Axial Spondyloarthritis: Patient-Reported Impact in Europe

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Marco Garrido-Cumbrera
Universidad de Sevilla
Seville, Spain

Christine Bundy
Cardiff University
Cardiff, UK

Souzi Makri
Cyprus League Against Rheumatism
Nicosia, Cyprus

Pedro Plazuelo-Ramos
Spanish Federation of Spondyloarthritis
Associations (CEADE)
Madrid, Spain

Victoria Navarro-Compán
University Hospital La Paz
Madrid, Spain

Raj Mahapatra
Axial Spondyloarthritis
International Federation (ASIF)
London, UK

Carlos J. Delgado-Domínguez
Universidad de Sevilla
Seville, Spain

Denis Poddubnyy
Charité-Universitätsmedizin Berlin
Berlin, Germany

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Executive Summary

Objectives and Scope of the Project

- The European results of the International Map of Axial Spondyloarthritis (IMAS) project hopes to create evidence of axial spondyloarthritis (axSpA) to raise awareness of the impact of the disease on patients.
- The project is a collaboration between the Health & Territory Research (HTR) group of the University of Seville, the Spanish Federation of Spondyloarthritis Associations (CEADE), the Axial Spondyloarthritis International Federation (ASIF), a steering committee composed of patient representatives and internationally recognized rheumatologists, and psychologists specialized in the field of axSpA, and Novartis.
- This European report of the IMAS 2020 presents the results of a survey completed by European patients with axSpA.

Survey Overview

- Participants were recruited between July 2017 and March 2018 and were eligible if aged 18 years or more, with a self-reported diagnosis of axSpA, ankylosing spondylitis (AS), or non-radiographic axSpA. Participants were also required to have visited a healthcare professional (HCP) for axSpA in the prior 12 months.
- Participants were asked questions about their condition and how it impacts their daily lives and physical and emotional well-being.
- Information was collected on various aspects of the disease, including
    - spinal stiffness, using the Spinal Stiffness Index;
    - functional limitation, using the Functional Limitation Index;
    - disease activity, using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI);
    - psychological distress, using the 12-item General Health Questionnaire (GHQ-12).

Overview of Respondents

- The IMAS European survey was completed by 2,846 participants with axSpA across 13 European countries (Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK).
- More than three out of five participants were female. The fact there were more female than male participants should be considered when interpreting the survey findings.
- Participants' ages ranged from 18 to 85 years; the average (mean) age was 44 years. Relatively, a few patients (3%) were over 68 years old, and as such the elderly population was under-represented in this survey.
- More than half of participants (52%) were categorized as overweight or obese.
- More than two-thirds of participants reported being married, and four out of five participants reported living in a relationship (whether they were married or not), indicating good access to this vital source of social support.
- Participants were well educated, with most having completed high school or university; levels of education in this population were in accordance with those of the general population of Europe.
- In general, the demographics of the participants was similar to those in previous studies in axSpA.
- Results of the survey suggest that axSpA did not negatively impact participants' marriage rate, fertility rate, educational achievement, or body mass index compared with the overall European population.
- On average, the monthly income per household member for IMAS participants was lower than the minimum monthly wage in their country, highlighting the considerable impact of axSpA on work productivity.

Diagnosis

- Most (83%) IMAS participants visited a general practitioner (GP) before diagnosis, reflecting the key role that these primary healthcare providers play in identifying possible cases of axSpA and referring patients to a rheumatologist.
- However, participants also frequently reported visiting other specialists, such as physiotherapists (46%) and orthopedists (35%) prior to diagnosis, suggesting that the recommended referral to a rheumatologist was not always/immediately followed, which may have contributed to delays in the diagnosis and initiation of effective treatment.
- The diagnostic test most frequently performed was X-ray imaging, followed by HLA-B27 genetic testing and magnetic resonance imaging (MRI) scans, which is in agreement with current recommendations from the European League Against Rheumatism (EULAR).

- The mean (average) delay in diagnosis was 7.4 years.
    - The diagnostic delay was 2 years longer in females compared with males.
- Although there was evidence suggesting that the delay in diagnosis may have improved over time, further efforts are required to raise awareness of the disease amongst primary care physicians to ensure patients with suspected axSpA are referred for specialist diagnosis and treatment by rheumatologists as early as possible.

Physical Health

- Active disease (measured using BASDAI, which indicates the degree of fatigue/tiredness, pain, and morning stiffness participants are experiencing), was reported by almost three-quarters of participants, suggesting that their disease was not being optimally managed.
- Approximately 80% of participants reported spinal stiffness, which was classed as moderate to severe in 45% of cases.
    - Spinal stiffness was less severe in participants who reported participating in physical activities (such as gymnastics, Pilates, and swimming).
    - Spinal stiffness was most severe in those participants who had experienced diagnostic delay, highlighting the importance of early diagnosis and treatment to reduce the burden of AxSpA.
- The most common sites of inflammation were the lower back, sacroiliac joints, and hips, with inflammation of peripheral sites (i.e. joints other than those of the spine, pelvis, and hips) also common.
- Participants reported considerable impairment in basic activities of daily living, particularly with physical exercise, cleaning, going up the stairs, and getting up from bed.
- Participants reported frequently requiring assistance with activities of daily living, with a high proportion making adaptations (such as customizing shoes and modifying their workplace) to overcome these difficulties.
- Many participants reported that they were suffering from one or more conditions in addition to axSpA (comorbidities); the additional conditions most frequently reported by participants were linked to psychological distress: sleep disorders (50%), anxiety (39%), and depression (34%).
- It was also relatively common for participants to report that areas of the body other than their spine and joints were affected (these are known as extra-articular manifestations). The most common areas affected other than the spine and joints were the eyes (uveitis, reported in 22% of participants), and the gut (ulcerative colitis was reported in 8% of participants and Crohn's disease was reported in 7% of participants).

- The findings serve to highlight the enormous impact that axSpA has on patients' lives. Maximizing health-related quality of life by improving physical health is a key aim of disease management.

Psychological Health

- The mental health of participants in the IMAS survey showed that 62% were at risk of psychological distress (assessed using the GHQ-12 index), illustrating the considerable negative impact of axSpA on psychological health.
- Co-occurring mental health conditions were common: 50% of participants reported sleep disorders, 39% anxiety, and 34% depression.
- The risk of psychological distress was significantly higher:
  - in female versus male participants;
  - in single or divorced participants compared with those who were married;
  - in younger than in older participants;
  - in individuals with lower compared with higher incomes.
- Participants who were at risk of psychological distress reported:
  - higher disease activity;
  - more severe spinal stiffness;
  - reduced ability to perform daily activities;
  - higher numbers of comorbidities (medical conditions other than axSpA).
- The findings highlight the importance of recognizing and including mental health as part of a complete approach to treating axSpA.

Social Support

- Almost half of the IMAS survey participants reported that axSpA had worsened their relations with work colleagues, and one-third reported worsened relations with friends.
- Participants also reported that axSpA had a negative impact on their ability to socialize, with two-thirds engaging less in sports, and around half reporting that they were traveling, engaging in intimate relations, going to the cinema, or visiting museums less, as a consequence of having axSpA.
- Patient organizations recruited approximately 70% of participants to the IMAS survey.
  - Patient organizations play a key role in providing patients and their families with the tools and resources (e.g. advice, education, and support) they need to face the challenges of living with a serious and chronic disease such as axSpA.

- These findings illustrate the significant impact of axSpA on the social lives of individuals with the disease.
- Preservation of social engagement should be an important component of a holistic approach to axSpA management. Indeed, treatment guidelines state that maximizing health-related quality of life by preservation of social engagement is a key goal of disease management.

Health Care

- The vast majority of participants reported having public health insurance suggesting that the costs of axSpA are primarily covered by healthcare systems.
- Patients with more active disease (those patients with a BASDAI of 4 or greater) made more visits to HCPs than those with lower disease activity (BASDAI less than 4).
- Most participants reported that their axSpA was being managed by a rheumatologist, which is in agreement with current guidelines for managing patients with axSpA.
  - 11% of participants were not managed by a rheumatologist, which represents a relatively large proportion who were not being optimally managed; this may reflect a lack of access to a rheumatologist.
- Of all healthcare appointments in the prior 12 months, participants reported visiting a physiotherapist most frequently.
  - Physical therapy can help to relieve pain and spinal stiffness and improve mobility, as well as help with other symptoms including tendon pain and painful joints—key for maintaining long-term mobility and health.
- Despite the lack of evidence showing benefits of complementary medicines in axSpA, these therapies, in particular acupuncture, were used by more than one-third of survey participants, which may be an indicator of inadequacies in the participants' current treatment pathway.

