 1.** Monthly sessions of the main complementary treatments (N: 123)

	Mean	Standard deviation	Median	Max	Min
<b>Aquatic therapy</b>	6.9	5.7	6	20	1
<b>Water aerobics</b>	6.5	5.3	6	20	1
<b>Homoeopathy</b>	3.1	3.1	2	12	1
<b>Acupuncture</b>	2.2	1.4	1	5	1

Source: 2017 Atlas patient survey

In the 2017 Atlas survey it was observed that just over one-third of the patients with Ax-SpA had visited a spa in the last year (Figure 2).

**Figure 2.** Percentage of patients who have attended a spa due to their illness in the last year (N: 583)



Source: 2017 Atlas patient survey

Another treatment that is showing good results in the management of AS is balneotherapy, which, in combination with other treatments, has been used for patients with rheumatologic diseases for some time (9). However, to date, only a few studies have been carried out on the effect of this type of treatment on patients affected by rheumatic diseases (10,11). Specifically, the efficacy of balneotherapy therapy in AS has been little investigated. However, both in the study by Tishler et al. (12) and in the one by Van Tubergen et al. (13) positive effects were observed in the use of balneotherapy combined with active exercise programmes.

Most of these treatments or therapies are not covered by public healthcare and, in most cases, they are not covered by private insurance either, so patients devote part of their personal budget to cover the payment for such treatments.

The patients interviewed reported spending on average €115.3 per month on rehabilitation therapies or physical exercise. When the spending is broken down into bands, 29.9% spent more than €100, 42.1% spent between €41 and €100 and 28% spent less than €41 each month.

**Table 2.** Monthly expenditure on rehabilitation therapies or physical exercise for patients with Ax-SpA (N: 311)

<b>Mean</b>	€115.3
<b>Standard deviation</b>	165.7
<b>Median</b>	70
<b>Max</b>	€1,600
<b>Min</b>	0
<b>Range</b>	
€0 ≤ €20	10.3%
€21 ≤ €40	17.7%
€41 ≤ €60	19.3%
€61 ≤ €80	9.6%
€81 ≤ €100	13.2%
€101 ≤ €150	10.3%
€151 ≤ €200	9.3%
€201 ≤ €300	7.1%
≥ €301	3.2%

Source: 2017 Atlas patient survey

## 11.2 Physiotherapeutic care

Visits to the physiotherapist deserve a special section within the therapies to help patients suffering from SpA. Table 3 shows the percentage and number of patients surveyed who used the services of a physiotherapist in each of the different types of healthcare provision (public system, private insurance and private consultations). As can be seen, one-third of the patients had visited a physiotherapist in the last twelve months.

**Table 3.** Visits to a physiotherapist for people with Ax-SpA in the last 12 months (N: 680)

<b>Physiotherapist</b>	<b>Frequency</b>	<b>Percentage</b>
No	452	66.5
Yes	228	33.5

Source: 2017 Atlas patient survey

In addition, as shown in Table 4, women opted for this therapy more often, showing a chi-square test significance level of 0.005.

**Table 4.** Visits to a physiotherapist for people with Ax-SpA by sex (N: 680)

		Visits to a physiotherapist		
		No	Yes	Total
<b>Sex</b>	Men	71.8%	28.2%	100%
	Women	61.6%	38.4%	100%
	Total	66.5%	33.5%	100%

Source: 2017 Atlas patient survey

By age, the youngest people are the most frequent users of the services provided by a physiotherapist, while only 20% of people of retirement age had used this service in the last twelve months.

**Table 5.** Visits to a physiotherapist for people with Ax-SpA in the last 12 months by age group (N: 680)

		Visits to a physiotherapist		
		No	Yes	Total
<b>Age</b>	16 to 31	52.7%	47.3%	100%
	32 to 47	65.1%	34.9%	100%
	48 to 64	69.8%	30.2%	100%
	≥65	80.0%	20.0%	100%
	Total	66.5%	33.5%	100%

Source: 2017 Atlas patient survey

However, a more important aspect is to see if the use of physical therapy has some kind of relationship with the level of disease activity using the BASDAI score as an indicator. Therefore, the average BASDAI score was compared for those people who visit a physiotherapist and those who do not. The results show that patients with Ax-SpA who visit a physiotherapist have a significantly higher average BASDAI ( $p < 0.001$ ) than those who do not visit one (Table 6). This fact could indicate that those patients with the most active disease need more physiotherapeutic attention.

**Table 6.** Average BASDAI score in relation to visits to a physiotherapist for people with Ax-SpA (N: 442)

Physiotherapist	Mean BASDAI
Yes	5.91
No	5.19
Total	5.49

Source: 2017 Atlas patient survey



At this point, it is interesting to analyse the use of physical therapy by patients depending on their employment status. This will allow determination of whether people who feel their work life is affected by the disease use this therapy more or less frequently than other patients. Table 7 shows some very revealing data: a much higher percentage of people on temporary sick leave from work visit a physiotherapist than the rest of the groups. In fact, this is the only group where a majority of people use this therapy. Conversely, for people who are engaged in housework, only 1 in 5 goes to a physiotherapist.

**Table 7.** Visits to a physiotherapist for people with Ax-SpA in relation to their work situation

		Visit a physiotherapist		
		No	Yes	Total
Employment Status	Worker	66.5%	33.5%	100%
	Temporary sick leave	46.0%	54.0%	100%
	Permanent sick leave	67.2%	32.8%	100%
	Early retirement	90.0%	10.0%	100%
	Unemployed	65.6%	34.4%	100%
	Retired	69.8%	30.2%	100%
	Housework (%)	79.3%	20.7%	100%
	Student	55.6%	44.4%	100%
	Do not know / No answer	70.0%	30.0%	100%
	Total	65.6%	34.4%	100%

Source: 2017 Atlas patient survey

On the other hand, physical therapy is a therapy that has associated costs that in many cases are not covered by public healthcare so it is interesting to study the use of physical therapy in different income brackets.

Table 8 shows those patients visiting a physiotherapist in relation to their income level.

**Table 8.** Visits to a physiotherapist by people with Ax-SpA in relation to monthly income in the home (N: 468)

Physiotherapist	Not known / No answer	No income	≤ €500	€501 to ≤ €1,000	€1,001 to ≤ €2,000	€2,001 to ≤ €3,000	> €3,000	Total
Yes	21	6	10	27	70	33	24	191
	45.70%	60%	37%	37.50%	41.70%	37.50%	42.10%	40.81%
No	25	4	17	45	98	55	33	277
	54.30%	40%	63%	62.50%	58.30%	62.50%	57.90%	59.19%
Total	46	10	27	72	168	88	57	468
	100%	100%	100%	100%	100%	100%	100%	100%

Source: 2017 Atlas patient survey

### 11.3 Physical activity

Ax-SpA is a chronic disease that usually progressively erodes a patient's quality of life by limiting their mobility. Exercise, besides improving symptoms, performance status and quality of life, can also prevent the development of deformities (14). Exercise can have beneficial effects on multiple symptoms and signs of the disease, such as vertebral and joint mobility, fatigue, stiffness, self-care and sleep (15). Combined treatment involving an anti-TNF agent with an intensive spa rehabilitation programme has been shown to contribute to a reduction in disability and an improvement in the quality of life of patients with AS (16).

Physical activity and exercise along with pharmacological treatment are increasingly considered an important part of treatment for AS (17). In fact, exercise contributes substantially to the treatment of AS by preserving vertebral flexibility, preventing postural deformities, improving muscle strength and reducing pain (18,19). The importance of exercise in Ax-SpA is such that ASAS / EULAR includes it in its recommendations (17).

It is important that patients with Ax-SpA remain physically active. Sports activities are the best way to achieve physical toning, stabilise blood pressure and heart rate, improve lung capacity and reduce cardiovascular risk. However, not all sports are beneficial for Ax-SpA and it is, therefore, necessary to identify those sports that are particularly appropriate, depending on the state of the disease and previous experience in the practice of each sport (20). Physical activities that promote good posture are recommended, as well as those that extend and rotate the trunk (21). On the other hand, it is not advisable to practice sports that have a greater potential for injury (such as boxing, football, etc.) (22).

Aquatic exercise in a swimming pool has beneficial effects on various musculoskeletal conditions (23). The pilates method developed by Joseph H. Pilates during World War I and improved over the next 50 years, consists of more than 500 stretching and strengthening exercises. Altan et al. (4) demonstrated how pilates exercises represent an effective and safe method to improve the physical capacity of patients with AS. Swimming is a physical activity recommended for patients with AS (6).

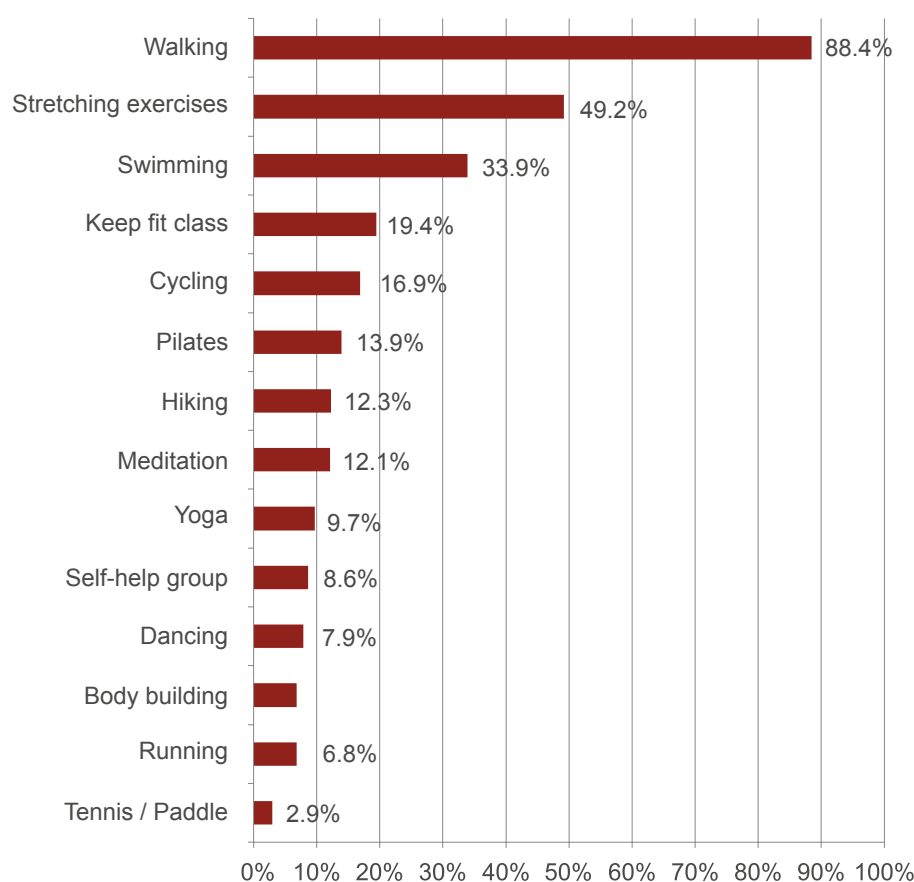
The demonstrated importance of physical activity in patients with AS indicates that it is necessary to develop customised programmes of physical exercise that take patients' personal aspects into account such as possible pain, degree of stiffness and time available (24,25). Although rheumatologists consider exercise a fundamental part of the treatment of rheumatic patients, a greater knowledge and development of specifically prescribed exercise strategies is needed in rheumatology. In fact, in the study by Zarco et al. (15) it was found that referral to physical exercise and sports specialists by the 106 professionals who make up SER's Ax-SpA work group (GRESSER) is not very high. This may be due to different factors, such as that in some centres sufferers may have to go on a waiting list before gaining access to the exercise, or that there are no referral protocols, or there is a lack of specific training for rheumatologists in this regard (15).

Each patient requires an individualised physical programme based on their physiology and their own characteristics. However, rheumatologists do not usually have the necessary training in physical activity techniques, so their recommendations are usually generic and lacking in detail (26). Therefore, it is necessary to improve training in the prescription of individualised physical exercise, since this activity is considered a fundamental part of the treatment for patients with AS by rheumatologists (15).

Patients with Ax-SpA were asked about physical activity in the 2017 Atlas survey. A total of 88.4% of the patients stated that they walked as a physical activity, this percentage being 70.6% for the general population according to data from the Sports Habits in Spain Survey (27). Likewise, the percentage of the Ax-SpA population that swim (33.9%) is higher than the general population (28.8%). On the other hand, activities such as cycling or keep-fit classes were less common among the Ax-SpA population than the general population (27).

In general, and despite the lack of knowledge among rheumatologists regarding the most beneficial physical activities for patients (15), the results (Figure 3) show that patients mostly practice physical activities that are the most suitable for the treatment of AS (4,6,22,23).

**Figure 3.** Activities performed by people with Ax-SpA on a weekly basis (N: 545)



Source: 2017 Atlas patient survey

When analysing the weekly hours dedicated to each of the physical activities, it can be seen that the most common activity on average was walking, followed by self-help groups, keep-fit classes, swimming, hiking and meditation (Table 9).

**Table 9.** Hours per week dedicated to different activities by people with Ax-SpA (N: 418)

	Mean	Standard deviation	Median	Max	Min
<b>Walking</b>	6.2	5.9	5	82	0.5
<b>Self-help group</b>	4.3	6.7	2	40	1
<b>Keep-fit classes</b>	3.5	3.3	2	25	1
<b>Swimming</b>	3.4	4.1	2	45	1
<b>Hiking</b>	3.4	4.2	2	30	1
<b>Meditation</b>	3.3	2.5	3	10	1
<b>Stretching exercises</b>	3.2	2.9	2	20	1
<b>Cycling</b>	3.1	2.9	2	20	1
<b>Body building</b>	3.0	2.1	2	10	1
<b>Yoga</b>	2.9	3.3	2	15	1
<b>Running</b>	2.8	2.1	2	10	1
<b>Dancing</b>	2.5	2.0	2	12	1
<b>Tennis/Paddle</b>	2.3	1.2	2	4	1
<b>Pilates</b>	2.0	0.8	2	5	1

Source: 2017 Atlas patient survey

## 11.4 Beneficial activities

Some activities are considered to be especially beneficial for Ax-SpA patients, including water aerobics, aquatic therapy, walking, meditation, swimming, pilates and yoga. The following table shows the number and percentage of people who reported performing any of these beneficial activities. Table 10 shows that three quarters (75.6%) of the patients surveyed performed one of the activities considered to be beneficial.

**Table 10.** Practice of beneficial activities for people with Ax-SpA (water aerobics, aquatic therapy, walking, meditation, swimming, pilates and yoga) (N: 680)

	Frequency	Percentage
<b>Yes</b>	514	75.6
<b>No</b>	166	24.4

Source: 2017 Atlas patient survey

Table 11 shows the distribution of the activities carried out, distinguishing between men and women. It can be seen that in general, the total percentage of men and women who practice some activity is similar, although water aerobics, meditation, pilates and yoga are practised mostly by women.

**Table 11.** Practice of activities beneficial for people with Ax-SpA by sex (N: 680)

	Men	Women	Total
<b>Walking</b>	50.9%	49.1%	100%
<b>Pilates</b>	23.7%	76.3%	100%
<b>Yoga</b>	26.4%	73.6%	100%
<b>Meditation</b>	30.3%	69.7%	100%
<b>Swimming</b>	52.7%	47.3%	100%
<b>Aquatic therapy</b>	54.2%	45.8%	100%
<b>Water aerobics</b>	36.0%	64.0%	100%
<b>Any beneficial activity</b>	50.2%	49.8%	100%

Source: 2017 Atlas patient survey

By age, the age group between 32 and 64 years of age is the one most likely to practice these beneficial activities, especially pilates, swimming and water aerobics. This is partly because it is the stage when the disease is most active.

**Table 12.** Practice of activities that are beneficial for people with Ax-SpA by age group (N: 680)

	From 16 to 31	From 32 to 47	From 48 to 64	≥65
<b>Walking</b>	7.7%	50.9%	37.0%	4.4%
<b>Pilates</b>	5.3%	64.5%	30.3%	0.0%
<b>Yoga</b>	17.0%	45.3%	28.3%	9.4%
<b>Meditation</b>	9.1%	43.9%	40.9%	6.1%
<b>Swimming</b>	8.2%	48.4%	39.1%	4.3%
<b>Aquatic therapy</b>	12.5%	37.5%	50.0%	0.0%
<b>Water aerobics</b>	4.0%	68.0%	28.0%	0.0%
<b>Any Activity</b>	7.4%	52.1%	36.4%	4.1%

Source: 2017 Atlas patient survey

Since these beneficial activities are fully funded by patients (except for walking), it is interesting to know the distribution of the people who participate in them by economic level, which is shown in the following table. Walking has been excluded, since it does not imply any type of cost and has no relationship with income level. Table 13 shows that people with no income and those earning less than 500 euros a month have stated that they do these activities less than the other strata ( $p < 0.001$ ).

**Table 13.** Practice of activities that are beneficial for patients with Ax-SpA (pilates, yoga, swimming, aquatic therapy, water aerobics and meditation) except for walking by monthly income level (N: 680)

	No income	€500 or less	€501 - €1,000	1,001 - €2,000	2,001 - €3,000	€3,001 or more	Total
<b>Yes</b>	40.0%	44.4%	54.0%	38.1%	42.0%	59.6%	48.1%
<b>No</b>	60.0%	55.6%	46.0%	61.9%	58.0%	40.4%	1.9%
<b>Total</b>	100%	100%	0.0%	100%	100%	100%	100%

Source: 2017 Atlas patient survey

Another point to bear in mind is that some of the patient associations provide information to members to encourage the practice of beneficial activities or they even finance them directly, thereby increasing access for all patients regardless of income. The following table lists the practice of beneficial activities in relation to membership of a patient association.

**Table 14.** Practice of activities that are beneficial for people with Ax-SpA in relation to membership of a patient association.

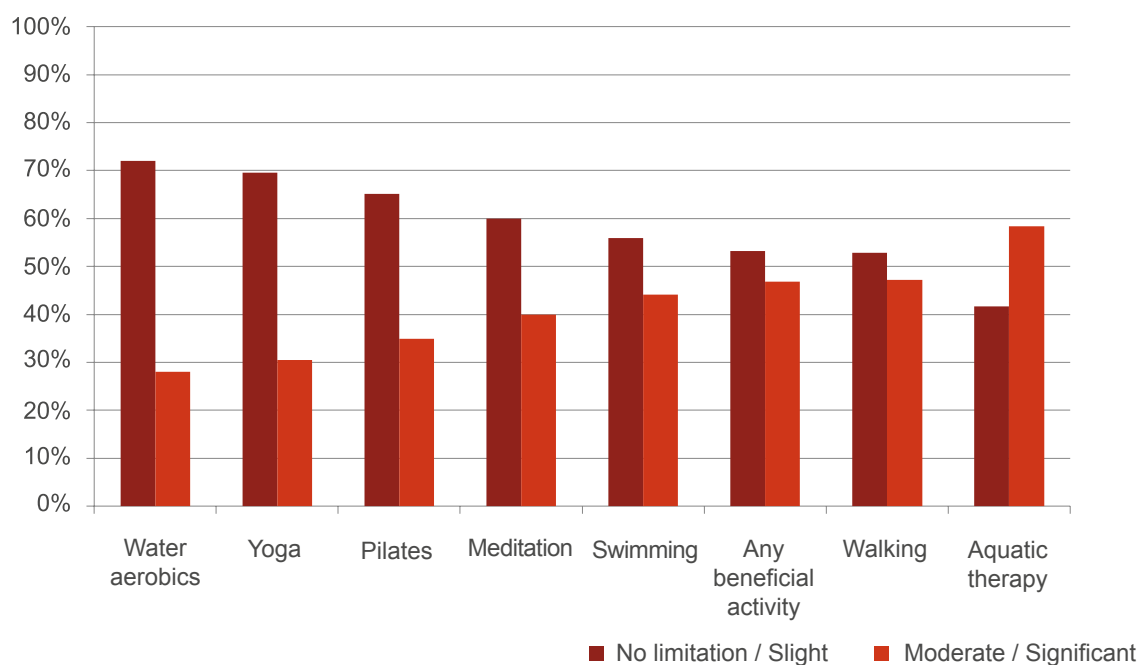
Activities	Member of association		
	Yes	No	Total
Walking	45.64%	54.36%	100%
Pilates	34.21%	65.79%	100%
Yoga	39.62%	60.38%	100%
Meditation	43.94%	56.06%	100%
Swimming	55.14%	44.86%	100%
Water aerobics	64.00%	36.00%	100%
Aquatic therapy	62.50%	37.50%	100%
Any Activity	45.45%	54.55%	100%

Source: 2017 Atlas patient survey

The data show that, except for the case of water aerobics ( $p = 0.04$ ) and aquatic therapy ( $p = 0.07$ ), membership in a spondylitis patients' association does not influence the performance of activities considered to be beneficial to the disease.