Habits and Lifestyle

- The most frequently reported physical activities by participants included walking (58%), stretching (28%), swimming (25%), hiking (19%), and cycling (18%). The vast majority (85%) of participants met World Health Organization (WHO) physical activity recommendations ($\geq$ 150 minutes per week).
- Exercise forms an integral part of the management of axSpA and all patients should be encouraged to discuss their exercise regime with their HCP to find a level and activity that best suits their needs.

- Almost one-third of participants were smokers despite current Assessment of SpondyloArthritis international Society-EULAR treatment recommendations encouraging all patients with axSpA to give up smoking.
- Alcohol consumption was reported by the majority (73%) of participants, with most reporting occasional or moderate consumption.

Employment Status and Productivity

- Amongst IMAS survey participants,
  - more than half were employed at the time of the survey;
  - employment rates amongst male and female participants were lower than the overall European population;
  - both absenteeism (absence from work due to sick leave) and presenteeism (impairment while at work) were commonly reported;
  - axSpA was considered an obstacle when looking for and applying for a job.
- Almost all participants on temporary or permanent sick leave at the time of the survey reported that their sick leave was related to axSpA.
- Compared with participants without work-related issues, those with work-related issues generally had higher:
  - disease activity;
  - levels of functional limitation (i.e. reduced ability to perform everyday tasks);
  - psychological distress.
- The survey results highlight the significant negative impact of axSpA on employment prospects and the need for patients to be supported accordingly.

Fears and Hopes

- The most frequently stated fears amongst participants were disease progression (33%), suffering pain (31%), loss of mobility (30%), and loss of independence/disability (29%), which were reflected in the two most frequently reported hopes to halt disease progression (33%) and eliminate pain (31%).
- The treatment goals most commonly reported by the survey participants were to eliminate or reduce pain (29%) and improve mobility (19%), but more than one-third of participants reported that they had not talked to their managing physician about their personal treatment goals.
- These findings highlight that both HCPs and patients should be encouraged to discuss expectations and goals for treatment to ensure optimal management of the disease and to make sure patients receive the education and information they need to make informed decisions.

Conclusions

- The IMAS survey has highlighted several opportunities for optimizing the care of patients with axSpA:
  - The delay in diagnosis of axSpA remains too long and further efforts are required to raise awareness of the disease amongst patients, HCPs, and the general public to ensure faster referral to a rheumatologist, accurate diagnosis, and administration of appropriate treatment.
  - Recognizing those at risk of psychological distress is vital in ensuring that adequate support can be given to optimize treatment outcomes.
  - A greater appreciation of the impact of axSpA on work productivity and development of interventions to help individuals with axSpA remain in productive work which are also vital for reducing the costs of the disease to both patients and society as a whole.

In terms of disease management, the report highlights that both HCPs and patients should be encouraged to engage in a proactive discussion regarding expectations and goals for axSpA treatment to enable effective shared decision-making and the design of individualized treatment strategies that provide optimal management of the disease.

Contents

Contributors

The European IMAS working group consisted of members of Health & Territory Research group (HTR) of the University of Seville, Spain, collaborating with Novartis Pharma AG, the Axial Spondyloarthritis International Federation (ASIF) and a multi-stakeholder steering committee of axial spondyloarthritis experts.

Health & Territory Research (HTR)

- Prof. Ph.D. Marco Garrido-Cumbrera
- Prof. Ph.D. David Gálvez Ruiz
- Ph.D. Olta Braçe
- M.Sc. Sergio Sanz Gómez
- M.Sc. José Correa Fernández

Novartis Pharma AG

- M.Sc. Laura Christen
- Mrs. Patricia Pertel
- Mrs. Monia Steenackers

Steering Committee

- Prof. Ph.D. Marco Garrido-Cumbrera, Health & Territory Research (HTR) group of the University of Seville, Spain
- Dr. Dennis Poddubnyy. Rheumatologist at Charité-Universitätsmedizin Berlin, Berlin and German Rheumatism Research Centre, Berlin, Germany
- Dr. Victoria Navarro-Compán. Rheumatologist at University Hospital La Paz (IdiPaz), Madrid, Spain
- Dr. Christine Bundy, School of Healthcare Sciences, Cardiff University, Wales, UK
- Mr. Raj Mahapatra, Chairman at Axial Spondyloarthritis International Federation (ASIF), London, UK
- Mrs. Souzi Makri, President of the Cyprus League Against Rheumatism, Nicosia, Cyprus

- Ph.D. Carlos J. Delgado-Domínguez, Health & Territory Research (HTR) Group at the University of Seville, Spain
- Mr. Pedro Plazuelo-Ramos, Spanish Federation of Spondyloarthritis Associations (CEADE), Madrid, Spain

Patient Advocacy Groups

The following organizations also supported this project:

- Ankilozan Spondilit Hasta Derneği (ASHAD)
- Axial Spondyloarthritis Association of South Africa
- Axial Spondyloarthritis Association of the Philippines (ASAPH)
- Ankylosing Spondylitis Society in Russia
- Ankylosing Spondylitis Welfare Society
- AntarDhwani
- Arthrites
- Association Française de Lutte Antirhumatismale (AFLAR)
- Assocation of Ankylosing Spondylitis, R.O.C
- Associazione Nazionale Persone con Malattie Reumatologiche (APMAR)
- Bechterevo Liga Sergančiųjų Draugija
- Canadian Spondylitis Association (CSA)
- Coordinadora Española de Asociaciones de Espondiloartritis (CEADE)
- Fundación de Espondilitis Anquilosante en Colombia
- FUNDARE
- National Axial Spondyloarthritis Society (NASS)
- Reumanet
- Reumatikerförbundet
- Spondyloartrittforbundet Norge (SPAFO)
- Spondylitis Association of America (SAA)
- Stand for AS
- VVSA

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Abbreviations

AS	Ankylosing Spondylitis
ASAS	Assessment of SpondyloArthritis International Society
ASIF	Axial Spondyloarthritis International Federation
axSpA	Axial spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
BMI	Body mass index
CEADE	Spanish Federation of Spondyloarthritis Associations
csDMARD	Conventional synthetic disease-modifying anti-rheumatic drug
CT	Computerized tomography
EMAS	European Map of Axial Spondyloarthritis
EULAR	European League Against Rheumatism
GESPIC	German Spondyloarthritis Inception Cohort
GHQ-12	12-item General Health Questionnaire
GP	General practitioner
HCP	Healthcare professional
HLA	Human leukocyte antigen
HTR	Health & Territory Research group of the University of Seville
IBD	Inflammatory bowel disease
IBP	Inflammatory back pain
IMAS	International Map of Axial Spondyloarthritis
MRI	Magnetic resonance imaging
N	Number of participants
nr-axSpA	Non-radiographic axial spondyloarthritis
NSAIDs	Non-steroidal anti-inflammatory drug
PAG	Patient Advocacy Group (patient organization)
SD	Standard deviation
SpA	Spondyloarthritis
WHO	World Health Organization

Introduction

1

Axial spondyloarthritis (axSpA), a chronic inflammatory condition that encompasses radiographic (also known as ankylosing spondylitis [AS]) and non-radiographic (nr-axSpA) forms of the disease (Rudwaleit et al. 2009), can lead to chronic pain, structural damage, and disability. While understanding of the pathophysiology of axSpA and its management (classification, diagnosis, monitoring, and treatment) has increased over recent years (Sieper and Poddubnyy 2017), still relatively little is known about the disease from the perspective of the patient. Further research efforts are required to better understand the patient journey to diagnosis, the functional limitations associated with living with axSpA, and its effects on work productivity, quality of life, and psychological well-being (Garrido-Cumbrera et al. 2017).

The International Map of Axial Spondyloarthritis (IMAS) European project, a collaboration between the Health & Territory Research (HTR) group of the University of Seville, the Axial Spondyloarthritis International Federation (ASIF), the Spanish Federation of Spondyloarthritis Associations (CEADE), a steering committee composed of patient representatives and internationally recognized rheumatologists, psychologists, and physiotherapists specialized in the field of axSpA, and Novartis, was conceived to address these unmet needs (Fig. 1.1) (Garrido-Cumbrera et al. 2019a).

IMAS has an overarching aim of expanding our knowledge of axSpA to raise awareness of the impact of the disease on patients. The hope is that the data gathered will help inform long-term plans and treatment goals to ultimately improve quality of life and optimize clinical outcomes for patients, while fostering closer relationships between patient organizations, healthcare professionals (HCPs), and policy makers across Europe.

As part of the IMAS European project, a detailed questionnaire was conducted to gather data from patients with axSpA across 12 European countries: Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Slovenia, Sweden,

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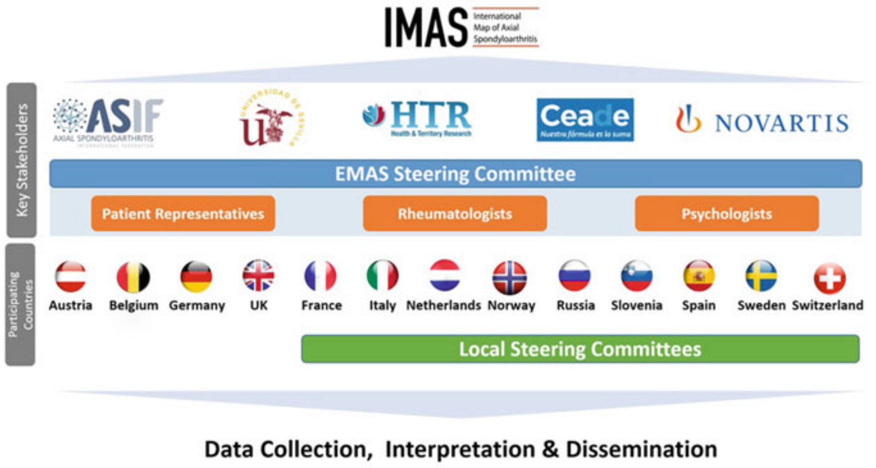

Fig. 1.1 Overview of the IMAS European project, including the key stakeholders and participating countries. *IMAS* International Map of Axial Spondyloarthritis

Switzerland, Russia, and the UK. In 8 of the 12 participating countries (all except Austria, Belgium, Germany, and the UK), country-specific steering committees supported local interpretation and dissemination of the data. The survey results provide a snapshot of the current status of axSpA across Europe and build upon the pilot questionnaire conducted as part of the Atlas of Ankylosing Spondylitis in Spain 2017 (Garrido-Cumbrera et al. 2019b), the data from which were added to the IMAS database retrospectively. Since its publication, the Atlas of axSpA in Spain has been used to support discussions with the Spanish health authorities (Autonomous Communities of Madrid, Catalonia, Andalusia, Basque Country and Castille La-Mancha) to put axSpA on the health policy agenda and implement solutions at the national level that improve patients' health.

This International Atlas of Axial Spondyloarthritis 2020 presents the key data from the IMAS questionnaire. The results are arranged thematically and have been critically analyzed, reviewed, and interpreted by the IMAS expert steering committee.

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Objectives

2

The overarching aim of the IMAS European project was to expand the knowledge of axSpA in Europe by gathering the perspectives of patients diagnosed with the disease.

The specific objectives were as follows:

Research Objectives

- To assess the diagnostic delay in axSpA and any barriers to early detection.
- To understand the physical and psychological impact of axSpA.
- To evaluate impact of axSpA on patients' social and professional lives.
- To describe current employment status of patients with axSpA.
- To describe the management of patients with axSpA across Europe, including pharmacologic treatment, alternative therapies, HCP visits, medical tests, and treatment goals.
- To describe the disease-related hopes and fears of patients with axSpA.
- To assess inequalities in disease management among regions and countries participating in the project.

Long-term Objectives

- To assist axSpA patient support groups by providing data to inform activities that raise disease awareness.
- To establish recommendations for the promotion of healthy lifestyles and improvement of living conditions for patients with axSpA.
- To foster closer relationships between patient organizations, HCPs, and policy makers within Europe through collaboration on the project and subsequent awareness raising activities.

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Methodology

3

3.1 Questionnaire Design

This cross-sectional market research survey was adapted from the Spanish Atlas of Axial Spondyloarthritis 2017, a pilot survey conducted from January to March 2016 (Garrido-Cumbrera et al. 2019a).

The first draft of the questionnaire was completed by 25 patients with different sociodemographic profiles to assess the feasibility and adequacy of the questions. The questionnaire was subsequently translated into relevant local languages: English, Dutch, French, German, Italian, Norwegian, Russian, Swedish, and Slovenian. Participating countries could modify questions for local relevance, with guidance only to make essential changes in order to maintain consistency on a pan-European level (Garrido-Cumbrera et al. 2019b).

The final patient questionnaire contained a total of 108 items related to sociodemographic and anthropometric characteristics, patient organization membership, diagnostic delay (date of first symptoms and diagnosis with axSpA), healthcare resource use, comorbidities, drug treatments, employment and work productivity, disability benefits, functional limitations, complementary treatments, and patient experience of living with the disease (Garrido-Cumbrera et al. 2019b).

The study utilized relevant information from a literature search to validate and support the responses from both questionnaires. Documents developed by the Assessment of SpondyloArthritis international Society (ASAS) were also consulted to supplement literature searches.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_3.

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3.2 Implementation of the Survey

Patients meeting the following inclusion criteria were recruited between July 2017 and March 2018:

- Aged ≥ 18 years.
- Residents in the specified country.
- A diagnosis of axSpA, AS, or nr-axSpA (self-reported).
- Visit to HCP for axSpA in the 12 months prior to participation.

Participants from Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Sweden, Switzerland, and the UK were recruited by GfK through their existing database of respondents. In Austria, France, Norway, Slovenia, Sweden, the Netherlands, Italy, and Russia, patient organizations also supported recruitment by distributing the survey to members. The Spanish database from the Atlas of Axial Spondyloarthritis 2017 was retrospectively added.

The survey conducted in Spain was administered via SurveyMonkey, an online platform for survey data collection, and conducted by HTR. Coordination of the patient survey and data collection in European countries other than Spain was led by Ipsos (formerly GfK).

3.3 Supplementary Instruments

A range of supplementary indices were collected in the questionnaire.

1. **Spinal Stiffness Index**: an index developed by the University of Seville specifically for the IMAS European survey (Garrido-Cumbrera et al. 2019a) to assess the degree of spinal stiffness experienced by patients in the spinal column, distinguishing between the cervical, dorsal, and lumbar areas.
2. **Functional Limitation Index**: a measure designed by the University of Seville specifically for the IMAS European survey (Garrido-Cumbrera et al. 2019a) to assess the degree of functional limitation in 18 activities of daily life: dressing; bathing; grooming; tying shoe laces; moving about the house; climbing stairs; getting into/out of bed; using the bathroom; shopping; preparing meals; eating; household cleaning; walking down the street; using public transportation; going to the doctor; driving; doing physical exercise; having sex.
3. **Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)** (Garrett et al. 1994): a self-administered questionnaire that evaluates disease activity in patients with axSpA. 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; areas of localized tenderness (also called enthesitis, or inflammation of tendons and ligaments); and the level and duration of stiffness in the morning.

4. **12-item General Health Questionnaire (GHQ-12)** (Goldberg 1972): is a screening instrument for assessing risk of psychological distress that has been widely used in various settings across different cultures.

3.4 Statistical Analysis

Data from completed questionnaires were harvested to compile the study database, which underwent data cleaning, homogenization, and normalization of the variables prior to analysis.

Different statistical tests were applied depending on the nature of the variable (qualitative or quantitative) and the sample distribution (parametric or non-parametric).

3.4.1 Quantitative Analysis

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:

- Mann–Whitney U test for independent samples (2 groups).
- Kruskal–Wallis H test for independent samples (>2 groups).
- Pearson χ^2 test to verify whether there is a relationship between two categorical variables.
- Spearman's rank correlation coefficient was used to measure the association or relationship of monotony between pairs of quantitative variables.
- The Pearson correlation coefficient was used for cardinal quantitative variables to measure the linear relationship between two variables.

3.4.2 Qualitative Analysis

The questionnaire included the following open questions:

1. Please describe your fears in relation to your spondylitis/spondyloarthritis.
2. Please describe your hopes in relation to your spondylitis/spondyloarthritis.
3. Please describe your personal treatment goals for spondylitis/spondyloarthritis.

In France, the third question was excluded and the first two questions were multiple choice.

The qualitative answers were homogenized (taking into account the options presented in the case of France), standardized, and grouped into several areas, including the frequency of each type of response. This allowed qualitative questions to be converted into quantitative, count percentages of answers, and thus assess patients' priorities in relation to their hopes and fears in general, as well as their goals with respect to their treatments.

3.5 Steering Committee

A multi-stakeholder steering committee of axSpA experts (rheumatologists, psychologists, researchers, and patient representatives) from several European countries was selected to:

- Guide strategy and data analysis.
- Provide expert responses to any questions emerging during the project.
- Interpret the results (both quantitative and qualitative).
- Provide scientific documents to support report preparation (including scientific literature and official reports).
- Support dissemination of the results.

The members of the steering committee for the IMAS European project are listed in the Contributors section.

Steering committees at the country level were organized in 8 of the 12 participating countries (all except Austria, Belgium, Germany, and the UK) to support local interpretation and dissemination of results.

3.6 Literature Review

The study utilized relevant information identified from a literature search to validate and support the responses from both questionnaires.