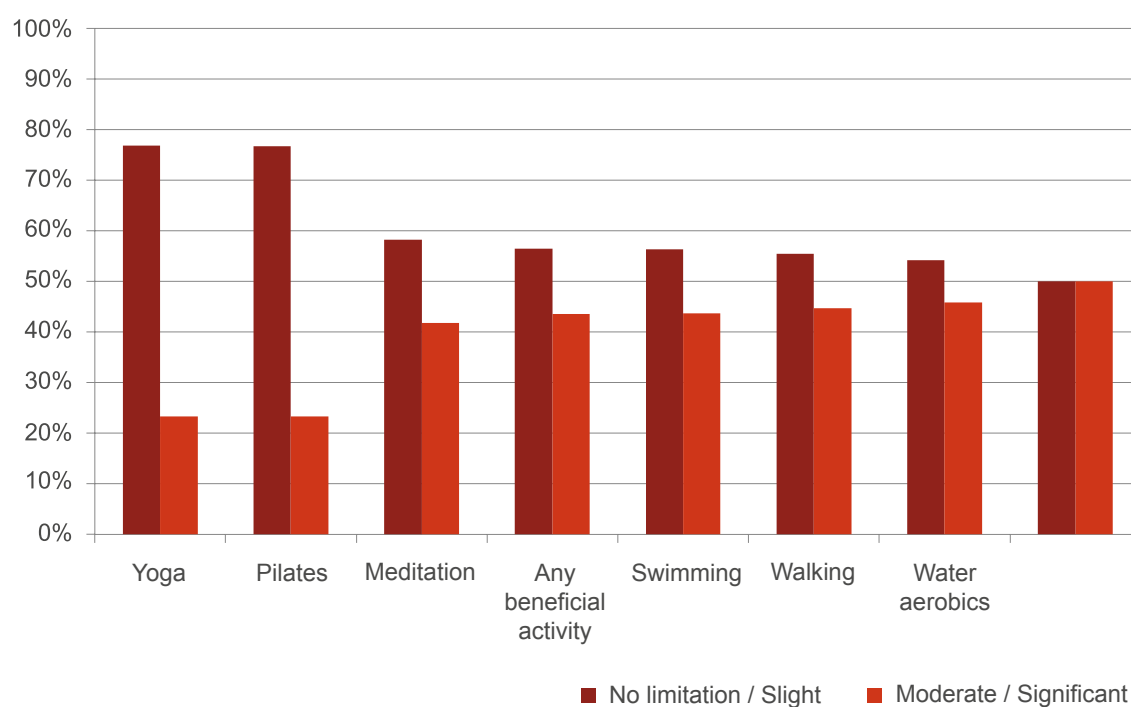
In relation to the degree of disease progression measured through stiffness in the different areas of the spine, the chi-square test indicates that walking, pilates and yoga have a significant relationship with a lower degree of dorsal and lumbar stiffness. The other activities do not show any relationship with different levels of stiffness.

**Figure 4.** Degree of cervical stiffness in relation to the performance of some beneficial activity

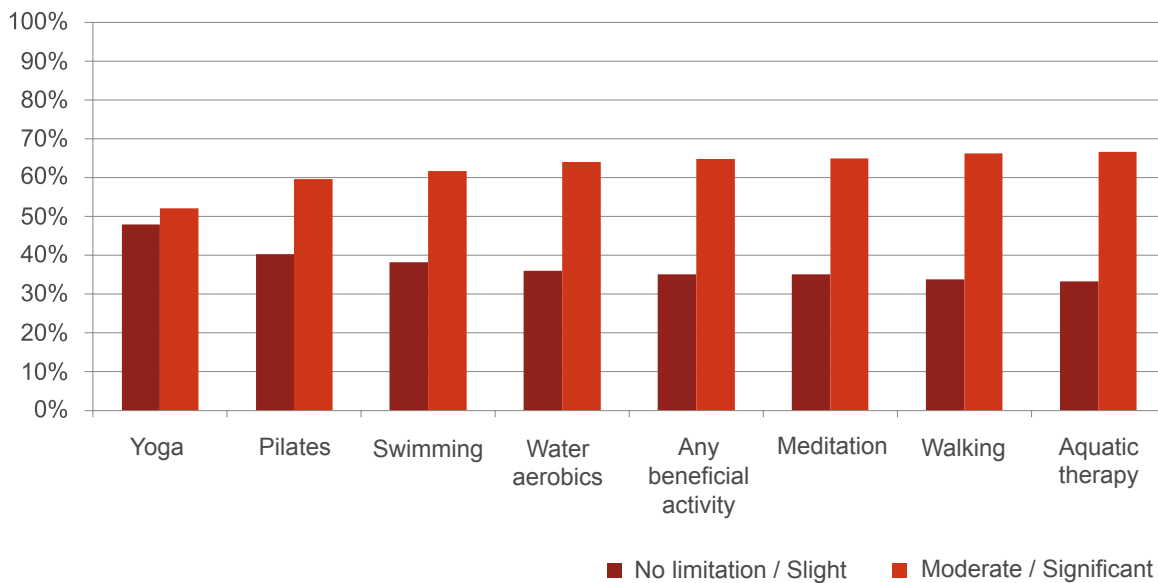


Source: 2017 Atlas patient survey

**Figure 5.** Degree of dorsal stiffness in relation to the performance of some beneficial activity



Source: 2017 Atlas patient survey

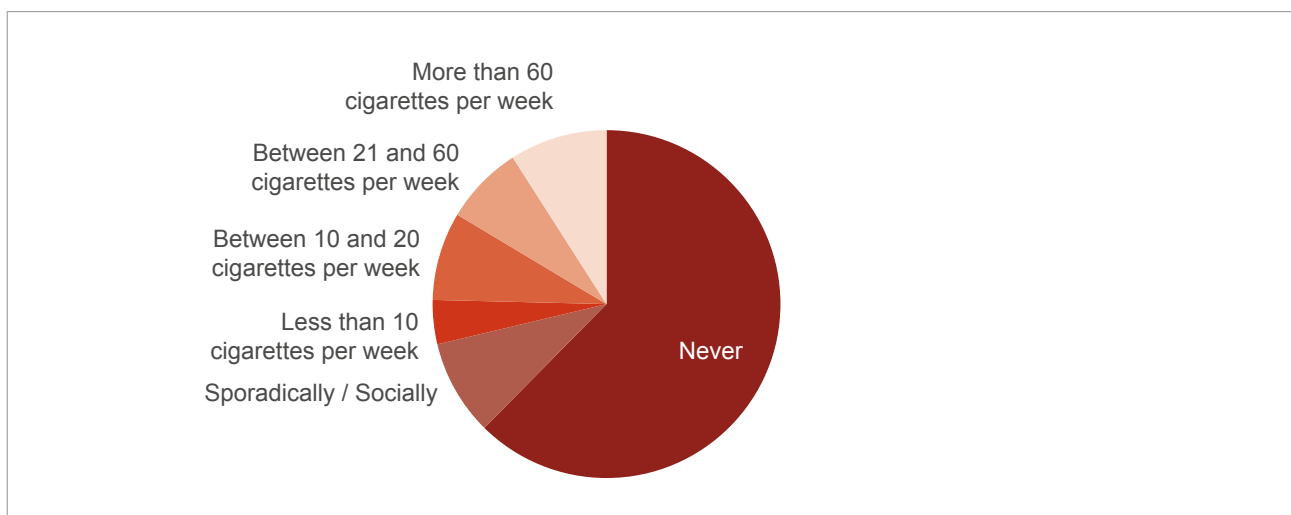
**Figure 6.** Degree of lumbar stiffness in relation to the performance of some beneficial activity

Source: 2017 Atlas patient survey

## 11.5 Bad habits

The relationship between smoking and AS has been studied in recent years (28-30). Smoking is a risk factor for the appearance and progression of Ax-SpA, causing a worsening of performance status and quality of life in patients in the long term (31-33). Smoking has been associated with a more rapid progression in functional disability and with higher levels of functional limitation in people with AS (34). Smoking has been shown to have a negative impact on the quality of life and activity of patients with Ax-SpA (35) and with AS (33). It has also been shown to cause a more rapid progression towards the functional disability of these patients (30). Therefore, avoiding smoking is one of the main recommendations for patients with AS (20).

In this study, 62.4% of the patients with Ax-SpA reported that they were not smokers, 8.9% were occasional smokers and 28.7% were regular smokers.

**Figure 7.** Smoking by people with Ax-SpA (N: 585)

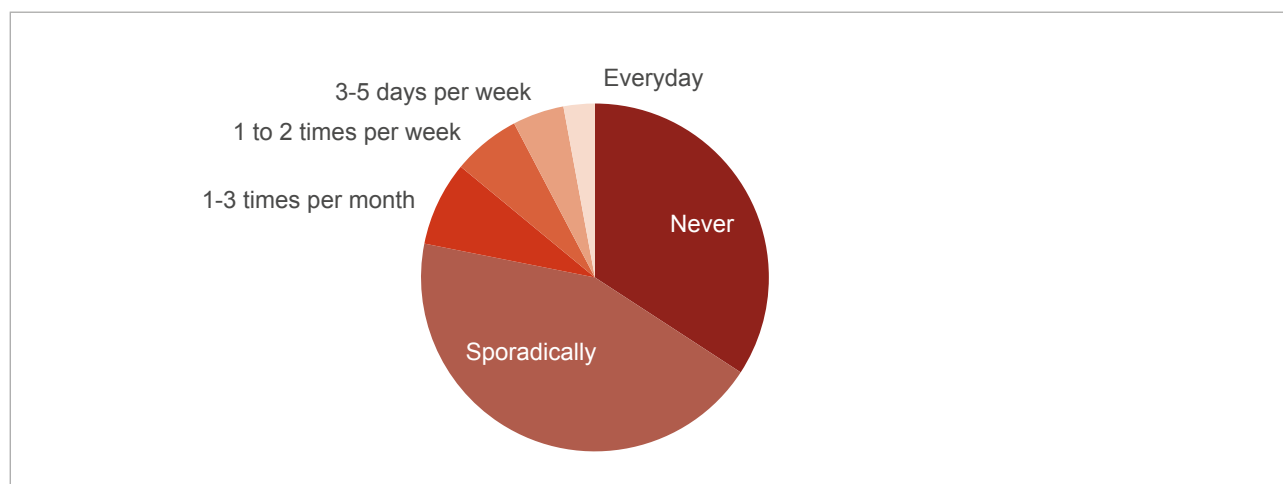
Source: 2017 Atlas patient survey



These percentages are similar to those in the general population, with 65.9% non-smokers, 3.2% occasional smokers and 30.9% regular smokers (36).

Patients who participated in the 2017 Atlas survey reported low alcohol consumption. Specifically, 34.2% reported that they never consume alcohol, while only 7.7% did so on a daily or almost daily basis. In the general population, 32.7% of the general population never drink alcohol, while 19.8% did so on a daily or almost daily basis (36).

**Figure 8.** Alcohol consumption by people with Ax-SpA (N: 585)



Source: 2017 Atlas patient survey

The relationship between alcohol consumption and a worsening of the disease has generated controversy in previous research. While the study by Myllykangas-Luosujärvi et al. (37) showed that alcohol consumption had negative effects on the population with AS in Finland, the study that Zhang et al. (38) conducted in China showed that alcohol consumption reduced night back pain.

- ▶ Despite the importance of non-pharmacological treatments for the treatment and monitoring of the disease, most are not included within the portfolio of services offered by the public health service and, therefore, patients spend an average €115 per month on this type of treatment.
- ▶ Besides walking, the main activities listed by surveyed patients were stretching exercises, swimming, pilates, keep-fit classes, aquatic therapy and water aerobics.

## References

- Liang H, Li W-R, Zhang H, Tian X, Wei W, Wang C-M. Concurrent Intervention With Exercises and Stabilized Tumor Necrosis Factor Inhibitor Therapy Reduced the Disease Activity in Patients With Ankylosing Spondylitis: A Meta-Analysis. *Medicine (Baltimore)*. December 2015;94(50):e2254.
- Dagfinrud H, Kvien TK, Hagen KB. The cochrane review of physical therapy interventions for ankylosing spondylitis. *J Rheumatol*. 2005;32(10):1899-906.
- Hidding A, Van der Linden S, De Witte L. Therapeutic effects of individual physical therapy in ankylosing spondylitis related to duration of disease. *Clin Rheumatol*. 1993;12(3):334-40.
- Altan L, Korkmaz N, Dizdar M, Yurtkuran M. Effect of Pilates training on people with ankylosing spondylitis. *Rheumatol Int*. 2012;32(7):2093-9.
- Roşu MO, Țopa I, Chiriac R, Ancuta C. Effects of Pilates, McKenzie and Heckscher training on disease activity, spinal motility and pulmonary function in patients with ankylosing spondylitis: A randomized, controlled trial. *Rheumatol Int*. 2014;34(3):367-72.
- Karapolat H, Eyigor S, Zoghi M, Akkoc Y, Kirazli Y, Keser G. Are swimming or aerobic exercise better than conventional exercise in ankylosing spondylitis patients? A randomized, controlled trial. *Eur J Phys Rehabil Med*. 2009;45(4):449-57.
- Ministry of Health, Social Services and Equality. Spanish National Health Survey 2011/12 (ENSE 2011/12) [Internet]. 2011 [cited 14 February 2017]. Available on: <https://www.msssi.gob.es/estadEstudios/estadisticas/encuestaNacional/encuesta2011.htm>
- Torres TM, Ferraz MB, Ciconelli RM. Resource utilisation and cost of ankylosing spondylitis in Brazil. *Clin Exp Rheumatol*. 2010;28(4):490-7.
- Sukenik S, Neumann L, Flusser D, Kleiner-Baumgarten A, Buskila D. Balneotherapy for rheumatoid arthritis at the Dead Sea. *Isr J Med Sci*. 1995;31(4):210-4.
- Nguyen M, Revel M, Dougados M. Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized, controlled trial. *Rheumatology*. 1997;36(1):77-81.
- Franke A, Reiner L, Pratzel HG, Franke T, Resch KL. Long-term efficacy of radon spa therapy in rheumatoid arthritis—a randomized, sham-controlled study and follow-up. *Rheumatology*. 2000;39(8):894-902.
- Tishler M, Bostovski Y, Yaron M. Effect of Spa Therapy in Tiberias on Patients with Morning stiffness. *Clin Rheumatol*. 1995;14(1):21-5.
- Tubergen AVAN, Landewe R, Wolter N, Asscher MAX, Falkenbach A, Genth E, et al. Combined Spa – Exercise Therapy Is Effective in Patients With Ankylosing Spondylitis : A randomized, controlled trial. *Arthritis Care Res*. 2001;430-8.
- Aytekin E, Caglar NS, Ozgonenel L, Tutun S, Demiryontar DY, Demir SE. Home-based exercise therapy in patients with ankylosing spondylitis: effects on pain, mobility, disease activity, quality of life, and respiratory functions. *Clin Rheumatol*. 2012;31(1):91-7.
- Zarco P, Florez M, Almodovar R. Opinion of Spanish rheumatologists who are expert in spondyloarthritis on the role of exercise in ankylosing spondylitis and other rheumatic diseases. *Reumatol Clin*. 2016;12(1):15-21.
- Colina M, Ciancio G, Garavini R, Conti M, Trotta F, Govoni M. Combination Treatment with Etanercept and an Intensive SPA Rehabilitation Program in Active Ankylosing Spondylitis. *Int J Immunopathol Pharmacol*. 2009;22(4):1125-9.
- Zochling J, van der Heijde D, Burgos-Vargas R, Collantes E, Davis JC, Dijkmans B, et al. ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis*. 2006;65(4):442-52.
- Zochling J. Assessment and treatment of ankylosing spondylitis: current status and future directions. *Curr Opin Rheumatol*. julio de 2008;20(4):398-403.
- van Tubergen A, Hidding A. Spa and exercise treatment in ankylosing spondylitis: fact or fancy? *Best Pract Res Clin Rheumatol*. 2002;16(4):653-66.
- Feldtkeller E, Lind-Albrecht G, Rudwaleit M. Core set of recommendations for patients with ankylosing spondylitis concerning behaviour and environmental adaptations. *Rheumatol Int*. 2013;33(9):2343-9.
- Lubrano E, Helliwell P, Moreno P, Griffiths B, Emery P, Veale D. The assessment of knowledge in ankylosing spondylitis patients by a self-administered questionnaire. *Rheumatology*. 1998;37(4):437-41.
- Khan MA. Ankylosing spondylitis: introductory comments on its diagnosis and treatment. *Ann Rheum Dis*. December 2002;61 Suppl 3(suppl 3):iii3-7.
- Dundar U, Solak O, Toktas H, Demirdal US, Subasi V, Kavuncu V, et al. Effect of aquatic exercise on ankylosing spondylitis: a randomized controlled trial. *Rheumatol Int*. 2014;1-7.
- Haines TP, Russell T, Brauer SG, Onlinefirst CR. Effectiveness of a video-based exercise programme to reduce falls and improve health-related quality of life among older adults discharged from hospital: a pilot randomized controlled trial. 2009;
- Kingston GA, Williams G, Gray MA, Judd J. Does a DVD improve compliance with home exercise programs for people who have sustained a traumatic