Searches were conducted using PubMed and Scopus with the keywords 'axial spondyloarthritis' and 'ankylosing spondylitis' together with other terms depending on the topic, such as:

- Employment: 'labour', 'employment', 'disability', 'absenteeism', or 'presenteeism'.
- Treatment: 'pharmacological treatments', 'drugs', or 'physical activity'.
- Health status: 'disease activity', 'stiffness', or 'functional limitation'.
- Well-being: 'mental health', 'psychological', 'psychiatric', 'anxiety', or 'depression'.
- Daily life: 'unhealthy habits', 'smoking', or 'alcohol'.
- Patient perspective: 'support group' or 'patient perspective'.

The search was limited to articles published between 2000 and 2018, giving priority to studies conducted in Europe compared with the rest of the world.

Documents developed by the Assessment in SpondyloArthritis international Society (ASAS) were also consulted to supplement literature searches.

3.7 Report

The data gathered using the questionnaire were used to prepare two types of report: a) an axSpA Country Profile for each country and b) an axSpA Pan-European report. The reports were prepared by the University of Seville. All members of the steering committee critically reviewed and approved the reports prior to publication.

Funding The IMAS European project was funded by Novartis Pharma AG, Basel, Switzerland (Supplemental Information for Chap. 3).

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4 Demographic Profile of Survey Respondents

The IMAS European survey was conducted across 13 European countries and included a wide range of patients with axSpA from varying sociodemographic backgrounds. Understanding the demographic characteristics of the survey participants allows the comparison of data from the IMAS cohort with data from other real-world studies and provides the context within which the IMAS data should be interpreted. In this chapter, the demographic characteristics of the European IMAS participants is presented.

4.1 IMAS European Patient Survey: Geographic Distribution

The IMAS European survey was completed by 2,846 participants with axSpA from 13 European countries. The majority of participants were from Spain, France, and Norway (Fig. 4.1).

4.2 Age of European IMAS Participants

The average age of participants was consistent with other axSpA studies. Participants' age ranged between 18 and 85 years. The mean age (± standard deviation [SD]) of the survey participants was 44 ± 12 years, which is consistent with other axSpA studies (mean age of approximately 48 years) (Mease et al. 2018; Dougados et al. 2011; Rudwaleit et al. 2009; Reveille 2013). Almost half of participants in IMAS were aged 35–51 years (Fig. 4.2). Only 3% of participants were aged > 68

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_4.

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Country	Austria	Belgium	France	Germany	Italy	Netherlands	Norway
Number of participants	82	76	638	78	134	107	509
Proportion of survey participants	2.9%	2.7%	22.4%	2.7%	4.7%	3.8%	17.9%

Country	Russia	Slovenia	Spain	Sweden	Switzerland	UK
Number of participants	233	83	680	71	80	75
Proportion of survey participants	8.2%	2.9%	23.9%	2.5%	2.8%	2.6%

Fig. 4.1 Distribution of survey participants by country (N = 2,846)

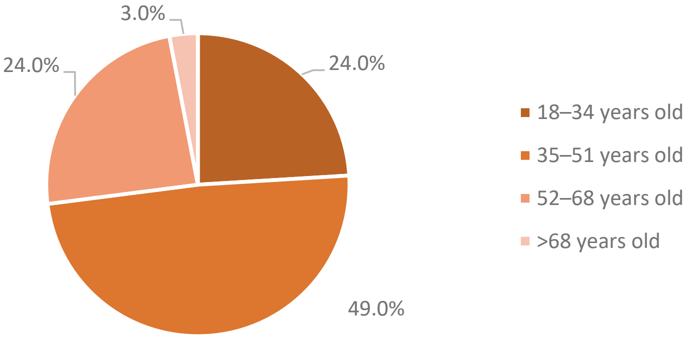


Fig. 4.2 Age of survey respondents by category (N = 2,846)

years, meaning that this age group is under-represented in the survey based on its proportion in the overall European population (Eurostat 2017a).

Reasons why more patients aged under 52 years took part in the IMAS European survey than older patients are unknown but may include greater internet access (and technical confidence) in younger versus older patients, greater concern about their disease (e.g. younger patients were at higher risk of psychological distress than older patients; see Chap. 7), and that younger patients were likely to have been more recently diagnosed with axSpA, and therefore may have been more interested in participating in research.

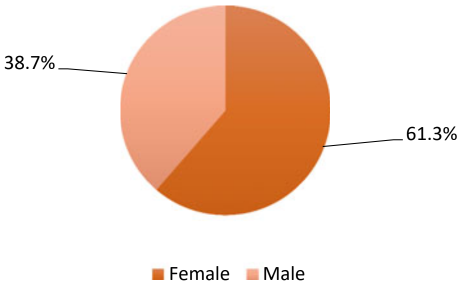


Fig. 4.3 Distribution of participants by gender (N = 2,846)

4.3 Gender Bias in European IMAS Population

While axSpA was historically thought to be more prevalent in men than women, this was predominantly due to under-diagnosis in women (potentially as a result of differences in symptoms, such as the more widespread pain reported by female patients with axSpA resulting in delayed or mis-diagnosis). More recent evidence suggests no difference in prevalence between genders (Slobodin et al. 2011; Polley and Slocumb 1947; West 1949; Rusman et al. 2018).

In the IMAS European survey, more than three out of five participants (61.3%) were female (Fig. 4.3). The reasons for the bias towards female participants is unclear but it could potentially be due to women being more comfortable sharing information/feelings and responding to online questionnaires (Smith 2008).

4.4 Weight of European IMAS Participants

Body mass index (BMI), a measure that reports an individual's weight according to their height, is commonly used to categorize individuals as underweight, within the normal range, overweight, or obese according to World Health Organization (WHO) criteria (2018).

The mean BMI of European IMAS participants was 26.1 kg/m^2, indicating that, overall, the study population was overweight. Half (52.2%) of the participants were categorized as overweight or obese (Fig. 4.4), which is similar to the general European population (51.6%) (Eurostat 2014).

Previous axSpA studies have reported similar BMIs (Mease et al. 2018) and there is evidence that obesity can increase the burden of inflammation and stiffness, decrease the benefits of exercise, and reduce the effectiveness of certain pharmacological treatments (Durcan et al. 2012). All patients with axSpA should therefore be encouraged to maintain a healthy BMI.

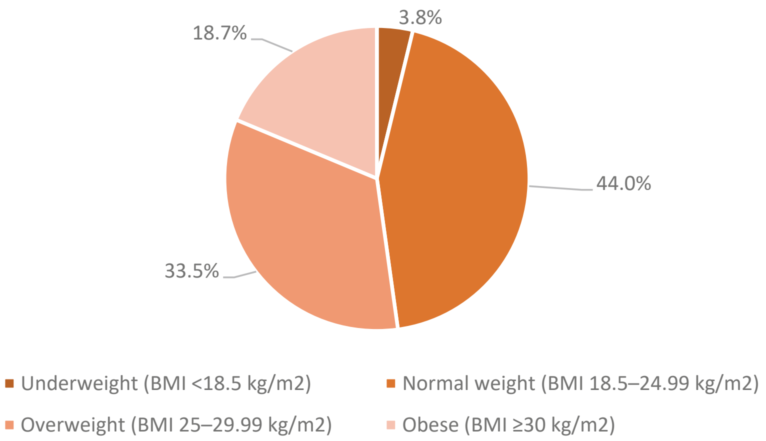


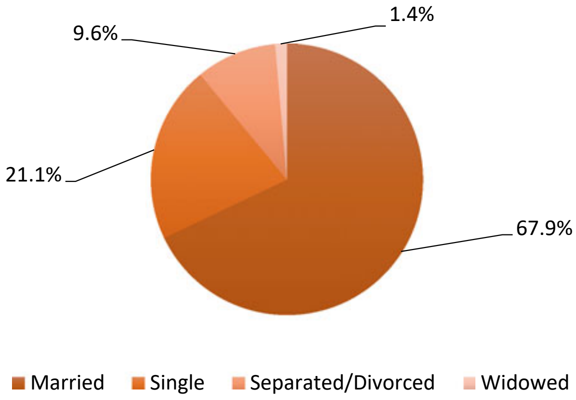
Fig. 4.4 Distribution of participants according to WHO classification of BMI categories (N = 2,846). *BMI* body mass index, *WHO* World Health Organization

4.5 Relationship Status of Participants in the IMAS European Survey

Like any chronic illness, axSpA can have a negative effect on relationships (Ward et al. 2008); in a US study, patients with axSpA were 50% more likely not to get married and 30% more likely to get divorced than healthy individuals. The reasons for these findings were not explored and further data of the impact of chronic rheumatic diseases on the likelihood of marriage or divorce are lacking (Ward et al. 2008).

Marriage or relationships may provide a primary source of social support that has beneficial effects on physical and mental health outcomes in patients with rheumatic disease, including axSpA (Strating et al. 2006; Ward and Leigh 1993; Ward 2002). In IMAS, more than two-thirds of participants were married (Fig. 4.5),

Fig. 4.5 Distribution of participants according to marital status (N = 2,846)



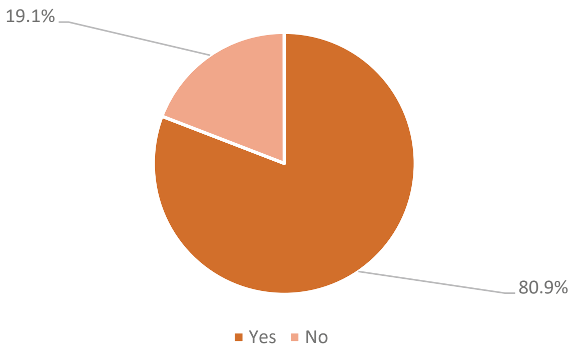


Fig. 4.6 Distribution of participants according to relationship status (N = 2,826)

which is higher than the overall marriage rate in Europe (55.3% (Eurostat 2015)), and four out of five participants were in a relationship (whether they were married or not) (Fig. 4.6), indicating good access to this vital source of social support.

4.6 Impact of axSpA on Participants' Fertility Rate

axSpA did not negatively impact the participants' fertility rate: the mean (±SD) number of children per household reported by participants was 1.4 ± 1.2, which is in accordance with the gross fertility rate (number of children per woman) in Europe (1.6) (Eurostat 2017b). Participants reported a mean (±SD) number of family members per household of 2.9 ± 1.3.

4.7 Education Level of European Participants in IMAS

Although there is some evidence to suggest that patients with axSpA are more likely to have a lower level of education due to their disease (Exarchou et al. 2015), the IMAS European data presented in Fig. 4.7 are in accordance with the levels of education across Europe (Eurostat. Educational attainment statistics 2018).

The mean monthly income of participants per household member was €1,122.58 (N = 2,289), which is lower than the minimum monthly wage reported in many of the countries participating in IMAS (Eurostat. Minimum wages 2015). The common manifestations of axSpA, such as pain fatigue, stiffness, and functional limitation, can greatly diminish work productivity and career prospects (Franke et al. 2009; Boonen et al. 2002, 2003a, b, 2010; Boonen and Linden 2006). Further information on the demographic profiles of IMAS European survey respondents can be found in the Supplement.

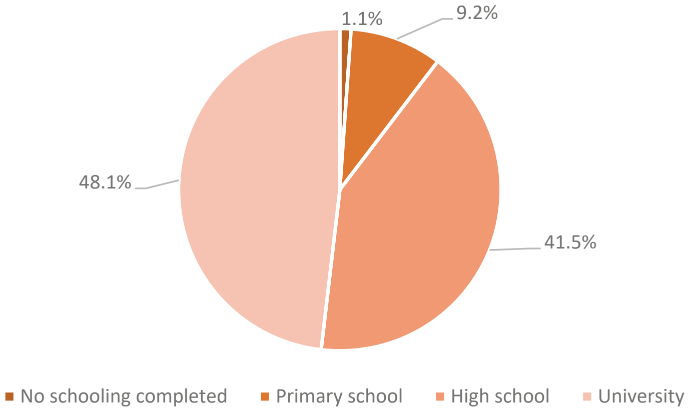


Fig. 4.7 Distribution of participants by educational level (N = 2,846)

4.8 Conclusions

- The IMAS European patient survey was completed by 2,846 participants with self-reported axSpA across 13 European countries (Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK).
- In general, the demographic profile of the European IMAS population was broadly similar to axSpA populations reported previously. There was a slight predominance of female and younger participants, which should be considered when interpreting the data.
  - The average (mean) age was 44 years; almost half were aged between 35 and 51 years, and nearly a quarter were young adults aged between 18 and 34 years.
  - More than three out of five participants were female.
  - More than half (52.2%) of participants were categorized as overweight or obese.
- More than two-thirds of participants reported being married, and four out of five participants reported living in a relationship (whether they were married or not), indicating good access to this vital source of social support.
- Participants were well educated, with most having completed high school or university; levels of education in this population were in accordance with those across Europe.
- The mean monthly income of European IMAS participants per household member was lower than the minimum monthly wage reported in many of the countries participating in IMAS.

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Diagnosis

5

The diagnosis of axSpA is challenging and is usually based on a combination of clinical symptoms (e.g. unexplained inflammatory back pain), patient characteristics (e.g. age <45 years, family history of axSpA, presence of genetic risk factors [human leukocyte antigen allele B27 (HLA-B27) positivity]), and the presence of inflammation on imaging (e.g. sacroiliitis on magnetic resonance imaging [MRI] or X-ray) (Sieper and Poddubnyy 2017; Rudwaleit and Sieper 2012; Rudwaleit et al. 2004). A number of other characteristics of axSpA that may be useful in diagnosis are captured in the ASAS axSpA classification criteria outlined in Fig. 5.1 (Rudwaleit et al. 2011).

Primary healthcare providers often treat patients who suffer from back pain but, as generalists, they can easily miss the signs of axSpA (Seo et al. 2015; Dincer et al. 2008). Early diagnosis and access to effective treatment are critical to reduce the burden of axSpA and prevent disease progression; delays in diagnosis mean that appropriate treatment is also delayed, which could potentially lead to a worse outcome (Seo et al. 2015; Dincer et al. 2008; Mandl et al. 2015). When axSpA is suspected or in all patients with unexplained inflammatory back pain for more than 3 months, referral to a rheumatologist is essential to ensure an accurate diagnosis and appropriate treatment (Rudwaleit and Sieper 2012).

In this chapter, the results from the IMAS European survey relating to diagnosis of axSpA are presented, including the personnel involved, the tests carried out, and the diagnostic delay experienced by participants.

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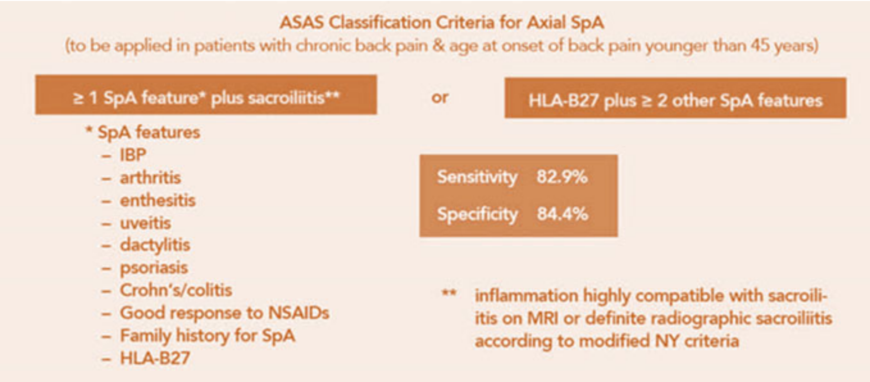

ASAS Classification Criteria for Axial SpA
(to be applied in patients with chronic back pain & age at onset of back pain younger than 45 years)

≥ 1 SpA feature* plus sacroiliitis**

or

HLA-B27 plus ≥ 2 other SpA features

* SpA features
- IBP
- arthritis
- enthesitis
- uveitis
- dactylitis
- psoriasis
- Crohn's/colitis
- Good response to NSAIDs
- Family history for SpA
- HLA-B27

Sensitivity 82.9%
Specificity 84.4%

** inflammation highly compatible with sacroiliitis on MRI or definite radiographic sacroiliitis according to modified NY criteria

Fig. 5.1 ASAS classification criteria for axSpA. *ASAS* Assessment of SpondyloArthritis International Society, *axSpA* axial spondyloarthritis, *HLA-B27* Human leukocyte antigen B27, *IBP* inflammatory back pain, *MRI* magnetic resonance imaging, *NSAID* non-steroidal anti-inflammatory drug, *NY* New York, *SpA* spondyloarthritis

5.1 Profile of HCPs Consulted by Patients with axSpA Prior to Receiving Diagnosis

Almost 80% of survey participants reported being diagnosed with axSpA by a rheumatologist (Fig. 5.2).