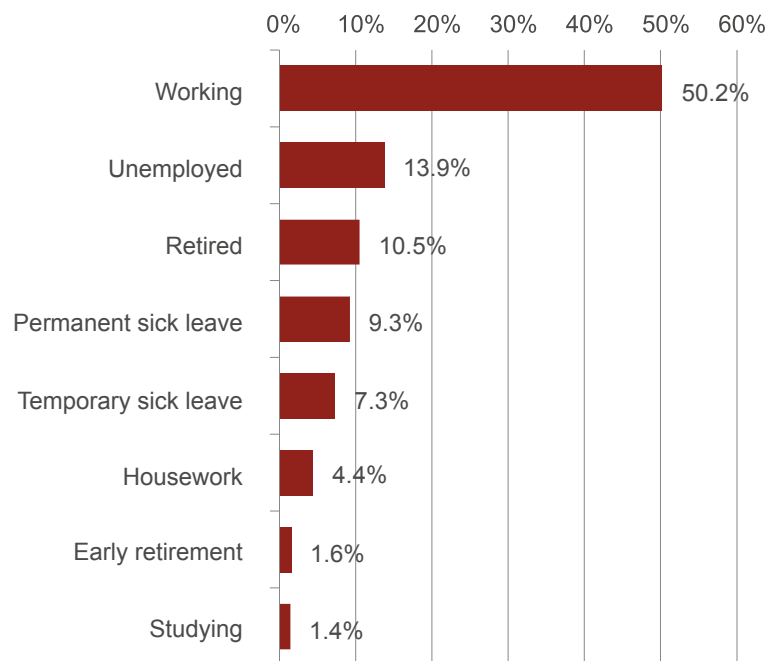
- hand injury? Results of a feasibility study. *Disabil Rehabil Assist Technol*. 2014;9(3):188-94.
26. O'Halloran P, Tzortziou Brown V, Morgan K, Maffulli N, Perry M, Morrissey D. The role of the sports and exercise medicine physician in the National Health Service: a questionnaire-based survey. *Br J Sports Med*. 2009;43(14):1143-8.
  27. Ministry of Education, Culture and Sports. Survey of Sports Habits in Spain [Internet]. 2015 [cited 14 February 2017]. Available on: <http://www.mecd.gob.es/servicios-al-ciudadano-mecd/estadisticas/deporte/en-cuesta-habitos-deportivos.html>
  28. Aaverns HL, Oxtoby J, Taylor HG, Jones PW, Dziedzic K, Dawes PT. Smoking and Outcome in Ankylosing Spondylitis. *Scand J Rheumatol*. 1996;25(3):138-42.
  29. Mattet DL, Dawson SR, Healey EL, Packman JC. Relationship Between Smoking and Patient-reported Measures of Disease Outcome in Ankylosing Spondylitis. *J Rheumatol*. 2011;38(12).
  30. Chung HY, Machado P, Heijde D Van Der, Agostino MD, Dougados M. Smokers in early axial spondyloarthritis have earlier disease onset , more disease activity , inflammation and damage , and poorer function and health-related quality of life : results from the DESIR cohort. *Ann Rheum Dis*. 2012;71(6):809-16.
  31. Kaan U, Ferda Ö. Evaluation of clinical activity and functional impairment in smokers with ankylosing spondylitis. *Rheumatol Int*. 2005;25(5):357-60.
  32. Ward MM, Weisman MH, Davis JC, Reveille JD. Risk Factors For Functional Limitations in Patients With Long-Standing Ankylosing Spondylitis. 2005;53(5):710-7.
  33. Bodur H, Ataman S, Rezvani A, Buğdayci DS, Cevik R, Birtane M, et al. Quality of life and related variables in patients with ankylosing spondylitis. *Qual Life Res*. 2011;20(4):543-9.
  34. Ward MM. Functional disability predicts total costs in patients with ankylosing spondylitis. *Arthritis Rheum*. 2002;46(1):223-31.
  35. Haglund E, Petersson IF, Bremander A, Bergman S. Predictors of Presenteeism and Activity Impairment Outside Work in Patients with Spondyloarthritis. *J Occup Rehabil*. 2015;25(2):288-95.
  36. Spanish National Statistics Institute (INE) European Survey on Health in Spain (ESES) 2014 [Internet]. 2014 [cited 14 February 2017]. Available on: [https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc\\_Eur\\_Salud\\_en\\_Esp\\_2014.htm](https://www.msssi.gob.es/estadEstudios/estadisticas/EncuestaEuropea/Enc_Eur_Salud_en_Esp_2014.htm)
  37. Myllykangas-Luosujärvi R, Aho K, Lehtinen K, Kautiainen H, Hakala M. Increased incidence of alcohol-related deaths from accidents and violence in subjects with ankylosing spondylitis. *Br J Rheumatol*. 1998;37(6):688-90.
  38. Zhang S, Li Y, Xu X, Feng X, Yang D, Lin G. Effect of cigarette smoking and alcohol consumption on disease activity and physical functioning in ankylosing spondylitis : a cross-sectional study. 2015;8(8):13919-27.

## 12. EMPLOYMENT STATUS

### 12.1 Employment status of the patient

This chapter describes the employment status of patients with AS and the repercussions of the disease in terms of work. Figure 1 shows that almost half of the patients (50.2%) were working at the time of the survey. The other half was divided between 13.9% unemployed, 10.5% retired, 9.3% people on permanent sick leave, 7.3% on temporary sick leave, 4.4% dedicated to household chores, 1.6% in early retirement and 1.4% studying. These results are in line with those obtained by Casals-Sánchez et al. (2012), their data shows that approximately 53% of the patients with Ax-SpA in Spain were actively working during the two-year duration of the study (1). The findings also concur with the patients included on the REGISPONSER register, where 52.4% of the patients were working while 36% were unemployed (2). At the international level, it has been documented that 45% of people with SpA in Italy were working full time, 8% part-time and 15% unemployed (3).

**Figure 1.** Current employment status (N: 562)

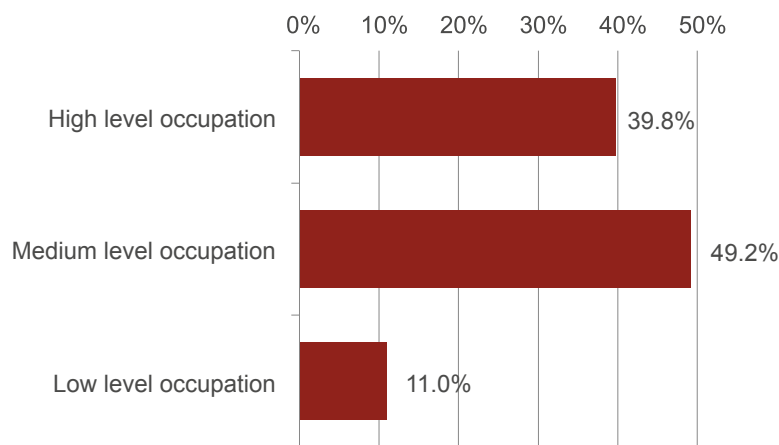


Source: 2017 Atlas patient survey

### 12.2 Working patients

In the working population of the sample, 49.2% belonged to a middle level occupation (government employees, catering, security and business, qualified workers in agriculture, fishing, industry and construction). Of the remaining percentage, 39.8% belonged to a higher level occupation (middle and senior management, professions associated with a college degree, technicians and support professionals) and 11% are framed as having lower level occupations (machinery installers and operators and unqualified workers) (Figure 2). The average weekly working hours were 37.9 hours (Table 1).

**Figure 2.** Workers: Main occupation (N: 264)



Source: 2017 Atlas patient survey

**Table 1.** Workers: Number of hours per week in their main occupation (N: 273)

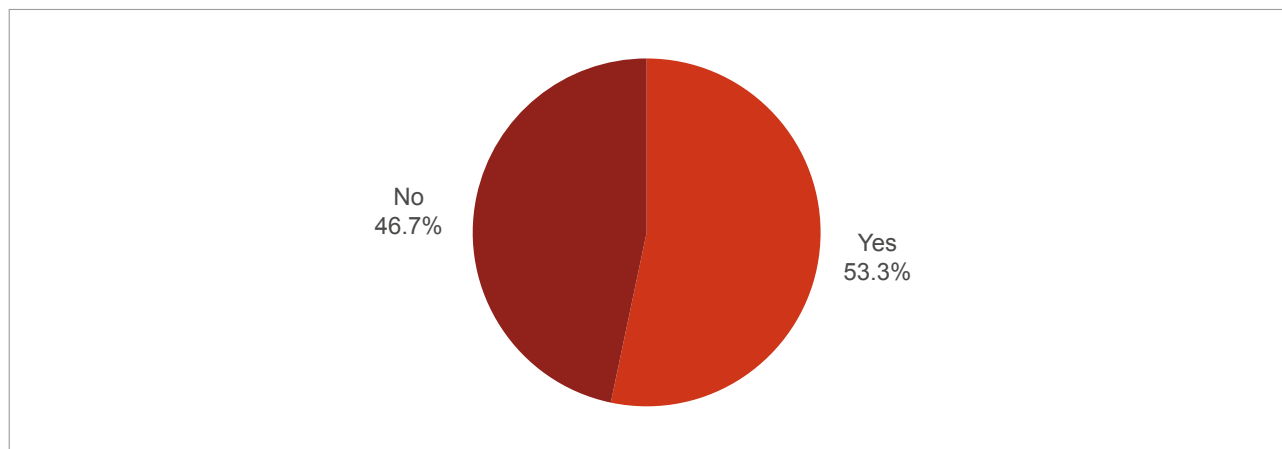
	Mean	Standard deviation	Median	Max	Min
Working hours/week	37.9	10.8	40.0	90.0	3.0

Source: 2017 Atlas patient survey

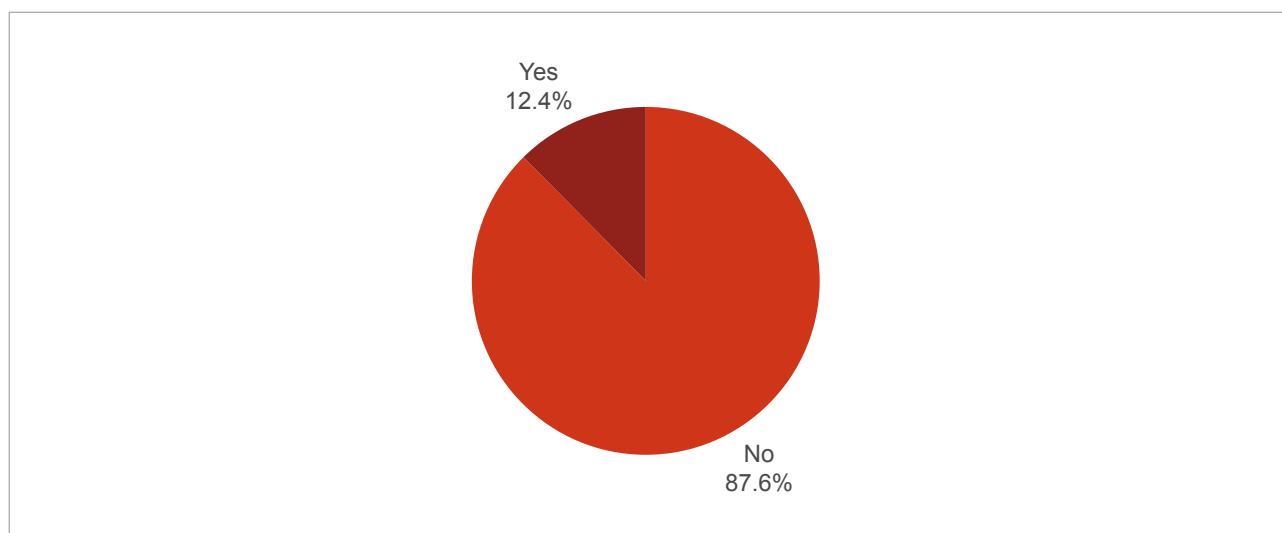
The literature has shown that absenteeism is frequent among workers with AS, particularly during periods with increased disease activity (4). A literature review revealed that, although absenteeism caused by AS has decreased during the past 15 years, the average number of days of work lost ranges from 8 to 46 days per patient, which means a rate three times higher than that of the general population (4). Similarly, a Dutch study estimated that patients with AS lost 5% of working days because of their illness, which meant an average of 10 days of absenteeism over and above the 12 days of the national average (5). A later study showed that in the Netherlands patients with AS lose 9.5% of official work hours due to absenteeism in general and another 7.2% due to absenteeism related to their illness (6).

The results of our survey showed that more than half of the working patients (53.3%) said they had had some kind of absenteeism in the last 12 months as a result of their AS (Figure 3). Of these:

- 12.4% had to request days of paid or unpaid leave (Figure 4), with an average of 5.5 days (Table 2).
- 35.2% had sick leave (Figure 5), with the average length 29.4 days (Table 3).
- 13.1% had to reduce their working hours (Figure 6) by an average of 15.9 hours per week for a period of 10.3 days on average (Table 4).

**Figure 3.** Workers: Work problems due to AS in the past 12 months (N: 272)

Source: 2017 Atlas patient survey

**Figure 4.** Workers: Paid/unpaid leave due to AS in the past 12 months (N: 145)

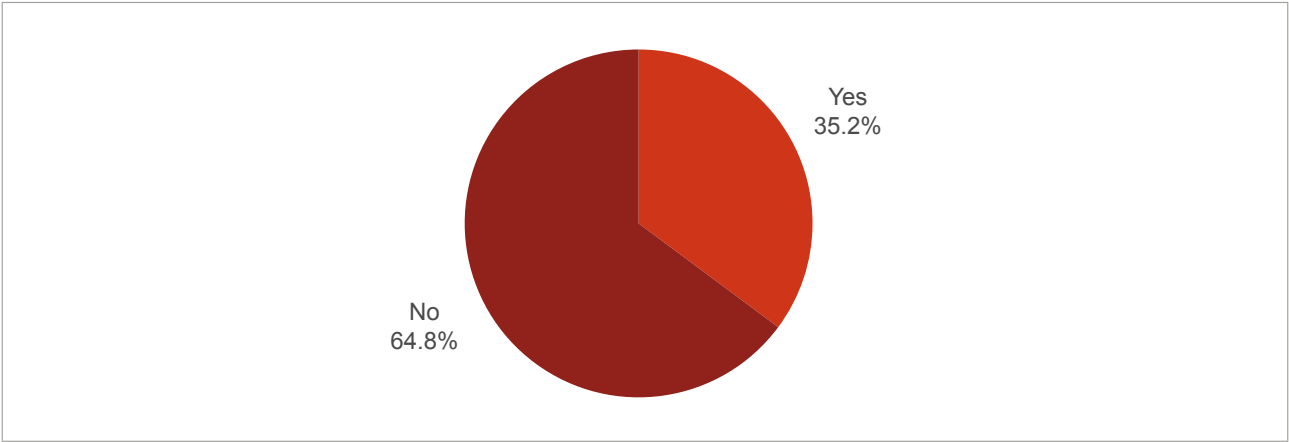
Source: 2017 Atlas patient survey

**Table 2.** Workers: Number of days of paid/unpaid leave due to AS in the past 12 months (N: 17)

	Mean	Standard deviation	Median	Max	Min
Days of paid/unpaid leave	5.5	3.7	5.0	15.0	1.0

Source: 2017 Atlas patient survey

**Figure 5.** Workers: Sick leave due to AS in the past 12 months (N: 145)



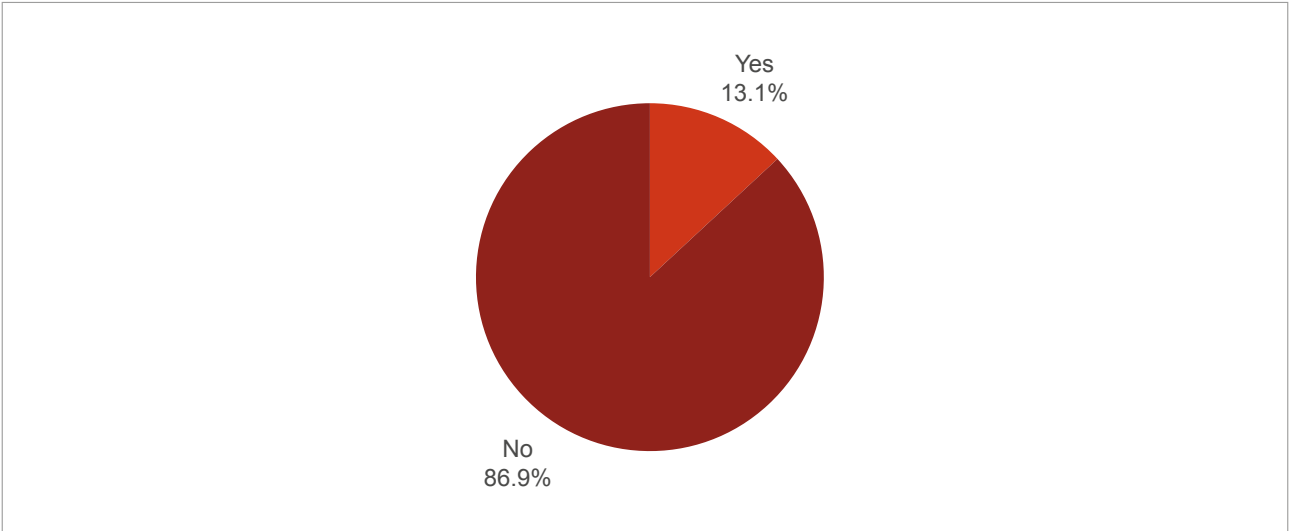
Source: 2017 Atlas patient survey

**Table 3.** Workers: Number of days of sick leave due to AS in the past 12 months (N: 48)

	Mean	Standard deviation	Median	Max	Min
Days of sick leave	29.4	27.8	18.5	90.0	1.0

Source: 2017 Atlas patient survey

**Figure 6.** Workers: Reduction in working hours due to AS in the past 12 months (N: 145)



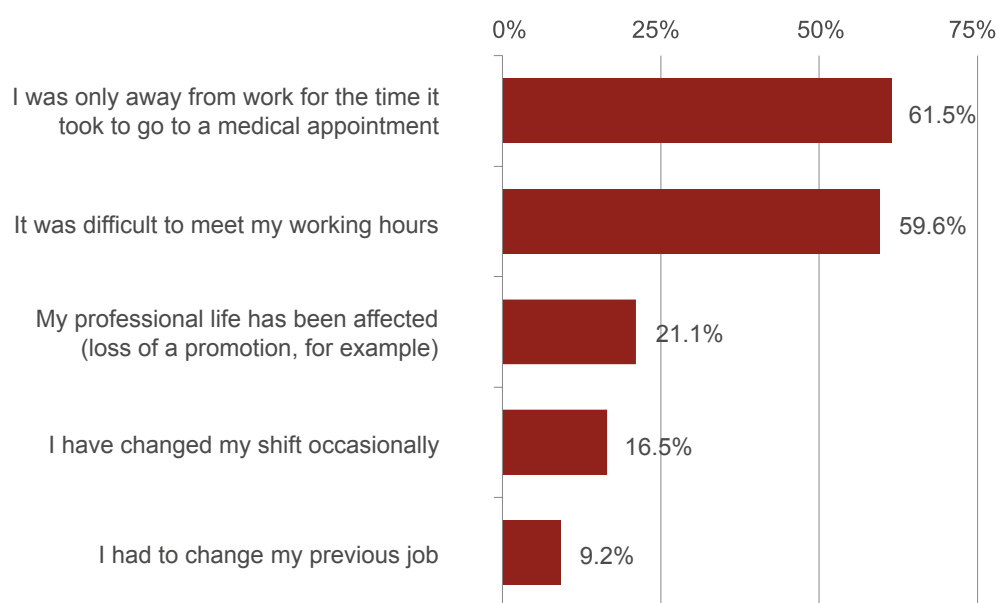
Source: 2017 Atlas patient survey

**Table 4.** Workers: Number of hours and days reduced per week due to AS in the past 12 months (N: 18-8)

	Mean	Standard deviation	Median	Max	Min
<b>Hours / week</b>	15.9	11.5	12.0	50.0	3.0
<b>Days</b>	10.3	20.1	3.0	60.0	1.0

Source: 2017 Atlas patient survey

Furthermore, 61.5% missed work on occasion to go to a medical consultation, 59.6% had difficulties complying with their work hours, 21.1% stated that their professional life had been affected, 16.5% had to change their work hours and 9.2% had to change their previous employment (Figure 7). These findings are consistent with a literature review published in 2015, according to which half of the people with Ax-SpA suffered from job instability, and 15% of them had had to reduce their working hours or change jobs because of their illness. This same review found that both psychological and physical factors played an important role in patients' job instability (7).

**Figure 7.** Workers: Problems related with work due to AS in the past 12 months (N: 109)

Source: 2017 Atlas patient survey

In the survey patients did not evaluate "work presenteeism", understood as a decrease in the effectiveness of the work done by a worker suffering from the disease. The literature shows that presenteeism is an important predictive factor for future sick leaves; (8,9) however, as it is a more diffuse concept than absenteeism, its identification and measurement is much harder, so it is not usually quantified (10). An exception is the study of Boonen et al. (2010), carried out in The Netherlands, where the authors estimated that 53% of workers with AS were experiencing a discomfort which affected them adversely at work. This was causing below-normal efficiency at work, with a score of 7.7 out of 10, where 10 is equivalent to normal efficiency. In turn, this resulted in 1.2 hours per week of inefficiency at work. Therefore, 22% of patients surveyed in the study by Boonen et

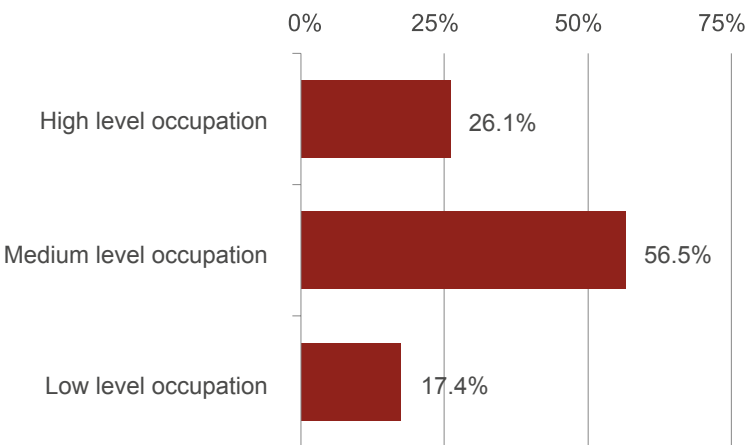


al. (2010) considered that they had to work almost an extra hour a week to compensate for the loss caused by presenteeism. For these patients, the authors quantified presenteeism as costing 1,947 euros a year. The average estimated for the general group of patients with AS, whether they had experienced presenteeism or not, was 967 euros per year (6). Another study, in this case British, concluded that presenteeism represented 1.4% of the total costs associated with AS (11).

### 12.3 Patients on temporary sick leave

Among patients who were on temporary sick leave at the time of the survey, 56.5% belonged to a middle level occupation (government employees, catering, security and business, qualified workers in agriculture, fishing, industry and construction). In addition, 26.1% belonged to a higher level occupation (middle and senior management, professions associated with a college degree, technicians and support professionals) and another 17.4% to a lower level occupation (machinery installers and operators and unqualified workers) (Figure 8). The average working hours usually performed by these people before their sick leave was 37.1 hours per week (Table 5).

**Figure 8.** Temporary sick leave: Main occupation (N: 23)



Source: 2017 Atlas patient survey

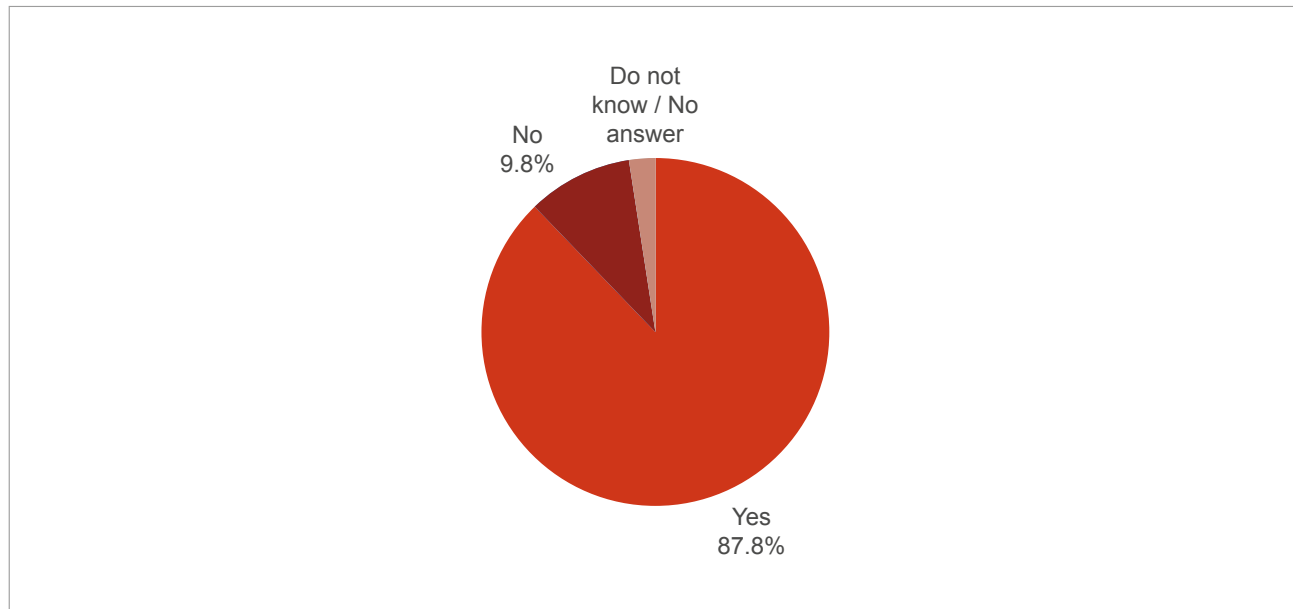
**Table 5.** Temporary sick leave: Number of hours per week in their main job (when not on sick leave) (N: 41)

	Mean	Standard deviation	Median	Max	Min
Working hours/week	37.1	12.3	40.0	80.0	8.0

Source: 2017 Atlas patient survey

According to the people surveyed, in 87.8% of the cases, their temporary sick leave was related to their AS (Figure 9). The average time spent on temporary sick leave, in the past 12 months, due to the disease was 7.0 months (Table 6)

**Figure 9.** Temporary sick leave as a consequence of AS (N: 41)



Source: 2017 Atlas patient survey

**Table 6.** Temporary sick leave: Number of months of temporary sick leave as a consequence of AS in the past 12 months (N: 35)

	Mean	Standard deviation	Median	Max	Min
<b>Months of temporary sick leave</b>	7.0	3.9	6.0	12.0	1.0

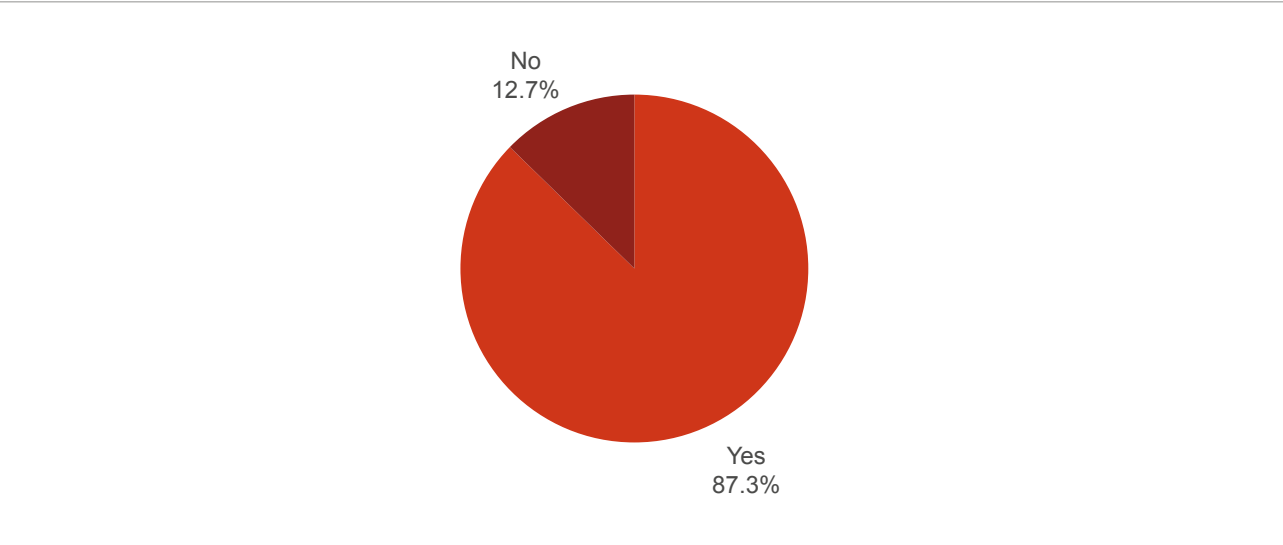
Source: 2017 Atlas patient survey

As this survey was a cross-sectional survey, it did not assess whether the frequency or duration of sick leave increased over time, as found in the study by Castillo-Ortiz et al. (2016). The authors followed a cohort of patients with AS in The Netherlands, France and Belgium for more than a decade and concluded that the prevalence of sick leave increased throughout the period. At the beginning of the survey it was estimated that, with respect to the general population, the likelihood of sick leave was 5.6 times higher among men with AS and 6.4 times higher among women with AS (12). Previous studies have revealed that the duration of sick leave as a result of AS tends to vary between 6 and 18 days (13). It has also been shown that it is conditioned by factors such as age at the time of diagnosis, type of work, treatment received, adaptation of the activities and the existence of help from relatives or third parties (5).

12.4
Patients on permanent sick leave or early retirement

In patients who were on permanent sick leave (either partial, total or absolute incapacity or serious disability) or in early retirement at the time of the survey, in 87.3% of cases their employment situation was related to their AS (Figure 10). The average number of months on permanent sick leave or in early retirement in the past 12 months due to the disease was 11.7 months (Table 7).

**Figure 10.** Permanent sick leave or early retirement as a consequence of AS (N: 63)



Source: 2017 Atlas patient survey

**Table 7.** Permanent sick leave or early retirement: Number of months permanent sick leave or early retirement because of AS in the past 12 months (N: 40)

	Mean	Standard deviation	Median	Max	Min
Months of permanent sick leave or early retirement	11.7	1.1	12.0	12.0	8.0

Source: 2017 Atlas patient survey

A total of 30.8% of patients with AS on permanent sick leave indicated receiving a payment for permanent sick leave from Social Security (reviewable or not), while 44.2% received a payment for absolute permanent disability (reviewable or not). At the national level, according to the REGISPONSER register, 26.5% of patients with Ax-SpA presented some form of work disability during their life, defined as a situation that legally allows them to receive a pension, with 3.9% temporary and 22.6% permanent (2).

The study by Ariza-Ariza et al. (2009) concluded that the main determinants of permanent disability in AS were age, duration of disease, structural damage and physical functioning (14).

## 12.5 Unemployed patients

Among the patients who were unemployed at the time of the survey, 61.3% stated that they had to stop working or that they had lost their job because of their AS. The average number of months unemployed in the past 12 months due to disease stood at 9.9 months (Table 8). It should be noted that a recent study concluded that the risk of withdrawal from the labour market is three times higher among people who suffer from AS than among the general population (7).

**Table 8.** Unemployed patients: Number of months unemployed as a result of AS in the past 12 months (N: 44)

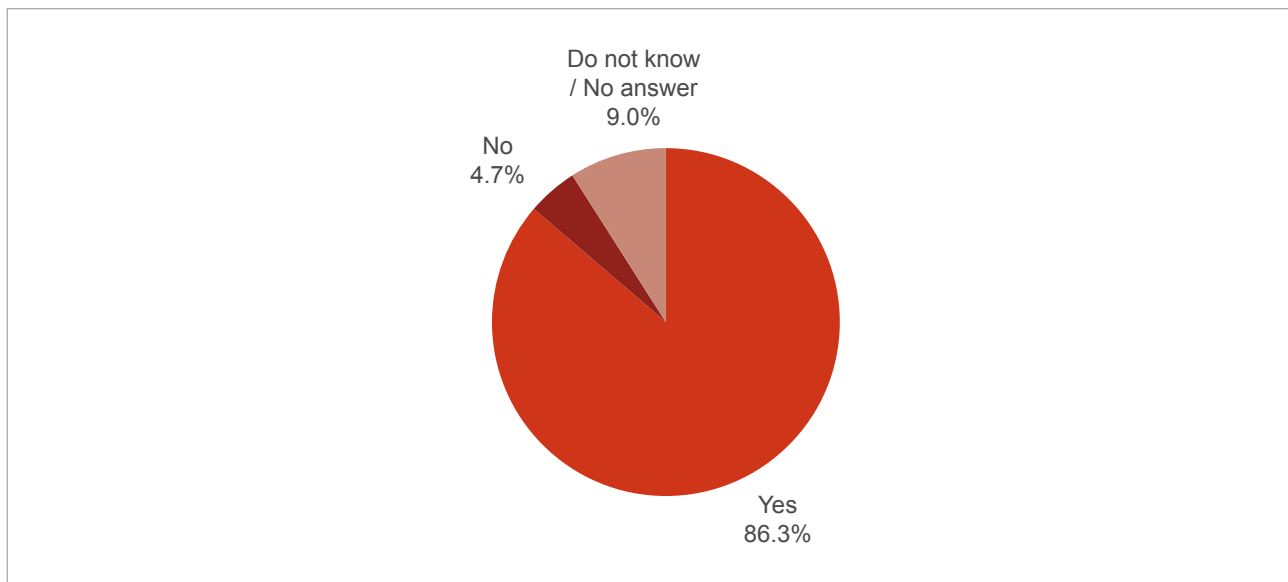
	Mean	Standard deviation	Median	Max	Min
Months unemployed	9.9	3.9	12.0	12.0	0.3

Source: 2017 Atlas patient survey

## 12.6 Difficulties accessing employment

The negative effects of AS can also translate into a lower probability of having a job. In this study, 86.3% of surveyed patients expressed the believe that they had or would have difficulties accessing employment because of their illness (Figure 11).

**Figure 11.** Difficulties accessing employment because of AS (N: 277)



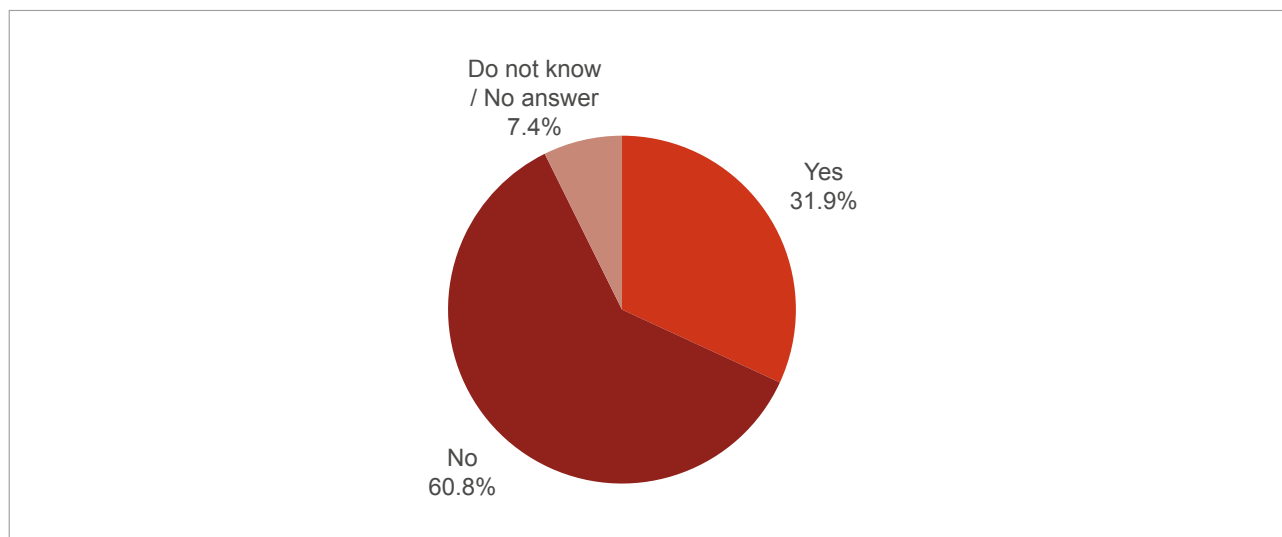
Source: 2017 Atlas patient survey

Previous studies have also pointed out the association between unemployment and diagnosis with AS in different countries, such as Argentina, Turkey, Brazil and the United Kingdom (15-18).

## 12.7 Choice of professional life

Finally, almost a third (31.9%) of the patients surveyed said that their choice of profession was conditioned in some way by their AS (Figure 12).

**Figure 12.** Choice of profession conditioned by AS (N: 505)



Source: 2017 Atlas patient survey

- ▶ People who suffer from AS usually experience problems associated with working.
- ▶ The results indicate high unemployment levels among patients with AS, as well as absenteeism problems for those who work. The latter are mainly due to attendance at medical appointments, problems complying with working hours and negative effects on their professional life.
- ▶ There is a significant link between temporary sick leave and this disease.
- ▶ AS is shown to be a disabling disease as it is associated with high rates of permanent disability.
- ▶ A large majority of patients perceived difficulties in gaining employment because of their illness.

## References

- Casals-Sánchez JL, García De Yébenes Prous MJ, Descalzo Gallego MÁ, Barrio Olmos JM, Carmona Ortells L, Hernández García C. Characteristics of patients with spondyloarthritis monitored in rheumatology units in Spain. EmAR II study. *Reumatol Clínica*. 2012;
- Collantes E, Zarco P, Muñoz E, Juanola X, Mulero J, Fernández-Sueiro JL, et al. Disease pattern of spondyloarthropathies in Spain: description of the first national registry (REGISPONSER)—extended report. *Rheumatology*. 8 January 2007;46(8):1309-15.
- Ramonda R, Marchesoni A, Carletto A, Bianchi G, Cuto M, Ferraccioli G, et al. Patient-reported impact of spondyloarthritis on work disability and working life: the ATLANTIS survey. *Arthritis Res Ther*. 2016;18(1).
- Frauendorf R, de Medeiros Pinheiro M, Ciconelli RM. Variables related to work productivity loss in patients with ankylosing spondylitis. *Rev Bras Reumatol Engl Ed*. 2013;53(3):303-309.
- Boonen A, Chorus A, Miedema H, van der Heijde D, van der Tempel H, van der Linden S. Employment, work disability, and work days lost in patients with ankylosing spondylitis: a cross sectional study of Dutch patients. *Ann Rheum Dis*. 2001;60(4):353-8.
- Boonen A, Brinkhuizen T, Landewe R, van der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. *Ann Rheum Dis*. 2010;69(6):1123-8.
- Martindale J, Shukla R, Goodacre J. The impact of ankylosing spondylitis/axial spondyloarthritis on work productivity. *Best Pract Res Clin Rheumatol*. 2015;29(3):512-23.
- Tran-Duy A, Nguyen TTV, Thijs H, Baraliakos X, Heldmann F, Braun J, et al. Longitudinal Analyses of Presenteeism and Its Role as a Predictor of Sick Leave in Patients With Ankylosing Spondylitis. *Arthritis Care Res*. 2015;67(11):1578-85.
- Haglund E, Petersson IF, Bremander A, Bergman S. Predictors of Presenteeism and Activity Impairment Outside Work in Patients with Spondyloarthritis. *J Occup Rehabil*. 2015;25(2):288-95.
- Skagen K, Collins AM. The consequences of sickness presenteeism on health and wellbeing over time: A systematic review. *Soc Sci Med*. 2016;161:169-77.
- Rafia R, Ara R, Packham J, Haywood KL, Healey E. Healthcare costs and productivity losses directly attributable to ankylosing spondylitis. *Clin Exp Rheumatol*. 2012;30(2):246-253.
- Castillo-Ortiz JD, Ramiro S, Landewé R, van der Heijde D, Dougados M, van den Bosch F, et al. Work Outcome in Patients With Ankylosing Spondylitis: Results From a 12-Year Followup of an International Study: AS Patients and Work Outcome Study Followup. *Arthritis Care Res*. 2016;68(4):544-52.
- Boonen A. A review of work-participation, cost-of-illness and cost-effectiveness studies in ankylosing spondylitis. *Nat Rev Rheumatol*. 2006;2(10):546-53.
- Ariza-Ariza R, Hernández-Cruz B, Collantes E, Batlle E, Fernández-Sueiro JL, Gratacós J, et al. Work disability in patients with ankylosing spondylitis. *J Rheumatol*. 2009;36(11):2512-6.
- Tamborenea MN, Pisoni C, Toloza S, Mysler E, Tate G, Pereira D, et al. Work instability in rheumatoid arthritis patients from Argentina: prevalence and associated factors. *Rheumatol Int*. 2015;35(1):107-14.
- Küçükdeveci AA, Ataman Ş, Genç A, Kutlay Ş, Elhan AH, HOztuna D, et al. Adaptation and validation of the Ankylosing Spondylitis Work Instability Scale (AS-WIS) for use in Turkey. *Rheumatol Int*. 2015;35(1):125-131.
- Frauendorf R, de Medeiros Pinheiro M, Ciconelli RM. Translation into Brazilian Portuguese, cross-cultural adaptation and validation of the Stanford presenteeism scale-6 and work instability scale for ankylosing spondylitis. *Clin Rheumatol*. 2014;33(12):1751-1757.
- Barkham N. The unmet need for anti-tumour necrosis factor (anti-TNF) therapy in ankylosing spondylitis. *Rheumatology*. 2005;44(10):1277-81.