Most participants visited a general practitioner (GP) before diagnosis, which reflects the key role that these primary healthcare providers play in identifying possible cases of axSpA (Fig. 5.3). However, participants also reported visiting a

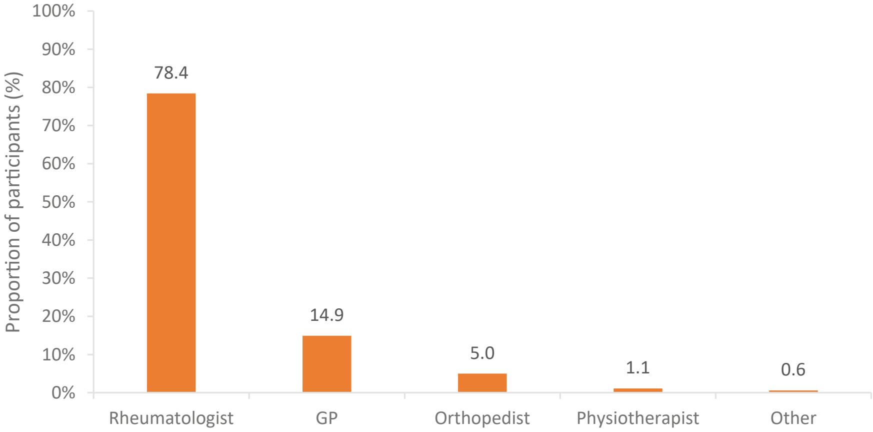

Fig. 5.2 HCP who diagnosed axSpA (N = 2,635). *axSpA* axial spondyloarthritis, *GP* general practitioner, *HCP* healthcare professional

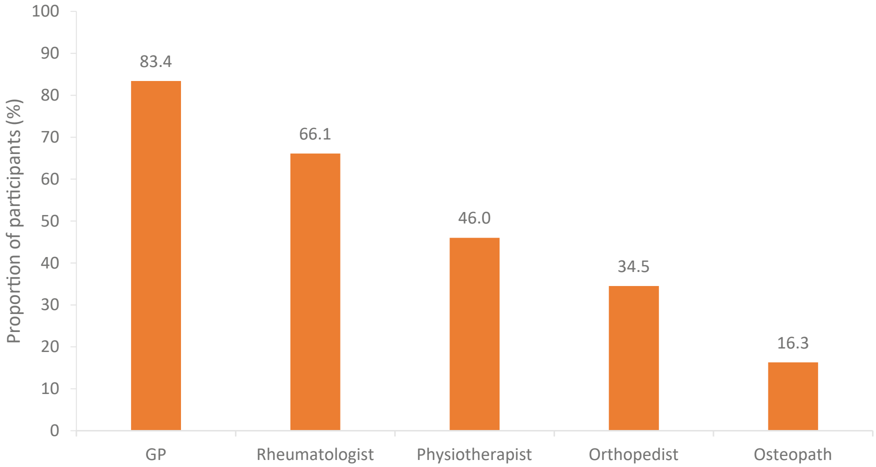

Fig. 5.3 HCPs visited by participants before diagnosis of axSpA (N = 2,706). *axSpA* axial spondyloarthritis, *GP* general practitioner, *HCP* healthcare professional

number of other specialists prior to diagnosis, including physiotherapists (46%), orthopedists (35%), and osteopaths (16%).

Participants frequently reported visiting more than one specialist prior to diagnosis, indicating that the path to diagnosis and treatment was not optimal. A primary care physician who suspects a high probability of axSpA should always refer patients directly to a rheumatologist for further investigation (Dincer et al. 2008).

5.2 Diagnostic Tests

The European League Against Rheumatism (EULAR) recommends that conventional radiography (i.e. X-rays) of the sacroiliac joints and spine should be performed to diagnose inflammation in the spine, sacroiliitis (inflammation of the sacroiliac joints), and assess any structural changes (Mandl et al. 2015). If diagnosis cannot be established based on clinical features and X-rays, MRI is recommended to detect both inflammation and structural changes (Mandl et al. 2015). Genetics plays a major role in susceptibility to axSpA, with inheritance of HLA-B27 being strongly implicated (Sieper and Poddubnyy 2017). Tests to identify the presence or absence of HLA-B27 are therefore also often used in the diagnostic work-up of axSpA (Rudwaleit et al. 2011).

The diagnostic test most frequently performed on European IMAS participants was X-ray imaging, followed by HLA-B27 genetic testing and MRI (Fig. 5.4), which is in broad accordance with the current diagnostic recommendations.

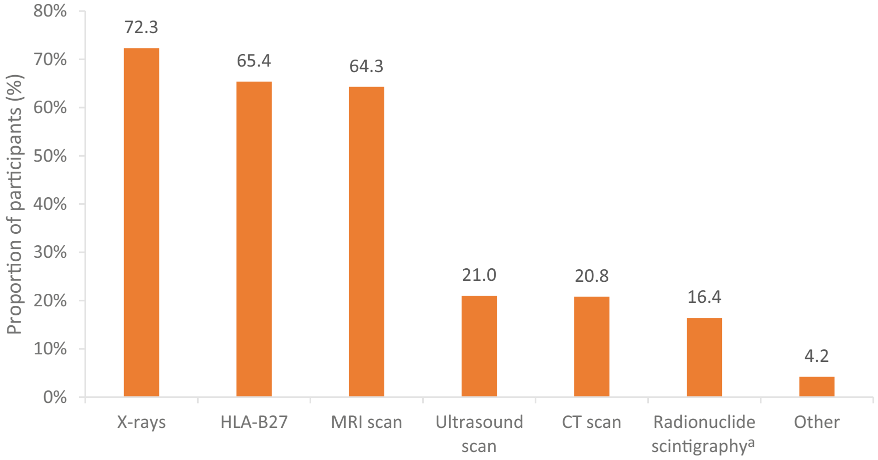

Fig. 5.4 Medical tests conducted in the diagnosis of axSpA in participants (N = 2,661). *axSpA* axial spondyloarthritis, *HLA-B27* Human leukocyte antigen B27, *MRI* magnetic resonance imaging, *CT* computerized tomography. ^{a}The number of patients undergoing radionuclide scintigraphy was not collected for participants from Norway

Almost 74% of the 1,735 participants who reported a genetic testing result were HLA-B27 positive, which is within the expected range based on published literature (Salvadorini et al. 2012; Glintborg et al. 2017).

5.3 Diagnostic Delay of European IMAS Participants

The mean (±SD) age of participants at symptom onset was 26.6 (±11.1) years, while the mean (±SD) age at diagnosis was 33.7 (±11.5) years. Diagnostic delay was defined, in accordance with previous studies (Masson Behar et al. 2017), as the time interval in years from the age at symptom onset to the age at diagnosis. The mean diagnostic delay of all European IMAS participants was 7.4 years and the median was 4.0 years (Table 5.1) (Garrido-Cumbrera et al. 2021), which is consistent with other European studies that reported an average diagnostic delay of approximately 8–11 years in patients with axSpA (Feldtkeller and Erlendsson 2008; Feldtkeller et al. 2003). In almost one-third of the survey participants, the diagnostic delay was more than 10 years (Table 5.2). A delay of 10 years or more has been associated with an increased probability of spinal structural damage (Haroon et al. 2013).

There was a large disparity in the diagnostic delay across participating countries (Fig. 5.5); this may be due to differences in patient characteristics or healthcare systems between the countries, and may also be influenced by the varying numbers

Table 5.1 Mean and median diagnostic delay in participants overall and by gender and age (N = 2,652)

	Diagnostic delay (years)		
	Mean	SD	Median
Overall	7.4	8.4	4.0
Gender			
Female	8.2	8.9	5.0
Male	6.1	7.4	3.0
Age at time of survey			
18–34 years	4.4	5.5	2.0
35–51 years	7.9	8.2	5.0
52–68 years	9.5	10.2	5.0
Over 68 years	7.3	9.7	4.0

SD standard deviation

Table 5.2 Diagnostic delay of participants classified by year categories (N = 2,652)

Diagnostic delay (years)	N	%
0–1	782	29.5
2–4	548	20.7
5–7	385	14.5
8–10	246	9.3
11–15	256	9.7
Over 15	435	16.4

of participants per country. Countries reporting the highest mean diagnostic delay were Norway (10.6 years), Spain (8.5 years), Slovenia (7.8 years), and Sweden (7.6 years). The lowest values were reported by participants in the UK (2.6 years), Germany (2.7 years), Switzerland (3.5 years), and Belgium (3.6 years). The diagnostic delay observed in the present study in Germany (2.7 years) was shorter than in previous studies such as the PROCLAIR study in which the mean diagnostic delay was 5.7 years (Redeker et al. 2019). This could be due to the larger sample of the PROCLAIR study compared to the IMAS German subgroup.