## 13. SOCIETAL BURDEN OF ANKYLOSING SPONDYLITIS

### 13.1 Introduction

AS is a disease that not only affects the physical, psychological and social well-being of the patients, but it also places an economic burden on society (1). As shown in earlier chapters, the impact of AS on patients' quality of life is significant. This impact may require a significant consumption of healthcare and social resources. AS is a chronic and degenerative disease that is diagnosed in early adulthood. The associated functional limitations, pain and impact on patients' quality of life can impair not only their work capacity (as shown in the previous chapter) but also lead to an increase in the consumption of healthcare services throughout their lives. This increase in the use of healthcare services, the need for care from professionals and/or family members and the reduction in their capacity to work due to structural changes, pain and functional limitations affects not only the patient and their family but also society as a whole (1-5).

The fact that AS does not directly affect patients' mortality rate or life expectancy, coupled with the significant delay in diagnosis, makes it a relatively invisible disease for the NHS. It is perhaps for this reason that, so far, health policies in Spain not have given the same priority to allocating resources for the early diagnosis and care of AS, as has occurred in the case of other chronic diseases affecting patients' overall survival, such as diabetes, cardiovascular diseases or cancers.

The economic and societal burden of a disease in a given period of time (e.g. one year) can be interpreted as the total benefit that society would have obtained if the disease did not exist or had previously been eradicated through a preventive programme (6). Therefore, the societal burden of AS in a year represents the maximum annual benefit that would have been obtained if AS had been completely eradicated.

Even though the eradication of AS is currently impossible because it is a congenital disease, the determination of the economic and societal burden of AS is important for several reasons. Firstly, a solid estimate of the societal costs throws light on the real dimension of the disease in economic terms, both for the NHS and for Spanish society. This would, in turn, quantify the importance of the timely treatment of patients. Secondly, knowing the magnitude of its socio-economic impact would give the disease its just importance in comparison with other more "visible" chronic diseases that are currently considered to be priorities. In fact, an estimation of the economic burden of AS would allow an informed assessment of the importance of allocating healthcare resources to its diagnosis and care, in a context of permanent competitive demands for limited healthcare resources. An estimation of the economic burden of AS can provide objective data and essential information both in determining resource use and funding priorities, but also in assisting in future economic assessments of new therapeutic approaches to AS from a societal perspective. This is all against a background in which both the medical community and healthcare payers are increasingly using a cost-effectiveness approach to analyse the growing number of therapeutic options to which the health budget can be allocated. Finally, knowing the dimensions of the different cost items associated with AS is fundamental when making optimal decisions on the allocation of resources for the early detection and management of this disease in the NHS. This can, in turn, have the effect of helping to decrease the societal impact of this condition in the near future.

Until now, an estimation of the economic burden associated with AS in Spain has been hindered by the scarcity of economic data related to the use of healthcare and non-healthcare resources, out-of-pocket costs and patient productivity losses. Thanks to the survey of patients diagnosed with AS we now have valuable, novel and recent information about patients' use of healthcare resources. This allows us to estimate the current socio-economic burden of this disease in our country.

This chapter aims to estimate the average annual cost per patient diagnosed with AS as well as the socio-economic impact. This will be carried out in terms of the direct and indirect costs of AS at the national level in Spain. The main source of data used is the survey questionnaire completed by patients with AS.

## 13.2 Diagnostic costs

Table 1 presents the costs related to diagnosis. It is worth noting that the average cost of visits to the doctor who diagnosed the disease (€109.5) was lower than the average cost of pre-diagnosis visits (€378), the latter accounting for 77.5% of total diagnostic expenditure. This highlights the cost generated as a result of delayed diagnosis, which could be avoided with an early diagnosis.

**Table 1.** Cost/diagnosis: visits to medical professionals (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Visit to the professional who made the definitive diagnosis	109.47	41.26	133.49	20.82	184.71
Visits to professionals prior to diagnosis	378.00	425.84	274.96	0.00	2,818.64
Total cost	487.47	439.35	392.74	39.61	2,952.13

Source: 2017 Atlas patient survey

In relation to the tests performed in order to diagnose the disease, the average total cost was €172.4. The average cost of magnetic resonance at €85.1 represents 49.4% of total expenditure (Table 2). It should be borne in mind that this average cost includes patients who were not given certain tests and others who were given several tests.

**Table 2.** Cost/diagnosis: diagnostic tests performed (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Magnetic resonance imaging	85.13	91.64	0.00	0.00	183.61
Radiography	11.45	8.69	18.04	0.00	18.04
Genetic analysis (HLA B27)	30.91	20.97	45.12	0.00	45.12
Ultrasound	7.99	21.55	0.00	0.00	66.00
Scintigraphy	29.75	55.27	0.00	0.00	132.27
Computerised tomography	5.56	21.27	0.00	0.00	86.81
Other diagnostic tests	1.55	11.40	0.00	0.00	131.93
Total cost	172.35	146.68	183.61	0.00	663.78

Source: 2017 Atlas patient survey

Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.



As a consequence of the diagnostic delay, as discussed in previous chapters, the average total cost for diagnosis was high for a number of the patients. This cost, which includes visits and tests, amounted to an average €659.8 per patient. This cost per patient ranged from €39 to €3,136 (Table 3), due to the difference in the time it took to diagnose a patient, represented by heterogeneous delay times. In fact, thanks to the implementation of the ESPERANZA programme, since 2009 it has been possible to reduce the diagnostic time, with a consequent reduction in this cost.

**Table 3.** Total cost of AS diagnosis per patient (N: 578)

	Mean	Standard deviation	Median	Min	Max
<b>Cost (€ 2015)</b>	659.82	515.83	576.77	39.61	3,135.74

Source: 2017 Atlas patient survey

In population terms, the total cost of diagnosing AS in Spain in the year 2015 was 2.21 million euros (Table 4).

**Table 4.** Total cost of AS diagnosis in Spain

	Total cost	Lower limit 95% CI	Upper limit 95% CI
<b>Cost (million € 2015)<sup>a</sup></b>	2.21	2.07	2.35

Source: 2017 Atlas patient survey

<sup>a</sup> Cost calculated for the total number of incident patients (3,350) estimated from incidence data obtained from the literature (7.2/100,000 inhabitants) and the census on 01/01/2016 (7,8).

Finally, it is important to note that the cost of diagnosis is not included in the calculation of the total annual costs for patients already diagnosed (prevalent patients), since this is a cost that is only assumed once in the life of a patient with AS.

## 13.3 Prevalent patient costs

### 13.3.1 Total costs

#### 13.3.1.1 Total cost per patient / year

The average cost of AS per patient per year was €11,462.3. Of this total, more than half (61.1%) were Direct Healthcare Costs, followed by costs associated with productivity losses (33.6%) (Table 5).

**Table 5.** Costs per patient / year and cost distribution by type

Cost (€ 2015)	Average cost / patient	Lower limit 95% CI	Upper limit 95% CI	% of Total cost
Direct Healthcare Costs	6,999.80	6,246.83	7,752.77	61.1%
Direct Non-Healthcare Costs	611.31	507.03	715.60	5.3%
Productivity losses	3,851.18	3,158.08	4,544.29	33.6%
Total cost	11,462.30	10,339.36	12,585.23	100.0%

Source: 2017 Atlas patient survey  
CI = confidence interval.

Comparison of these results with other studies is difficult because of methodological differences as well as differences between different health systems. Taking this into account, our results are lower than those of the previous study on AS costs for Spain, that of Kobelt et al. (2008), where it was estimated that the average total costs per patient amounted to 20,328 euros in a sample of patients seen in three Spanish hospitals in 2005. The difference between our total costs and those in this previous study may be due to several reasons. Firstly, Kobelt et al. (2008) included the costs of informal care and the costs of the infrastructure adaptations made by patients as part of direct non-healthcare costs. Without taking these two cost components into account, the average total costs of Kobelt et al. (2008) decrease to 11,483 euros per patient per year, a figure that coincides with that found in our study. Secondly, the remaining cost components analysed by Kobelt et al. (2008) are not exactly consistent with ours (9).

The total costs reported by other recent studies conducted in different countries also vary due to differences in methodology and cost types included. For example, Strömbeck et al. (2010) estimated the total costs associated with AS in Sweden at US\$26,024 per patient (approximately 24,500 euros) (10), Lee et al. (2014) estimated that in South Korea the average total costs per patient amounted to 11,646,180 Korean won (equivalent to 9,673 euros) (11), and Franke et al. (2009) estimated them at 9,374 euros per patient per year in The Netherlands (1).

### 13.3.1.2 Total cost per patient / year in relation to severity

The total cost per patient per year is influenced by the severity of the disease. The severity of AS, as demonstrated through the BASDAI scale, showed an average score of 5.4 ( $\pm 2.1$ ), where the group with the lowest inflammatory activity (BASDAI <4) showed an average score of 2.5 ( $\pm 1.1$ ) and patients with greater inflammatory activity (BASDAI  $\geq 4$ ) showed an average score of 6.4 ( $\pm 1.4$ ). Gender is a factor that influences this score, since women score statistically higher than men ( $p = 0.002$ ), with 5.8 ( $\pm 2$ ) against 5.1 ( $\pm 2.1$ ).

In addition, the mean total cost is higher in patients with BASDAI  $\geq 4$  than in patients with BASDAI <4, with average costs of €15,579.7 versus €10,575.8. These differences were significant in the case of Direct Healthcare Costs and productivity losses, although not in relation to Direct Non-Healthcare Costs (Table 6).

**Table 6.** Costs per patient/year according to severity (BASDAI scale)

	<b>BASDAI &lt; 4 (N: 91)</b>	<b>BASDAI ≥ 4 (N: 285)</b>	<b>p-value</b>
	<b>Cost (€ 2015)</b>	<b>Cost (€ 2015)</b>	
Direct Healthcare Costs	7,592.00	9,706.95	0.015*
Direct Non-Healthcare Costs	557.27	767.96	0.240
Productivity losses	2,426.50	5,104.76	0.002*
Total Costs	10,575.78	15,579.67	0.003*

Source: 2017 Atlas patient survey  
\* Statistically significant.

On average, the annual direct healthcare cost per patient is 22% lower for patients with a BASDAI <4, while the cost equivalent for productivity losses is 53% lower than that of patients with a BASDAI ≥4. This result is in line with that of Kobelt et al. (2008) who found that costs increase significantly as the disease worsens and, in particular, the patient's physical functioning (9).

### 13.3.1.3 Total cost per patient / year by sex

Sex was not an influential factor in the mean total cost per patient. Although this cost amounted to €12,167.9 for men and € 10,668.5 for women, the differences were not statistically significant. Once again, the highest expenditure was assumed by Direct Healthcare Costs in both groups (Table 7).

**Table 7.** Costs per patient/year by sex

	<b>Men N: 306)</b>	<b>Women N: 272)</b>	<b>p-value</b>
	<b>Cost (€ 2015)</b>	<b>Cost (€ 2015)</b>	
Direct Healthcare Costs	7,310.92	6,649.79	0.411
Direct Non-Healthcare Costs	551.25	678.88	0.447
Productivity losses	4,305.76	3,339.78	0.890
Total Costs	12,167.93	10,668.45	0.298

Source: 2017 Atlas patient survey

### 13.3.1.4 Total cost per patient / year in relation to the administration of biologics

Differences in the administration of medication to patients with AS can lead to different total costs per patient, both for the cost of the medication itself and for their use of resources and associated health outcomes. This means that significant differences were observed between the patients who were taking biologics and those

who were not. The average cost for the former was €21,752.6 compared to the latter at €5,849.4. These differences were observed both in relation to Direct Healthcare Costs and Direct Non-Healthcare Costs, with both types of costs showing higher values among patients taking biologics. In relation to productivity losses, no significant differences were observed between the two groups (Table 8).

**Table 8.** Costs per patient/year in relation to the administration of biologics

	<b>No treatment (N: 374)</b>	<b>With treatment (N: 204)</b>	<b>p-value</b>
	<b>Cost (€ 2015)</b>	<b>Cost (€ 2015)</b>	
Direct Healthcare Costs	1,847.77	16,445.18	<0.001
Direct Non-Healthcare Costs	598.52	634.76	0.018*
Productivity losses	3,403.14	4,672.60	0.081
<b>Total Costs</b>	<b>5,849.43</b>	<b>21,752.55</b>	<b>&lt;0.001</b>

Source: 2017 Atlas patient survey  
\* Statistically significant.

#### 13.3.1.5 Total cost of AS in Spain

From the official population data and the prevalence of AS in Spain obtained from the scientific literature, a total cost of managing AS in Spain was estimated at 2,666.4 million euros (Table 9).

**Table 9.** Annual total cost of AS management in Spain

	<b>Total cost</b>	<b>Lower limit 95% CI</b>	<b>Upper limit 95% CI</b>
Cost (million € 2015) <sup>a</sup>	2,666.42	2,405.19	2,927.64

Source: 2017 Atlas patient survey  
<sup>a</sup> Cost calculated for the total number of prevalent patients (232,625) estimated from data from scientific literature (12) and the census at 01/01/2016 (8).

### 13.3.2 Direct healthcare costs

#### 13.3.2.1 Medical visits

The specialist services that patients with AS visited as a consequence of their illness and which, therefore, represented a higher average cost were: rheumatology (26.3%), primary healthcare (20.1%), psychiatry/psychology (16.8%) and physical therapy (14.2%). The average cost per patient in 2015 for these specialists was: €244.7 (±293.7), €187.4 (±522.2), €156.5 (±780.7) and €132.1 (±399.4) respectively (Table 10).

**Table 10.** Cost/patient/year: AS-related medical visits in the last 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Rheumatology	244.72	293.73	156.90	0.00	3,922.50
Primary Healthcare	187.36	522.24	39.61	0.00	9,110.30
Nurse	49.63	200.43	0.00	0.00	2,460.00
Traumatology	38.82	156.85	0.00	0.00	2,353.50
Physical therapy	132.09	399.43	0.00	0.00	4,996.80
Ophthalmology	62.84	170.08	0.00	0.00	2,196.60
Pulmonology	13.57	59.75	0.00	0.00	784.50
Cardiology	13.84	60.04	0.00	0.00	627.60
Psychology / Psychiatry	156.49	780.65	0.00	0.00	13,650.30
Other specialities	31.07	172.26	0.00	0.00	3,294.90
Total cost	930.43	1,503.16	471.09	0.00	14,983.95

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.2.2 Medical tests

The total cost, per patient per year of medical tests related to AS was €422.5 ( $\pm 561.2$ ). Some medical tests involved higher costs due to their frequency or high cost. The tests with a higher average cost per patient were blood tests with €186.2 ( $\pm 229.4$ ) per patient per year (44.1% of the total cost of medical tests), followed by magnetic resonance imaging (25.3%), with an average annual cost per patient of €106.7 ( $\pm 241.6$ ) and radiographs with almost €64.7 ( $\pm 116.6$ ) (Table 11).

**Table 11.** Cost/patient/year: AS-related medical tests in the past 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Radiography	64.68	116.58	0.00	0.00	973.29
Magnetic resonance imaging	106.74	241.56	0.00	0.00	2,203.32
Ultrasound	16.79	53.11	0.00	0.00	528.00
Scintigraphy	12.82	56.85	0.00	0.00	529.08
Computerised tomography	3.45	21.71	0.00	0.00	260.43
Blood tests	186.16	229.41	122.76	0.00	2,148.30
Urinalysis	24.51	36.86	13.14	0.00	394.20
Other tests	7.32	48.13	0.00	0.00	734.44
Total cost	422.46	561.17	271.80	0.00	4,894.50

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.2.3 Radiography

Breaking the cost down by area tested, the highest cost was found in the radiography performed in the sacroiliac and lumbar areas, representing 19.3% and 17.8% of the total radiological cost, with a mean of €12.5 ( $\pm 34.7$ ) and €11.5 ( $\pm 29.2$ ) per patient per year respectively (Table 12).

**Table 12.** Cost/patient/year: breakdown of AS-related radiography in the last 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Cervical	7.85	18.43	0.00	0.00	180.00
Dorsal	7.85	18.69	0.00	0.00	156.45
Lumbar	11.49	29.22	0.00	0.00	440.00
Sacroiliacs	12.46	34.68	0.00	0.00	616.84
Whole column	6.54	20.42	0.00	0.00	300.60
Chest	4.84	12.63	0.00	0.00	100.00
Shoulders	2.08	8.80	0.00	0.00	87.36
Knees	3.15	14.41	0.00	0.00	200.30
Hips	5.37	15.63	0.00	0.00	220.33
Hands and fingers	2.31	8.38	0.00	0.00	72.16
Other radiography	0.72	6.01	0.00	0.00	72.16
Total cost	64.68	116.58	0.00	0.00	973.29

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.2.4 Use of emergency services

Visits to the accident and emergency department by patients with AS made for reasons related to the disease resulted in a cost per patient per year of €232.7 ( $\pm 617.2$ ). Most of the expenditure was concentrated in the most used services: 54.4% of the expenditure on hospital emergencies, with €126.6 ( $\pm 351.8$ ) and 40.3% in health centre emergencies with €93.9 ( $\pm 434.4$ ). Home emergencies and the use of emergency ambulances, despite their considerable unit price, represent the lowest average cost due to their low utilisation rate: €4.3 ( $\pm 41.2$ ) and €8 ( $\pm 101.4$ ) respectively per patient per year (Table 13).

**Table 13.** Cost/patient/year: visits to emergencies related to AS in the last 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Hospital emergencies	126.55	351.77	0.00	0.00	4,248.33
Health centre emergencies	93.87	434.44	0.00	0.00	7,057.60
Home emergencies	4.26	41.20	0.00	0.00	777.18
Emergency ambulance	8.01	101.38	0.00	0.00	2,137.86
Total cost	232.69	617.19	0.00	0.00	7,057.60

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.2.5 Hospital admissions

With respect to hospital admissions related to AS in the last year, the average cost per patient is €890.3 (±4,455.2) (Table 14).

**Table 14.** Cost/patient/year: hospital admissions related to AS in the last 12 months (N: 578)

	Mean	Standard deviation	Median	Min	Max
Cost (€ 2015)	890.34	4,455.23	0.00	0.00	66,402.24

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.2.6 Medication

Table 15 reflects the annual cost per patient for medication related to the disease. It can be seen that the average cost of biological treatment has an average of €4,445.6 (±6,676.4) and €40.4 (±90) in pharmacological and administration costs per patient per year, respectively. However, it should be remembered that although this type of medication has a higher cost only a third of the patients surveyed took biologics. On the other hand, the use of NSAIDs represents an average annual cost of €33.6 (±77.1) and DMARDs €4.3 (±13.6) per patient per year.

**Table 15.** Cost/patient/year: AS-related medication in the last 12 months (N: 578)

Cost (€ 2015)		Mean	Standard deviation	Median	Min	Max
NSAIDs		33.64	77.06	0.00	0.00	504.67
DMARDs		4.30	13.62	0.00	0.00	69.15
Biologics	Medication	4,445.56	6,676.39	0.00	0.00	31,802.71
	Administration cost	40.39	90.01	24.60	0.00	499.21
Total cost		4,523.88	6,720.24	38.65	24.60	31,823.22

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

Biologics, including the cost of administration, accounted for more than 99% of the total pharmacological cost, similar to that found in recent studies (1,2,10,11).

### 13.3.2.7 Total direct healthcare costs

The total direct healthcare costs per patient per year amounted to €6,999.8 ( $\pm 9,216.9$ ) (Table 16).

**Table 16.** Cost/patient/year: Direct healthcare costs (N: 578)

	Mean	Standard deviation	Median	Min	Max
<b>Cost (€ 2015)</b>	6,999.80	9,216.85	1,789.19	24.60	75,610.19

Source: 2017 Atlas patient survey

Most of this cost (64.6%) was for pharmacological treatment, followed by visits to professionals (13.3%) and hospital admissions (12.7%). The lowest average costs per patient were recorded for medical tests (6.0%) and the use of emergency services (3.3%) (Table 17).

**Table 17.** Distribution of Direct Healthcare Costs by type of cost

	Cost (€ 2015)	% of total DHC
<b>Visits to professionals</b>	930.43	13.3%
<b>Medical tests</b>	422.46	6.0%
<b>Use of emergency services</b>	232.69	3.3%
<b>Hospital admissions</b>	890.34	12.7%
<b>Medication</b>	4,523.88	64.6%
<b>Direct Healthcare Costs</b>	6,999.80	100.0%

Source: 2017 Atlas patient survey  
DHC = Direct Healthcare Costs.

On the other hand, almost all of the Direct Healthcare Costs (94.3%) were borne by the National Health System, representing a total of €6,603.2 of funding per patient per year (Table 18). The remaining 5.7% of these costs, which translates into €397 per patient per year, were financed privately through the payment for medical insurance or private consultation by the patient or their family.

**Table 18.** Cost/patient/year: Direct Healthcare Costs by type of financing (N: 578)

Cost (€ 2015)	Mean	Standard deviation	% of total cost
<b>NHS financed</b>	6,603.15	9,086.54	94.3%
<b>Privately financed</b>	396.65	1,439.46	5.7%
<b>DHC totals</b>	6,999.80	9,216.85	100.0%

Source: 2017 Atlas patient survey  
NHS = National Health System.  
DHC = Direct Healthcare Costs.

<sup>a</sup> Includes resources used through a private insurance system or private consultations.



A recent study by Greenberg et al. (2016) in the United States analysed the direct costs of patients with AS and reported costs for hospitalisations, use of emergency services and medical consultations at \$6,514 per patient (approximately 6,100 euros) (2). The average pharmacological cost amounted to \$11,214 per patient per year. These costs are higher than those found in our study. The differences may be mainly due to the difference in unit costs of healthcare resources existing between Spain and the United States. Lastly, the relative weight of hospital admissions obtained in this study (12.7%) coincides with that found by Kobelt et al. (2008) (9).

### 13.3.3 Direct Non-Healthcare Costs

#### 13.3.3.1 Alternative treatments

The main complementary therapies used were acupuncture and homoeopathy, which involved an average cost of €53.4 ( $\pm 324.8$ ) per patient per year. Less than 10% of patients followed this type of treatment, the rest had no expense in this heading (Table 19).

**Table 19.** Cost/patient/year: main alternative treatments related to AS in the last 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Acupuncture	26.47	158.22	0.00	0.00	1,500.00
Homoeopathy	26.89	271.23	0.00	0.00	5,040.00
Total cost	53.36	324.77	0.00	0.00	5,040.00

Source: 2017 Atlas patient survey  
Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

#### 13.3.3.2 Rehabilitation therapies and physical exercise

Rehabilitation therapy and physical exercise accounted for an average cost per patient per year of €558 ( $\pm 1,201.5$ ). Independently of the type, the maximum spending was €14,400 per patient per year (Table 20).

**Table 20.** Cost/patient/year: rehabilitation therapies and physical exercise related to AS in the past 12 months (N: 578)

Cost (€ 2015)	Mean	Standard deviation	Median	Min	Max
Total cost <sup>a</sup>	557.96	1,201.45	0.00	0.00	14,400.00

Source: 2017 Atlas patient survey a Cost provided directly by the patient.  
Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

### 13.3.3.3 Total Direct Non-Healthcare Costs

The total Direct Non-Healthcare Costs amounted to €611.3 ( $\pm 1,276.5$ ) per patient per year (Table 21). The greatest cost corresponded to rehabilitation therapy and physical exercise when compared with costs for acupuncture or homoeopathy (Table 22).

**Table 21.** Cost/patient/year: Direct Non-Healthcare Costs (N: 578)

	Mean	Standard deviation	Median	Min	Max
<b>Cost (€ 2015)</b>	611.31	1,276.49	0.00	0.00	14,400.00

Source: 2017 Atlas patient survey  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

**Table 22.** Distribution of Direct Non-Healthcare Costs by type of cost

	Cost (€ 2015)	% of total DNHC
<b>Alternative treatments</b>	53.36	8.7%
<b>Rehabilitation therapies and physical exercise</b>	557.96	91.3%
<b>Direct Non-Healthcare Costs</b>	611.31	100.0%

Source: 2017 Atlas patient survey  
 DNHC = Direct Non-Healthcare Costs.

It should be noted that these costs are limited to direct non-healthcare costs collected by the patient survey and they, therefore, do not include those relating to patient transport, informal care or adaptations made by patients (to housing, car, shoes, etc.).

The direct non-healthcare costs are assumed entirely by the patient. If we add to these costs the direct health-care costs financed by the patient (an average 396,65 euros per year), our results indicate that patients' expenditure amounted to 1,008 euros per year on average, without taking into account adaptations to their housing or car nor expenses incurred for transport.

## 13.3.4 Indirect costs

### 13.3.4.1 Loss of productivity

Productivity losses for patients with AS amounted to an average of €3,851.2 ( $\pm 8,484$ ) per patient per year. It is noteworthy that patients who had to prematurely leave the labour market, either through early retirement or permanent sick leave, were those with the greatest loss of productivity cost, with an average of €16,290.6 ( $\pm 11,813.5$ ). In second place were the unemployed with a productivity loss of €11,250.7 ( $\pm 11,598.5$ ). Lastly, even though some of the patients with AS were working, these also had losses in productivity due to absenteeism, equivalent to €483.6 ( $\pm 2,343.4$ ) per patient per year (Table 23).

**Table 23.** Cost/patient/year: annual labour productivity losses for patients with AS

Cost (€ 2015)	N valid	Mean	Standard deviation	Median	Min	Max
Working	282	483.58	2,343.43	0.00	0.00	34,412.00
Temporary sick leave	41	5,722.64	8,312.93	0.00	0.00	37,007.36
Early retirement <sup>a</sup>	60	16,290.56	11,813.48	22,447.36	0.00	26,224.64
Unemployed	78	11,250.65	11,598.50	4,991.31	0.00	26,224.64
Total	578	3,851.18	8,484.02	0.00	0.00	37,007.36

Source: 2017 Atlas patient survey

<sup>a</sup> Before the standard retirement age (65 years old). Includes permanent sick leave and early retirement.  
 Note: A median cost of zero euros indicates that 50% or more of the patients did not use this resource and, therefore, they are assigned a cost of zero euros.

These costs represent the monetary value that society as a whole loses on average annually due to the disability of patients with AS. The majority of patients in the sample (N = 282) stated they were working at the time of the survey. Even so, these patients suffered productivity losses due to absenteeism equivalent to 483.58 euros as an annual average.

Several studies addressing the impact caused by spondylitis have shown the existence of a direct relationship between the disease and loss in productivity, as well as the importance of using functional disability as a predictor in the evaluation of the costs associated with this disease (13-15). Studies have also been conducted outside Europe to measure the employment impact of AS in countries such as the US (16), Turkey (17), Tunisia (18), Brazil (19) and South Korea (11). In all these studies the indirect costs associated with the disease were high. Malinosvsky et al. (2015) conducted a systematic literature review, analysing 32 studies on loss of productivity among workers with AS in several countries and concluding that the monetary quantification of absenteeism is much more common than that of presenteeism (3). According to their meta-analysis, the average indirect costs associated with the disease range from 661 to 45,954 dollars a year per patient (mean 6,455 dollars). Other studies have obtained similar average magnitudes. For example, the work of Kobelt et al. (2008) placed the indirect costs produced by AS at around 6,840 euros per patient, which accounted for 33.7% of the total, much lower than in countries such as Canada or the UK, with which the results obtained were compared (9). In the Netherlands, Boonen et al. (2010) found that productivity losses for patients on temporary sick leave amounted to 1,451 euros (95% CI: €425 to €2,742), the losses to compensate for inefficient working hours, equivalent to presenteeism, was 967 euros (95% CI: €503 to €1,496) and the costs for replacing workers were around 1,930 euros on average (95% CI: €1,404 to €2,471) (20).

On the other hand, the labour impact caused by AS has also been compared with other rheumatic diseases such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA). In particular, studies by Malhan et al. (2011) and Huscher et al. (2006) showed that the indirect costs associated with workers with AS were superior to those who suffered from RA or PsA (21,22). In addition, presenteeism was greater in workers with spondylitis (10.8%) than among patients with RA (8.4%).

A key aspect in the reduction of average time lost to absenteeism and presenteeism in workers with AS may be the use of pharmacological treatments. However, our analysis showed no significant differences in the costs associated with productivity losses among patients treated with biologics and patients not treated with biologics.

ics. This contrasts with the findings of previous studies that examined the direct effect of certain anti-TNF $\alpha$  biologics (etanercept, infliximab, adalimumab) on indirect costs associated with the disease (13,23,24). These studies showed a direct relationship between the beginning of treatment with a biologic and a gradual reduction in indirect costs. Since our study is transversal and not longitudinal, we cannot rule out the possibility that the indirect costs for patients treated with biologics may decrease over time.

### 13.4 Health-related costs and quality of life

Patients with AS showed an average rating on the GHQ-12 mental health scale of 5.5 ( $\pm 4.4$ ). The level of inflammatory activity proved to be an influential factor in the psychological health of the patients. Thus, patients with BASDAI  $\geq 4$  show GHQ-12 scale scores ( $6.57 \pm 4.18$ ) statistically higher ( $p < 0.001$ ) than patients with BASDAI  $< 4$  ( $2.10 \pm 3.06$ ). Conversely, there is no significant difference in GHQ-12 score in relation to gender, reflecting averages of 5.28 ( $\pm 4.46$ ) and 5.75 ( $\pm 4.29$ ) points in men and women respectively.

The associations between costs, productivity losses and BASDAI and GHQ-12 scores are presented in Table 24. In the case of GHQ-12 score, it was found to have a significant positive association with all types of costs except with direct non-healthcare costs. Increased costs related to higher scores on the scale implying a worse state of mental health. Finally, both scales have a positive association, with  $\rho = 0.514$ , which associates higher BASDAI scores with higher GHQ-12, i.e. increased inflammatory activity with a worse state of mental health. The BASDAI scale score has a significant positive association with all costs associated with the disease. This means that higher levels of disability (highest score on the scale) are associated with higher direct, indirect and total costs.

In the case of GHQ-12 score, it was found to have a significant positive association with all types of costs except with direct non-healthcare costs. Increased costs related to higher scores on the scale implying a worse state of mental health. Finally, both scales have a positive association, with  $\rho = 0.514$ , which associates higher BASDAI scores with higher GHQ-12.

**Table 24.** Correlation between cost, disease activity (BASDAI) and mental health (GHQ-12) in patients with AS

	BASDAI score (N: 376)		GHQ-12 score (N: 406)	
	Correlation coefficient	p-value	Correlation coefficient	p-value
<b>Direct Healthcare Costs</b>	0.168*	0.001	0.184*	<0.001
<b>Direct Non-Healthcare Costs</b>	0.159*	0.002	0.091	0.068
<b>Loss of productivity</b>	0.234*	<0.001	0.134*	0.007
<b>Total Costs</b>	0.227*	<0.001	0.162*	0.001
<b>BASDAI score</b>	1.000	--	0.514*	<0.001
<b>GHQ-12 score</b>	0.514*	<0.001	1.000	--

Source: 2017 Atlas patient survey  
 \*\* Statistically significant at the 99% confidence level.

These results highlight the importance of improving patients' functionality and mental health, not only to see improvements in their daily quality of life, but also for the concomitant potential cost savings that less seriously ill patients with better mental health may represent for the NHS and for society as a whole.

## 13.5 Sensitivity analysis

This section compares the major costs of the base case, i.e. the costs set out in previous sections, against the sensitivity analysis.

The sensitivity analysis takes current practice in Spain into account in relation to the price of biologics (a 30% reduction on official prices, optimisation of vials and optimisation of management time for patients with more than one year of treatment). This results in a reduction in the cost of biological treatment to a total of €2,341.1 per patient per year, which is broken down into €2,304.2 for treatment costs and €36.9 for management costs (Table 25). This suggests that the average annual cost of treatment with biologics per patient could be 48% less in reality.

**Table 25.** Cost/patient/year: medication related to AS in the past 12 months. Comparison of base case versus sensitivity analysis (N: 578)

Cost (€ 2015)		Base case		Sensitivity analysis	
		Mean	Standard deviation	Mean	Standard deviation
NSAIDs		33.64	77.06	33.64	77.06
DMARDs		4.30	13.62	4.30	13.62
Biologics	Medication	4,445.56	6,676.39	2,304.25	3,428.43
	Administration cost	40.39	90.01	36.86	77.22
Total cost		4,523.88	6,720.24	2,379.06	3,467.23

Source: 2017 Atlas patient survey

These changes in biological treatment costs result in changes in direct healthcare costs that, after application of the sensitivity analysis, are reduced to €4,855, passing from 64.6% of total costs to 49% (Table 26).

**Table 26.** Distribution of Direct Healthcare Costs according to cost type. Comparison of base case versus sensitivity analysis

	Base case		Sensitivity analysis	
	Cost (€ 2015)	% of total DHC	Cost (€ 2015)	% of total DHC
<b>Visits to professionals</b>	930.43	13.3%	930.43	19.2%
<b>Medical tests</b>	422.46	6.0%	422.46	8.7%
<b>Use of emergency services</b>	232.69	3.3%	232.69	4.8%
<b>Hospital admissions</b>	890.34	12.7%	890.34	18.3%
<b>Medication</b>	4,523.88	64.6%	2,379.06	49.0%
<b>Direct Healthcare Costs</b>	6,999.80	100.0%	4,854.97	100.0%

Source: 2017 Atlas patient survey  
DHC = Direct Healthcare Costs.

Similarly, the total costs are modified, falling from €11,462.3 to €9,317.5, where the percentage representing the direct healthcare costs is approaching the percentage for productivity loss, with 52.1% and 41.3% respectively (Table 27).

**Table 27.** Costs per patient per year and distribution of the cost depending on type. Comparison of base case versus sensitivity analysis

Cost (€ 2015)	Base case		Sensitivity analysis	
	Average cost / patient	% of Total cost	Average cost / patient	% of Total cost
Direct Healthcare Costs	6,999.80	61.1%	4,854.97	52.1%
Direct Non-Healthcare Costs	611.31	5.3%	611.31	6.6%
Productivity losses	3,851.18	33.6%	3,851.18	41.3%
Total cost	11,462.30	100.0%	9,317.47	100.0%

Source: 2017 Atlas patient survey  
CI = confidence interval.

Therefore, the sensitivity analysis reduced the estimated annual cost of managing AS in Spain to a total of 2,167.5 million euros, compared to the figure of 2,666.4 million euros for the base case (Table 28).

**Table 28.** Total annual cost of managing AS in Spain. Comparison of base case versus sensitivity analysis

Cost (million € 2015) <sup>a</sup>	Total cost	Lower limit 95% CI	Upper limit 95% CI
Base case	2,666.42	2,405.19	2,927.64
Sensitivity analysis	2,167.48	1,937.05	2,397.91

<sup>a</sup> Cost calculated for the total number of prevalent patients (232,625) estimated from data from scientific literature (12) and the census at 01/01/2016 (8). Source: 2017 Atlas patient survey

This result should be interpreted with caution, since the patient sample analysed may not be representative of the population with AS in Spain. As it was an electronic survey that the patients completed voluntarily, it may contain a self-selection bias. This could mean that the sample represents those patients with access to the internet and/or motivated to answer the survey. The latter could be connected with their degree of severity and/or with the hope a patient may have that their responses will be useful, so that in the future treatments will exist that will improve their physical and mental condition.

The costs reflected in this analysis are, therefore, estimations based on relatively in-depth data on the consumption of resources by 578 patients diagnosed with AS. These costs can shed light on the true extent of the socio-economic burden of this disease. It should be noted that our total costs do not include a valuation of the intangible costs associated with the disease and also the costs for patients with AS who are still awaiting diagnosis. This could mean that the overall societal burden of the disease could be even greater.

## 13.6 Scenario analysis

This section details those costs which were not included in the patient questionnaire, but that are available in the literature and that can offer additional information of interest.

### Informal care

The literature data used in the estimation of this scenario are the percentage of patients with AS who needed informal care (26.6%) and the annual hours of care received by these patients (93.6 hours) (9). The unit price applied when it comes to informal care is equivalent to the cost per hour of a non-professional caregiver (equivalent to a household worker) (25). This is as opposed to the data used in the reference article, cost per hour of a professional caregiver, whose unit price is not specified. A cost of zero euros was applied to the patients who did not need informal care. The result obtained is a cost for informal care of €126.5 per patient per year, calculated for the total sample (Table 29).

**Table 29.** Scenario analysis. Cost/patient/year: informal care as a consequence of AS

	N valid	Mean
Cost (€ 2015)	578	126.48

Source: 2017 Atlas patient survey

### Investment in adaptation

The patient questionnaire obtains information regarding the percentage of patients who needed to invest in adaptations (house, car, shoes, etc.). However, the establishment of a standard unit price for each of these items is not considered to be feasible. For this reason, the average cost invested in adaptations related to AS published in the literature has been used (38). As the information regarding investments provided in this article is not broken down by items, the average cost has been applied directly to the whole of the sample. The average cost calculated for the investment in adaptation is €2,302.32 per patient per year (Table 30).

**Table 30.** Scenario analysis. Cost/patient/year: investment in adaptations

	Medium (2005)	Medium (2015)
<b>Cost (€)</b>	1,923.00 <sup>a</sup>	2,302.32 <sup>b</sup>

Source: 2017 Atlas patient survey

<sup>a</sup> Source of average cost of investment in adaptations: Kobelt 2008.

<sup>b</sup> Cost updated with general CPI.

### Total Direct Non-Healthcare Costs

Taking into account the data obtained from the literature (informal care and investment in adaptation), and together with the costs of other treatments from the patient survey, we can estimate a new Direct Non-Healthcare Cost that amounts to €3,040.1. This total is distributed in the following way: 75.7% investment in adaptations, 20.2% corresponds to alternative treatment and rehabilitation therapies and physical exercise, and 4.2% to informal care (table 31).

**Table 31.** Scenario analysis. Direct Non-Healthcare Costs: cost/patient/year and distribution according to cost type

	Cost (€ 2015)	% of total DNHC
Complementary treatments	53.36	1.8%
Rehabilitation therapies and physical exercise	557.96	18.4%
Informal care	126.48	4.2%
Investment in adaptations	2,302.32	75.7%
<b>Direct Non-Healthcare Costs</b>	<b>3,040.12</b>	<b>100.0%</b>

Source: 2017 Atlas patient survey

DNHC = Direct Non-Healthcare Costs.