5.4 Delay in Diagnosis by Gender

The diagnostic delay was statistically longer in female versus male participants (Table 5.1; mean delay 8.24 years versus 6.14 years; Mann–Whitney $p \leq 0.001$) (Garrido-Cumbrera et al. 1865). Similar data were shown in a recent systematic review and meta-analysis, where the mean diagnostic delay was 8.8 years for women and 6.5 years for men (Jovani et al. 2017). Although there are no obvious gender-based differences in the clinical manifestations of axSpA, these differences may be due to a later onset of disease in women, the more widespread pain reported

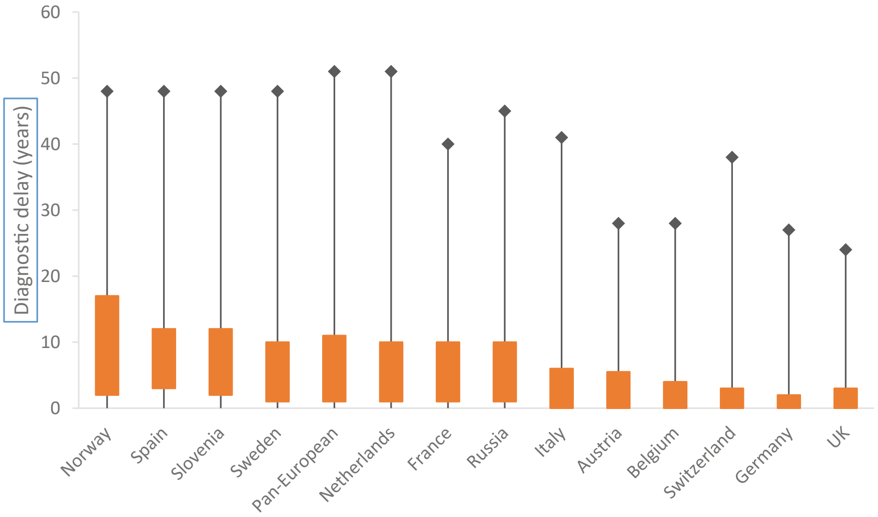

Fig. 5.5 Quartiles of diagnostic delay by country (N = 2,652)

by female patients with axSpA resulting in delayed diagnosis, or faster disease progression in men (Slobodin et al. 2011; Rusman et al. 2018).

5.5 Delay in Diagnosis by Time Since Symptom Onset

Diagnostic delay was significantly longer in older participants than younger ones (Table 5.1; Kruskal–Wallis $p \leq 0.001$). Furthermore, the delay was longer in participants who experienced symptom onset at a younger age, as indicated by a significant negative relationship between age at onset of symptoms and diagnostic delay (Fig. 5.6; Pearson's correlation −0.377, significant at the 0.01 level [bilateral]). These results may have been partly influenced by data from older participants who were undiagnosed for several years and later received a diagnosis following improvements in axSpA awareness, access to rheumatologists, and advances in imaging techniques (Salvadorini et al. 2012; Glintborg et al. 2017; Sorensen and Hetland 2015). Accordingly, the diagnostic delay was longer in patients diagnosed more recently (Pearson's correlation 0.163, significant at the 0.01 level [bilateral]).

Improvements in the diagnosis of axSpA over time are also the likely explanation for the significant relationship observed between year of onset of symptoms and diagnostic delay (Fig. 5.7; Pearson's correlation −0.545, significant at the 0.01 level [bilateral]); diagnostic delay was shorter in patients who experienced symptom onset more recently. More than half of the IMAS European survey sample were diagnosed between the years 2010 and 2017 (Table 5.3), highlighting the improvements in diagnosis that followed publication of the 2009 ASAS guidelines

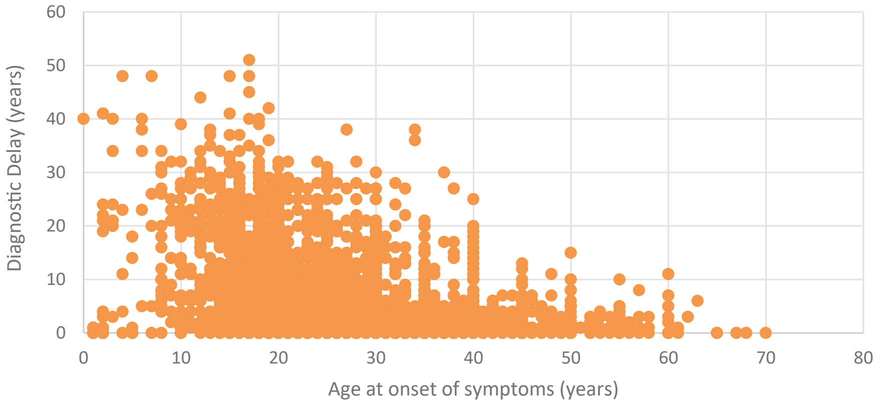

Fig. 5.6 Scatter diagram of age at onset of symptoms in participants versus diagnostic delay

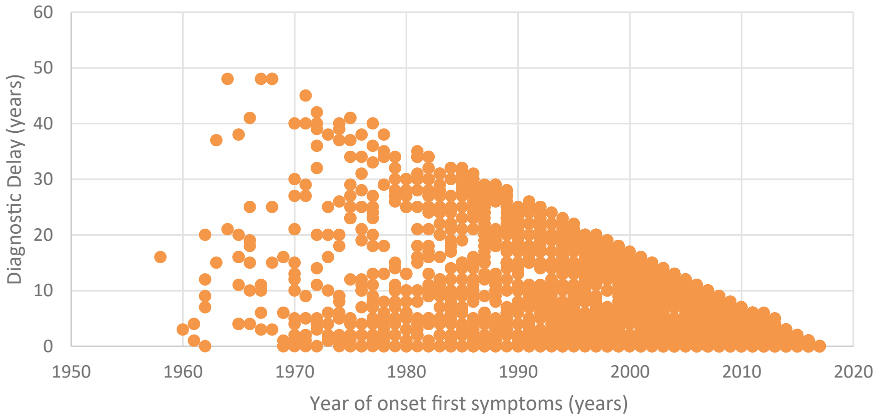

Fig. 5.7 Scatter diagram of year of onset of symptoms in participants versus diagnostic delay

Table 5.3 Number of diagnoses of axSpA per decade in IMAS European survey participants (N = 2,649)

Decade of diagnosis	n	%
1960–1969	10	0.4
1970–1979	66	2.5
1980–1989	145	5.5
1990–1999	284	10.7
2000–2009	647	24.4
2010–2017	1,497	56.5

axSpA axial spondyloarthritis, *IMAS* International Map of Axial Spondyloarthritis for the classification of axSpA (Rudwaleit et al. 2009). It is important to note that the IMAS European survey only included participants who had already been diagnosed with axSpA so does not provide information regarding the current diagnostic pathway/delay for undiagnosed patients with recent onset of symptoms.

5.6 Conclusions

- The mean delay in diagnosis reported by participants was 7.4 years, with more than half waiting 5 or more years for a diagnosis.
- Diagnosis was delayed by approximately 2 years longer in female versus male participants.
- The delay was shorter in patients who experienced symptom onset more recently, suggesting that the delay between symptom onset and diagnosis has improved over time.
- Most (83%) European IMAS participants visited a GP prior to receiving a diagnosis, reflecting an important role for primary healthcare providers in identifying possible cases of axSpA.
- Participants also frequently reported visiting other specialists, such as physiotherapists (46%) and orthopedists (35%), prior to diagnosis, suggesting that the preferred pathway to diagnosis (via a rheumatologist) was not followed.
- Although there is evidence that the delay in axSpA diagnosis has improved, it remains a poorly diagnosed disease and further efforts are required to raise awareness amongst patients, HCPs, and the general public to ensure faster diagnosis and treatment.

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Physical Health

6

In this chapter, the physical health of European IMAS participants is examined, including disease activity, spinal stiffness, inflammation, and comorbidities. The relationship between these parameters and a range of sociodemographic and clinical characteristics is also explored.

IMAS European survey participants were receiving a range of different treatments (e.g. non-steroidal anti-inflammatory drugs [NSAIDs], conventional synthetic disease-modifying anti-rheumatic drugs [csDMARDs], biologics, and combinations of different treatments) but there were insufficient numbers of participants receiving particular treatment(s) to stratify the results accordingly.

6.1 Disease Activity in European IMAS Participants

BASDAI is the most commonly used measure of disease activity in axSpA (Sieper and Poddubnyy 2017). The mean (±SD) BASDAI score across the 2,584 participants in the IMAS European survey was 5.5 (±2.0), and active disease (BASDAI score ≥ 4) was reported in 78.1% of participants overall (Fig. 6.1).

Spinal stiffness can affect any region of the spine from the neck to the lower back, and is one of the most frequent symptoms in patients with axSpA (Sieper and Poddubnyy 2017). Approximately 80% of European IMAS participants reported some degree of spinal stiffness, with more than 45% having moderate or severe stiffness (Fig. 6.2).