### Total cost per patient/year

Similarly, it is possible to recalculate the total cost per patient per year and compare its distribution according to cost type (Table 32).



**Table 32.** Scenario analysis. Average cost/year for a patient with AS in Spain and the cost distribution by type

	Base case <sup>a</sup>		Scenario 2 <sup>b</sup>	
	Cost (€ 2015)	% of total cost	Cost (€ 2015)	% of total cost
<b>Direct Healthcare Costs</b>	6,999.80	61.1%	6,999.80	50.4%
<b>Direct Non-Healthcare Costs</b>	611.31	5.3%	3,040.12	21.9%
<b>Productivity losses</b>	3,851.18	33.6%	3,851.18	27.7%
<b>Total cost</b>	11,462.30	100.0%	13,891.10	100.0%

Source: 2017 Atlas patient survey

<sup>a</sup> The Direct Non-Healthcare Costs have been calculated using data from the patient questionnaire.<sup>b</sup> The Direct Non-Healthcare Costs have been calculated using data from the patient questionnaire plus data from the literature relating to "informal care" and "investment in adaptations".

- ▶ As far as we know, this chapter introduces the first approach to the economic and societal burden of AS in Spain in the last 10 years.
- ▶ The total annual cost per prevalent patient amounted to €11,462.30, distributed between direct healthcare costs (61.1%), direct non-healthcare costs (5.3%) and indirect costs attributable to the loss of productivity (33.6%).
- ▶ The AS patients and their families assume part of these costs. The survey found that 5.7% of the direct healthcare costs, as well as all of the direct non-healthcare costs were funded privately, with an estimated outlay of 1,000 euros per patient per year.
- ▶ Losses in productivity equated to 3,851 euros per patient per year.
- ▶ Early diagnosis and appropriate management of patients with AS may contribute to reducing disability in patients thereby increasing their quality of life and mental health. In turn, this could result in a substantial reduction of the direct and indirect costs associated with this disease.

## References

1. Franke LC, Ament AJHA, van de Laar M a. FJ, Boonen A, Severens JL. Cost-of-illness of rheumatoid arthritis and ankylosing spondylitis. *Clin Exp Rheumatol*. August 2009;27(4 Suppl 55):S118-123.
2. Greenberg JD, Palmer JB, Li Y, Herrera V, Tsang Y, Liao M. Healthcare Resource Use and Direct Costs in Patients with Ankylosing Spondylitis and Psoriatic Arthritis in a Large US Cohort. *J Rheumatol*. 1 January 2016;43(1):88-96.
3. Malinowski KP, Kawalec P. The indirect costs of ankylosing spondylitis: a systematic review and meta-analysis. *Expert Rev Pharmacoecon Outcomes Res*. 2015;15(2):285-300.
4. Healey E, Haywood K, Jordan K, Garratt A, Packham J. Impact of ankylosing spondylitis on work in patients across the UK. *Scand J Rheumatol*. January 2011;40(1):34-40.
5. Palla I, Trieste L, Tani C, Talarico R, Cortesi PA, Mosca M, et al. A systematic literature review of the economic impact of ankylosing spondylitis. *Clin Exp Rheumatol-Incl Suppl*. 2012;30(4):S136.
6. Akobundu E, Ju J, Blatt L, Mullins CD. Cost-of-illness studies: a review of current methods. *Pharmacoeconomics*. 2006;24(9):869-90.
7. Muñoz-Fernández S, De Miguel E, Cobo-Ibáñez T, Carmona L, Steiner M, Descalzo MA, et al. Early spondyloarthritis: results from the pilot registry ESPI-DEP. *Clin Exp Rheumatol*. 2010;28(4):498.
8. Spanish National Statistics Institute Continuous Census Statistics. Provisional data as of 1 January 2016. Total population. [Internet]. 2016 [cited 7 November 2016]. Available on: <http://www.ine.es/jaxi/Datos.htm?path=/t20/e245/p04/provi/10/&file=00000002.px>
9. Kobelt G, Sobocki P, Mulero J, Gratacos J, Pocovi A, Collantes-Estevez E. The Burden of Ankylosing Spondylitis in Spain. *Value Health*. 2008;11(3):408-15.
10. Strömbeck B, Englund M, Bremander A, Jacobsson LTH, Kedza L, Kobelt G, et al. Cost of Illness from the Public Payers' Perspective in Patients with Ankylosing Spondylitis in Rheumatological Care. *J Rheumatol*. 11 January 2010;37(11):2348-55.
11. Lee T-J, Park B-H, Kim JW, Shin K, Lee EB, Song Y-W. Cost-of-Illness and Quality of Life in Patients with Ankylosing Spondylitis at a Tertiary Hospital in Korea. *J Korean Med Sci*. 2014;29(2):190-7.
12. Stolwijk C, van Onna M, Boonen A, van Tubergen A. Global Prevalence of Spondyloarthritis: A systematic review and meta-analysis. *Analysis of SpA Prevalence. Arthritis Care Res*. September 2016;68(9):1320-31.
13. Tran-Duy A, Nguyen TTV, Thijs H, Baraliakos X, Heldmann F, Braun J, et al. Longitudinal Analyses of Presenteeism and Its Role as a Predictor of Sick Leave in Patients With Ankylosing Spondylitis. *Arthritis Care Res*. 2015;67(11):1578-85.
14. Boonen A, van der Heijde D, Landewé R, Spoorenberg A, Schouten H, Rutten-Van Mölken M, et al. Work status and productivity costs due to ankylosing spondylitis: comparison of three European countries. *Ann Rheum Dis Lond*. 2002;61(5).
15. Strömbeck B, Jacobsson LTH, Bremander A, Englund M, Heide A, Turkiewicz A, et al. Patients with ankylosing spondylitis have increased sick leave -a registry-based case-control study over 7 years. *Rheumatology*. 2009;48(3):289-92.
16. Ward MM. Functional disability predicts total costs in patients with ankylosing spondylitis. *Arthritis Rheum*. 2002;46(1):223-31.
17. Akkoç N, Direskeneli H, Erdem H, Gül A, Kabasakal Y, Kiraz S, et al. Direct and indirect costs associated with ankylosing spondylitis and related disease activity scores in Turkey. *Rheumatol Int*. 2015;35(9):1473-8.
18. Younes M, Jalled A, Aydi Z, Zrour S, Korbaa W, Salah ZB, et al. Socioeconomic impact of ankylosing spondylitis in Tunisia. *Joint Bone Spine*. 2010;77(1):41-46.
19. Torres TM, Ferraz MB, Ciconelli RM, others. Resource utilisation and cost of ankylosing spondylitis in Brazil. *Clin Exp Rheumatol*. 2010;28(4):490.
20. Boonen A, Brinkhuizen T, Landewe R, van der Heijde D, Severens JL. Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. *Ann Rheum Dis*. 2010;69(6):1123-8.
21. Malhan S, Pay S, Ataman S, Dalkilic E, Dinc A, Erken E, et al. The cost of care of rheumatoid arthritis and ankylosing spondylitis patients in tertiary care rheumatology units in Turkey. *Clin Exp Rheumatol*. 2011;30(2):202-207.
22. Huscher D, Merkesdal S, Thiele K, Zeidler H, Schneider M, Zink A. Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany. *Ann Rheum Dis*. 2006;65(9):1175-83.
23. Kobelt G, Andlin-Sobocki P, Maksymowych WP. Costs and quality of life of patients with ankylosing spondylitis in Canada. *J Rheumatol*. 2006;33(2):289-295.
24. Fautrel B, Benhamou M, Breban M, Roy C, Lenoir C, Trape G, et al. Cost-effectiveness of two therapeutic regimens of infliximab in ankylosing spondylitis: economic evaluation within a randomized controlled trial. *Ann Rheum Dis*. 2009;
25. Spain. Royal Decree 1106/2014, of 26 December, establishing the national minimum wage for 2015. BOE no. 313, 27 December 2014. [Internet]. 2014 [cited 10 August 2016]. Available on: [http://www.boe.es/diario\\_boe/txt.php?id=BOE-A-2014-13518](http://www.boe.es/diario_boe/txt.php?id=BOE-A-2014-13518)

## 14. HOPES AND FEARS

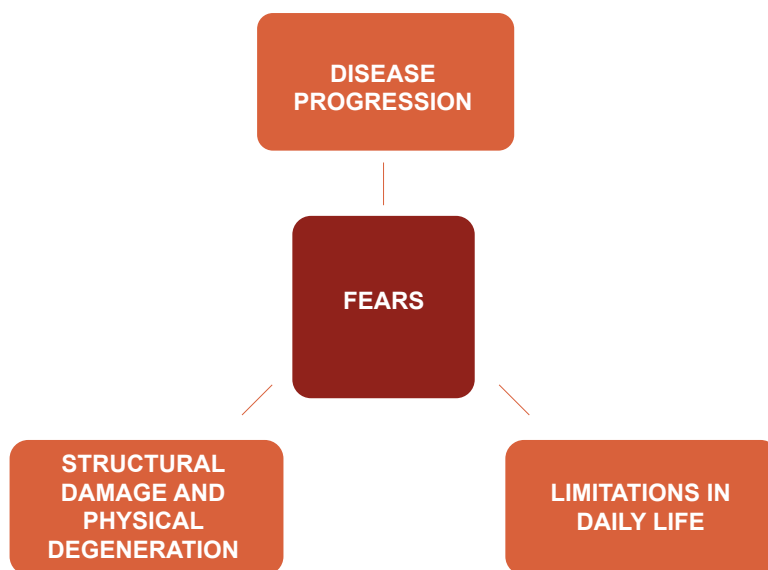
People with Ax-SpA face a number of fears but they also have hopes for the way their disease will progress and how to combat it. The desire of the majority is to achieve as normal a life as possible, with less pain and to be able to adopt a healthier lifestyle.

A recent study involving 199 patients with Ax-SpA analysed the importance to patients of different aspects of health (assessed through the ASAS health index, ASAS HI). The results of the study found that the aspects attracting the highest scores were (in order): pain, sleep and fatigue (1).

### 14.1 Fears in relation to the disease

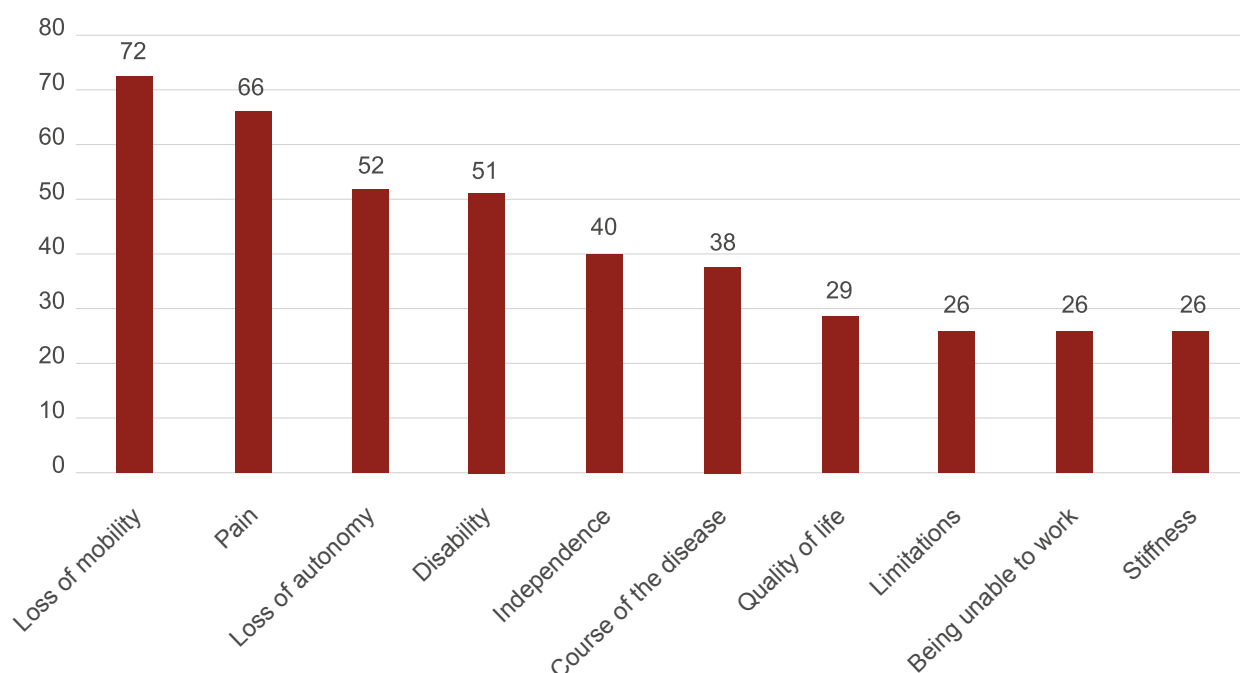
Among the 399 people with Ax-SpA who answered this question, their biggest concerns related to structural damage and physical degeneration (58%), disease progression (30%) and limitations in performing daily activities (28%) (See Figure 1).

**Figure 1.** Fears of people with EspA-ax in the survey



Source: Own elaboration

Figure 1 presents the 10 main fears of the people surveyed. Loss of mobility and pain are aspects that condition and limit the daily life of patients and which cause them the most concern. People with Ax-SpA think that if they fail to stop the disease they may suffer structural damage, organ damage or loss of vision. As a result of this damage they fear losing their mobility and autonomy and becoming dependent on people, without being free to perform tasks such as: work, play sports, going out with friends or just going for a walk without having someone's help.

**Figure 2.** Main fears of people with Ax-SpA (N: 399)

Source: 2017 Atlas patient survey

These people live with the fear of being socially excluded, of losing their job and with it the associated economic resources as well as the uncertainty of whether the state will recognise their situation of dependence or disability. Patients want the disease to be recognised, that the pains and difficulties they face in coping with daily life are valued and that medical professionals treat them in a more humane way.

Some of the women reported worrying that their children might develop the disease in the future or have complications during pregnancy as a result of the treatment they receive.

Getting better and the proper use of treatments are also points that most concern the people surveyed. Some are optimistic about the results of treatment with biologics, while others fear that the drugs they are taking may cause side effects in the future or that the treatments will become less effective. Respondents point out that non-pharmacological treatments such as physical therapy or activities such as swimming are essential and ask the state to subsidise these activities or integrate them into the Public Health System Services Portfolio.

## 14.2 Patients' hopes

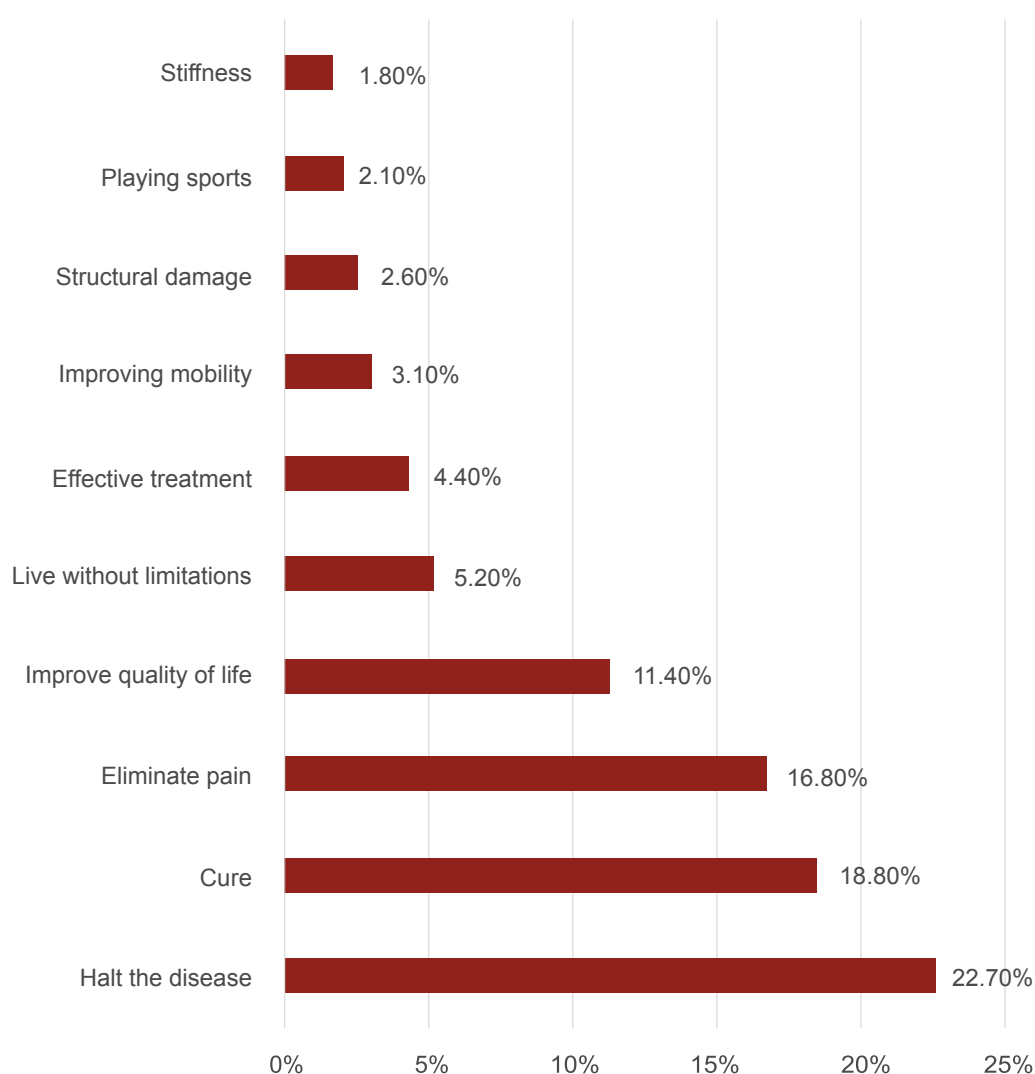
This question was answered by 387 people with Ax-SpA, of whom 75% said they had high hopes for research on the disease, of a cure being found and even of overcoming the disease. Scientific advances and the good results derived from the use of new biological treatments provide hope in finding a definitive cure. Therefore, they ask the state and pharmaceutical companies to not cut back on and even increase the resources for research.

One of the patients expressed it as follows: “The research should continue so that young people can have better and timely solutions, not like us where they arrived just in time although it's still not too late”.

Other areas that were important for patients were a reduction in the side effects derived from the use of drugs, ensuring the new treatments do not attack the immune system and controlling the transfer of the disease from a genetic point of view. One patient points out the following: “There should be more research and not only in pharmacological treatments ... and above all so that you can avoid passing the disease on to your children, which is the most painful part”.

The following figure shows the frequency of the top ten hopes that respondents have about the progression of their disease. A total of 22.7% hope the disease will not progress, 18.6% dream of a cure for the disease, 16.8% have eliminating pain as their main goal and 11.4% an improvement in their quality of life.

**Figure 3.** Main hopes of people with Ax-SpA (N: 387)



Source: 2017 Atlas patient survey

Despite these encouraging data, it should be noted that 13% of people with Ax-SpA have lost hope in medicine and that their health may improve in the future. These include people who have changed medications several times without their condition improving, with the pain they feel persisting and the disease progressing.

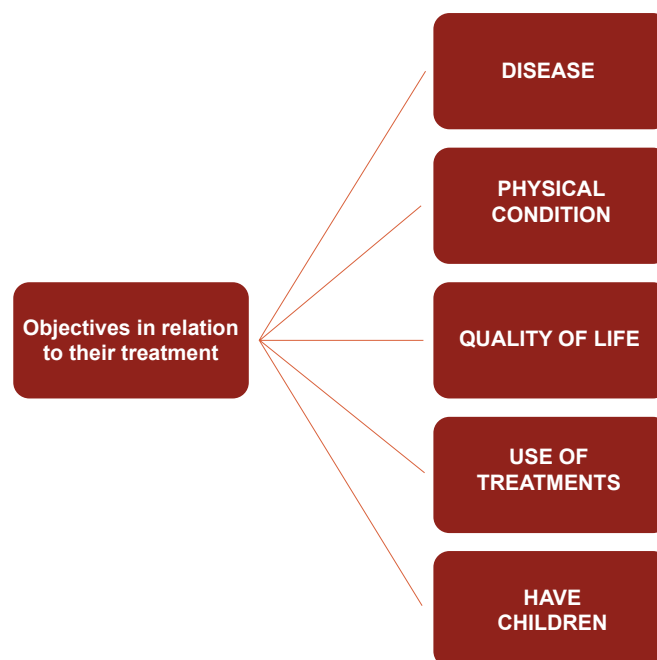
One of the patients who were pessimistic about their future expressed it in the following way: “At the moment I don't have much hope, I've suffered from this type of pain for many years and although I consider myself a strong and eager person, the discouragement is gradually taking its toll as time goes by”.

A total of 52 of the 387 respondents to the question about their hopes said they were encouraged and satisfied with the effects of using biological treatments as they had changed the process of their illness and improved their quality of life. Since beginning biological therapy, these patients stated they have experienced a reduction in the symptoms of the disease and, thanks to this, they have managed to enjoy a normal life, without limitations and almost forgetting that they suffer from the disease. Patients taking biologics are hopeful that they will be more effective, cause no side effects, and although they will not cure the disease, that they will at least slow down its progression and help reduce their pain.

### 14.3 Objectives in relation to treatment

In the qualitative question regarding personal goals in relation to their treatment (decreased pain, increased mobility, cure, structural damage, etc.) the respondents affirm that they have set goals regarding the treatment they are receiving, although these vary depending on their health and the development of their disease. As can be seen in the following figure, patients want their treatment to stop their disease, help improve their physical condition and improve their quality of life. They also want more effective treatments and to have a pregnancy that is not affected by their disease or medication.

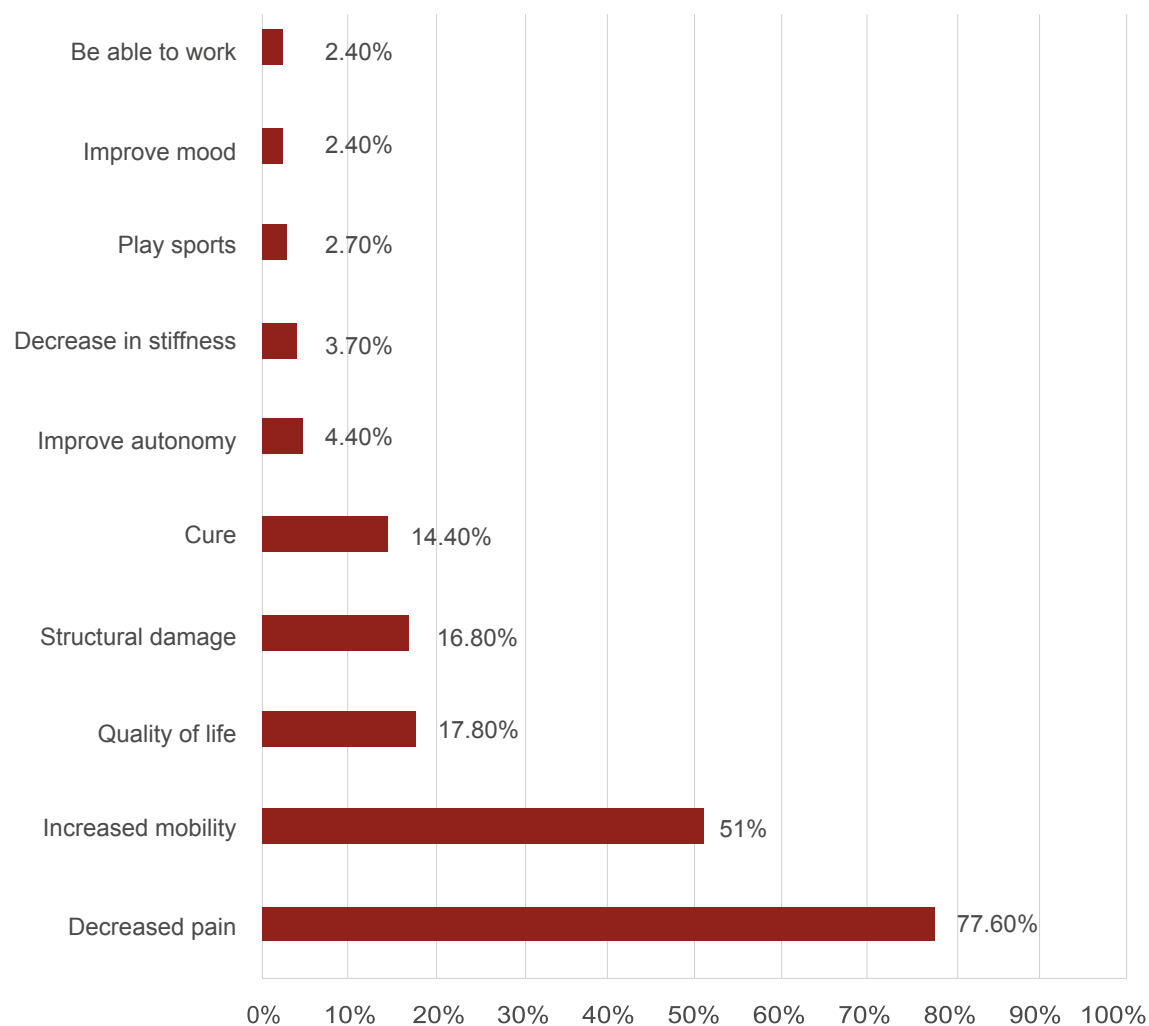
**Figure 4.** General objectives of people with Ax-SpA in relation to their treatment



Source: 2017 Atlas patient survey

Of the 410 respondents to this question, 77.6% want their treatment to reduce or eliminate their pain, 51% expect to recover mobility thanks to the treatment used, 17.8% to improve their quality of life, 16.8% to avoid structural damage and 14.4% for their disease to be cured (see Figure 3).

**Figure 5.** Main specific objectives of the respondents in relation to their treatment (N: 410)



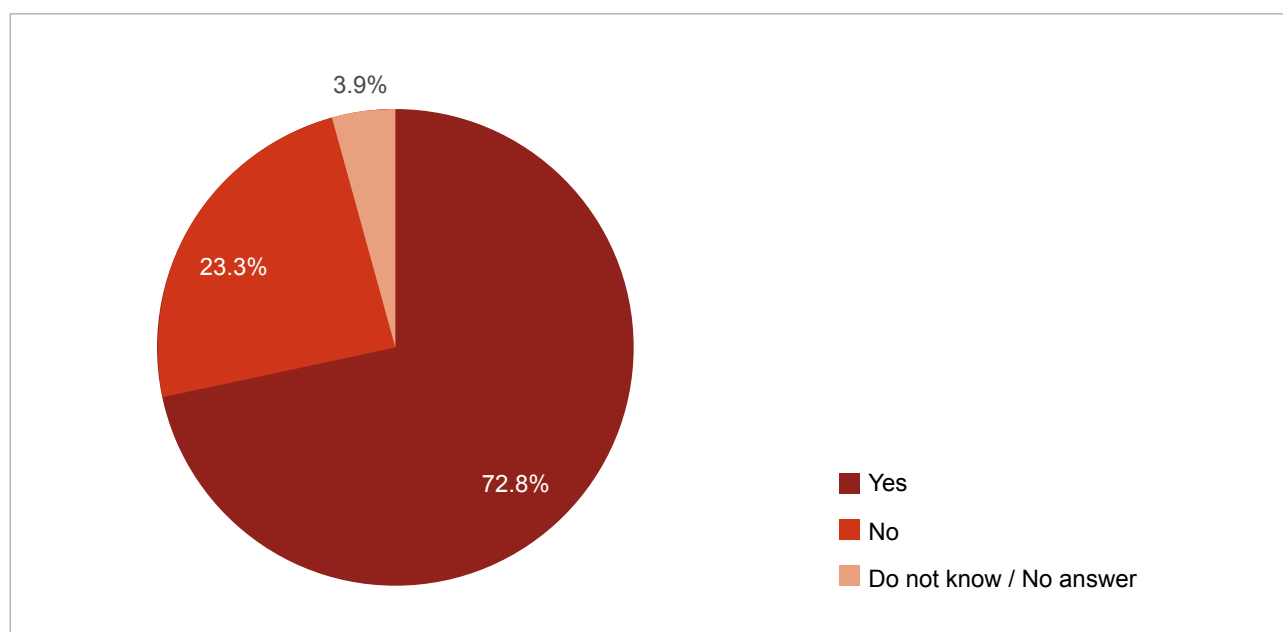
Source: 2017 Atlas patient survey

Another important goal that respondents want to achieve with their treatment is improving their quality of life. In order to achieve this it is important for them to improve aspects such as autonomy, mood, independence and rest.

## 14.4 Patient communication with their doctor

The communication and understanding between patients with Ax-SpA and their doctors is vital in managing the disease, ensuring compliance with the treatment and monitoring the effectiveness of the treatments. A total of 72.8% of the patients surveyed stated that they had talked to their doctor about their personal treatment goals (Figure 4). Patients are asking specialists to provide them with adequate treatment and, on the other hand, they are asking researchers to minimise the side effects caused by the treatments they are receiving. Around 25% of these people would like to cope with the disease without using drugs or at least use the minimum possible.

**Figure 6.** Patients with Ax-SpA that have spoken with their doctor about their personal goals (N: 464)



Source: 2017 Atlas patient survey

- ▶ The results obtained show that the respondents who suffer from Ax-SpA experience fears focused on three major areas: the progress of the disease, structural damage and physical degeneration that could rob them of their autonomy and make them dependent on others.
- ▶ Thanks to the new treatments and advances in science, a significant number of patients were hopeful that the progression of the disease would be halted in the near future, that a cure will be found, their pain will be removed and that this will improve their quality of life.
- ▶ It should be noted that the vast majority of the people surveyed have at some point spoken with their doctor about their personal goals relating to the treatment. The two main objectives that they want to achieve are relief from the pain they are suffering and an increase in mobility.



## References

1. Kiltz U, Essers I, Hilgsmann M, Braun J, Maksymowych WP, Taylor WJ, et al. Which aspects of health are most important for patients with spondyloarthritis? A Best Worst Scaling based on the ASAS Health Index. *Rheumatology*. October 2016;55(10):1771-6.

## 15. CONCLUSIONS AND RECOMMENDATIONS

- ▶ Planning for rheumatic diseases and specifically SpA is poor in the autonomous regions, only three have adopted or drafted specific rheumatology plans.
- ▶ The majority of the patients surveyed had ankylosing spondylitis, i.e. a form of the disease with irreversible structural damage.
- ▶ A total of 44.3% of respondents belonged to a patients' association, 36.9% had studied at university and 71.5% are married or in a civil partnership.
- ▶ Before being diagnosed, patients with Ax-SpA made more visits to physical therapists and orthopaedic surgeons than to rheumatologists, which may indicate incorrect referrals.
- ▶ Patients reported having suffered the first symptoms associated with the disease at age 24, on average, with diagnosis at age 33, on average.
- ▶ The delay in diagnosis for the surveyed patients was almost 9 years, on average, with a delay of over 6 years for 75% of the patients.
- ▶ Ax-SpA is being diagnosed earlier nowadays with a significant reduction in diagnostic delay. Thus, while before 2009 the average diagnostic delay was 9.5 years, after 2009 it dropped to 2.5 years.
- ▶ The patients surveyed reported having suffered inflammation in 21 areas of the body, with percentages ranging from 78% for patients with inflammation in the sacroiliac joints to 19.6% with pain in the back of the foot, with more than 50% of patients suffering pain in one or more of 8 specific areas.
- ▶ Ax-SpA causes a number of negative effects such as susceptibility to a large number of concomitant diseases, including anxiety, sleep disorders, uveitis, depression, overweight/obesity, high blood pressure, hypercholesterolemia, fibromyalgia, severe infections requiring antibiotic treatment and psoriatic arthritis.
- ▶ The main activities in which patients stated they experienced the greatest limitations during moments of crisis arising from their Ax-SpA were physical exercise, domestic cleaning, getting out of bed and climbing stairs.
- ▶ The main activities patients have been forced to do less often after suffering from Ax-SpA include practising sport, travelling and going to bars and restaurants.
- ▶ The majority of patients felt that their personal relationships (with neighbours, family and their partner) had not been affected as a result of their Ax-SpA, although there was a greater perception of a worsening in relationships in the work environment and with friends.
- ▶ The adaptation or purchase of a car was the action taken by the majority of patients, followed by the purchase of special or comfortable shoes.
- ▶ Half of the patients evaluated their degree of disability, of these patients 50% rated it as 38% (33% being the minimum threshold for obtaining a certificate of disability). This demonstrates the high level of disability associated with Ax-SpA.
- ▶ There is a correlation between disease activity, body stiffness and the limitations in daily activities and mental health problems in patients with Ax-SpA.

- ▶ The majority of patients surveyed (70% of women and 60% of the men) have mental health problems.
- ▶ Three psychological disorders (anxiety, sleep disorder and depression) are among the four most commonly described concomitant diseases.
- ▶ Members of associations for patients with Ax-SpA have fewer mental health problems than other patients.
- ▶ The majority of patients with Ax-SpA received public healthcare (95.5%) and 29.3% had private insurance, this percentage is double that for the general population.
- ▶ The main medical specialists involved in the management and monitoring of the disease are primary care doctors, rheumatologists, physiotherapists and psychologists/psychiatrists.
- ▶ A total of 36.3% of the patients were being treated with biologics, 31.5% took NSAIDs and/or DMARDs but without biologics and 32.2% were not taking any type of drug.
- ▶ A total of 51.5% of patients following biological therapy considered that the improvement due to this treatment was high, this figure was 29.8% for those that took NSAID and only 21.0% for those who took DMARD.
- ▶ A total of 83% of patients following biological therapy considered that they were appreciably better than before taking biologics.
- ▶ Despite the importance of non-pharmacological treatments for the treatment and monitoring of the disease, most are not included within the portfolio of services offered by the public health service and, therefore, patients spend an average €115 per month on this type of treatment.
- ▶ Besides walking, the main activities listed by surveyed patients were stretching exercises, swimming, pilates, keep-fit classes, aquatic therapy and water aerobics.
- ▶ People who suffer from AS usually experience problems associated with working.
- ▶ The results indicate high unemployment levels among patients with AS, as well as absenteeism problems for those who work. The latter are mainly due to attendance at medical appointments, problems complying with working hours and negative effects on their professional life.
- ▶ There is a significant link between temporary sick leave and this disease.
- ▶ Ax-SpA is a disabling disease, showing high rates of permanent disability.
- ▶ A large majority of patients perceived difficulties in gaining employment because of their illness.
- ▶ As far as we are aware, this Atlas presents the first estimation of the economic and societal burden of AS in Spain in over 10 years.
- ▶ The total annual cost per prevalent patient amounted to €11,462.30, distributed between direct healthcare costs (61.1%), direct non-healthcare costs (5.3%) and indirect costs attributable to the loss of productivity (33.6%).
- ▶ The AS patients and their families assume part of these costs. The survey found that 5.7% of the direct healthcare costs, as well as all of the direct non-healthcare costs were funded privately, with an estimated outlay of 1,000 euros per patient per year.

- ▶ Losses in productivity equated to 3,851 euros per patient per year.
- ▶ Early diagnosis and appropriate management of patients with AS may contribute to reducing disability in patients thereby increasing their quality of life and mental health. In turn, this could result in a substantial reduction of the direct and indirect costs associated with this disease.
- ▶ The results obtained show that the fears of the people surveyed who suffer from Ax-SpA are focused on three main areas: the progress of their disease, structural damage and physical degeneration that could rob them of their autonomy and make them dependent on others.
- ▶ Thanks to the new treatments and advances in science, a significant number of patients were hopeful that the progression of the disease would be halted in the near future, that a cure will be found, their pain will be removed and that this will improve their quality of life.
- ▶ It should be noted that the vast majority of the people surveyed have at some point spoken with their doctor about their personal goals relating to the treatment. The two main objectives that they want to achieve are relief from the pain they are suffering and an increase in mobility.



## APPENDIX

### UNIT PRICES



**Table 1.** Unit prices: visits to healthcare professionals

	Euros (2015)
Primary healthcare medicine (1st visit)	63.44
Primary healthcare medicine (successive visits)	39.61
Nursing (1st visit)	25.57
Nursing (successive visits)	24.60
Specialist (1st visit) <sup>a</sup>	133.49
Specialist (successive visits) <sup>a</sup>	78.45
Physical therapy	20.82

<sup>a</sup> Includes professionals in rheumatology, traumatology, ophthalmology, pneumology, cardiology, rehabilitation, psychology/psychiatry.

**Table 2.** Unit prices: diagnostic tests

	Euros (2015)
Magnetic resonance imaging	183.61
Cervical radiography	20.00
Dorsal radiography	22.35
Lumbar radiography	22.00
Pelvis / sacroiliac radiography	22.03
Whole column radiography	25.05
Chest radiography	20.00
Shoulder radiography	21.84
Knee radiography	20.03
Hip radiography	20.03
Hands / feet radiography	18.04
Genetic analysis (HLA B27)	45.12
Ultrasound	66.00
Scintigraphy	132.27
Computerised tomography	86.81
Blood tests	61.38
Urinalysis	13.14



**Table 3.** Unit prices: use of emergency services

	Euros (2015)
Health centre emergencies	88.22
Hospital emergencies	184.71
Home emergencies	129.53
Emergency ambulance	356.31

**Table 4.** Unit prices: hospital admissions according to CIE9: 720.0 Ankylosing spondylitis

	Euros (2015)
Ankylosing spondylitis	5,533.52

**Table 5.** Unit prices: AS-related medication

	Price/mg (euros 2015)
<b>NSAIDs</b>	
Ibuprofen	0.0000820833
Naproxen	0.0002170000
Etoricoxib	0.0106666667
Indometacin	0.0011240000
Diclofenac	0.0008250000
Celecoxib	0.0037133333
Meloxicam	0.0084666667
<b>DMARDs</b>	
Methotrexate	1.0886666667
Sulfasalazine	0.0316666667
<b>Biologics</b>	
Adalimumab	14.094625000
Certolizumab Pegol <sup>a</sup>	2.610175000
Etanercept <sup>a</sup>	4.925200000
Golimumab <sup>a</sup>	24.396600000
Infliximab <sup>a</sup>	6.158800000
Secukinumab <sup>a</sup>	4.156600000
Infliximab biosimilar <sup>a</sup>	5.102900000

<sup>a</sup> Variable price depending on induction or maintenance period.

**Table 6.** Unit prices: alternative treatments

	Euros (2015)
Acupuncture (session)	25.00
Homoeopathy (successive)	35.00

**Table 7.** Unit prices: hourly rate for normal hours

Sex	Occupation	Euros (2015)
Women	High <sup>a</sup>	18.60
	Middle <sup>b</sup>	10.50
	Low <sup>c</sup>	9.52
	All occupations	13.49
Men	High <sup>a</sup>	22.24
	Middle <sup>b</sup>	12.99
	Low <sup>c</sup>	12.11
	All occupations	15.76

<sup>a</sup> Includes large occupation groups 1, 2 and 3.<sup>b</sup> Includes large occupation groups 4, 5, 6 and 7.<sup>c</sup> Includes large occupation groups 8 and 9.**Table 8.** Unit prices: informal care

	Euros (2015)
One hour of informal care	5.08

Note: equivalent to one hour at the national minimum wage for domestic workers, it is not specialised care.