Inflammation was self-reported by answering the following question: "In which part of your body have you noticed inflammation at some point due to spondylitis/spondyloarthritis"? As inflammation is an objective measure detected by physicians during an examination, it is important to note that participants are

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M. Garrido-Cumbrera et al., *Axial Spondyloarthritis: Patient-Reported Impact in Europe*, https://doi.org/10.1007/978-3-030-97606-4_6

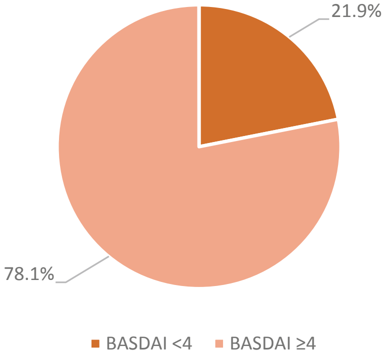

Fig. 6.1 Level of disease activity of participants (BASDAI <4 or ≥ 4) (N = 2,584). *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index

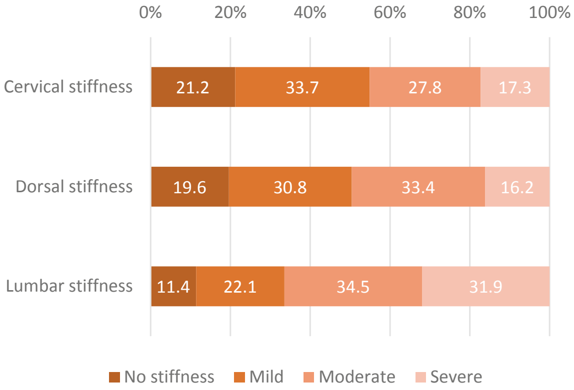

Fig. 6.2 Degree of spinal stiffness (cervical, dorsal, and lumbar) in participants

likely to have answered this question based on pain in a particular body area rather than inflammation specifically.

The majority of European IMAS participants reported inflammation in the lumbar region, sacroiliac joints, and hips (Fig. 6.3), regions of the body typically affected by axSpA (Sieper and Poddubnyy 2017). Other affected sites frequently reported by IMAS participants were the dorsal region of the spine, and the shoulders and knees, indicative of peripheral arthritis.

Disease activity levels were typically higher than those previously reported in axSpA registries, where BASDAI ranges from 4.0 to 4.3 (Rudwaleit et al. 2009; Gladman et al. 2011; Glintborg et al. 2017; Mease et al. 2018). High disease activity in axSpA can leave patients at risk of irreversible structural damage as well as having a negative impact on quality of life (Ramiro et al. 2014; Lopez-Medina et al. 2018). Consequently, targeting disease activity is a key aim of axSpA therapy (Heijde et al. 2017; Smolen et al. 2018). The high level of disease activity in the European IMAS population may be indicative of sub-optimal disease management. Differences in the way the data are collected in surveys (patient reported) and registries (often collected by the doctor) may potentially account for some differences in these different data sets.

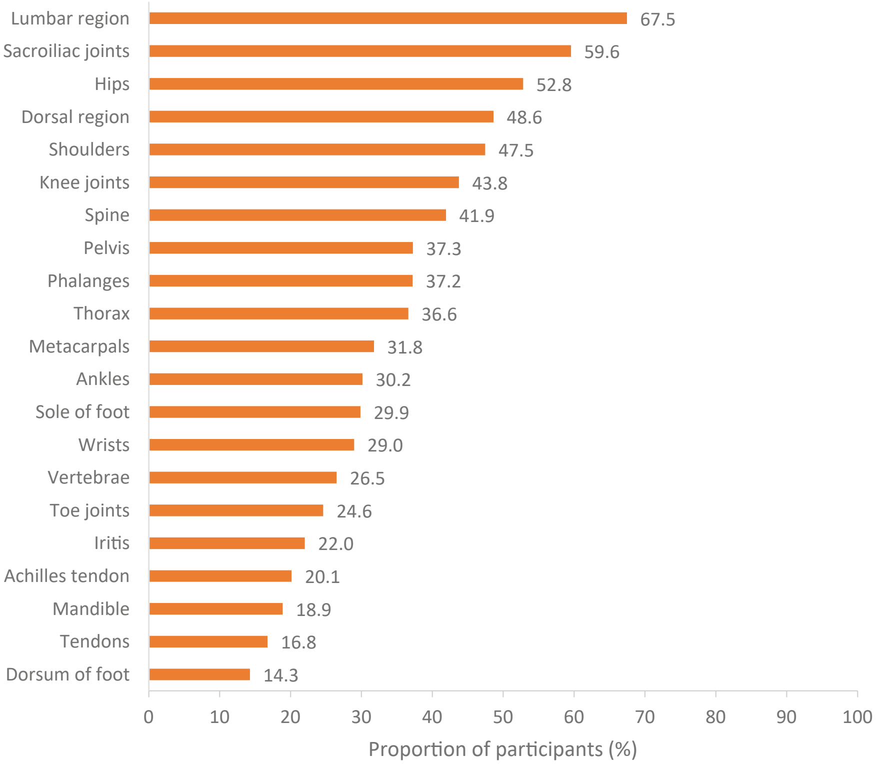

Fig. 6.3 Body areas where survey participants reported experiencing inflammation (N = 2,727)

In addition to spinal inflammation, many participants also reported inflammation at peripheral sites. This is in agreement with previous studies showing that 30–50% of axSpA patients present with peripheral inflammation, typically in the lower limbs (e.g. knees) (Sieper and Poddubnyy 2017). Peripheral disease manifestations contribute significantly to the burden of disease in axSpA, but are often largely ignored when it comes to disease monitoring. Greater consideration should be given to the management of these relatively common manifestations.

6.2 Impact of axSpA on Patients' Daily Activities

axSpA can cause severe limitations to patients' daily lives, affecting not only their quality of life but also their work productivity and social functioning (Rudwaleit et al. 2009; Gladman et al. 2011; Glintborg et al. 2017; Mease et al. 2018; Ramiro et al. 2014; Lopez-Medina et al. 2018; Heijde et al. 2017; Smolen et al. 2018; Horst-Bruinsma et al. 2012; Ward 1999; Ariza-Ariza et al. 2003; Boonen et al. 2001; Barlow et al. 2001; Ward and Kuzis 2001; Mengshoel 2008).

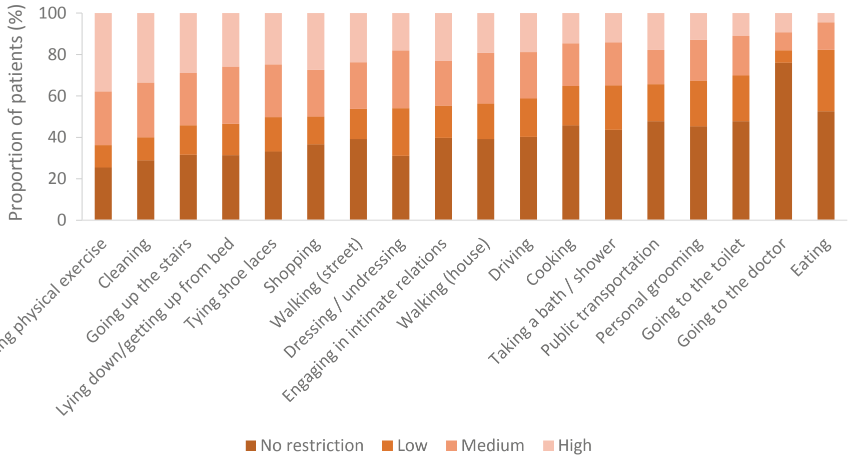

Fig. 6.4 Restricted daily activities reported by survey participants (N = 2,771)

The mean Functional Limitation Index of European IMAS participants was 20.4, indicating a medium level of limitation (Garrido-Cumbrera et al. 2019). Physical exercise, cleaning, going up stairs, and getting out of bed were the most commonly affected daily activities (Fig. 6.4). Almost 70% of participants felt their disease affected their ability to tie their shoelaces and over half reported that axSpA had affected their ability to have intimate relations, go to the toilet, and go shopping.

As a consequence of their functional limitations, participants reported needing assistance carrying out routine daily activities, such as cleaning, shopping, going to the doctor, and doing physical exercise (Fig. 6.5). Many participants reported needing help in having intimate relations (57.9%) and going to the toilet (46.6%).

Many participants reported making adaptations, such as customizing shoes and modifying their workplace, to overcome functional limitations and continue to carry out daily activities (Table 6.1).

A greater appreciation of the challenges faced by patients with axSpA in daily living can help promote understanding from friends, family, and work colleagues, in addition to informing strategies aimed at improving their quality of life.

6.3 Comorbidities Reported in Patients with axSpA

More than two out of five survey participants reported suffering from two or more physical comorbidities, while almost half reported having at least one psychological comorbidity (**Supplemental Table 6.1**). Sleep disorders, anxiety, and depression were the most frequently reported comorbidities overall, with other common comorbidities including obesity/overweight and hypertension (Fig. 6.6).

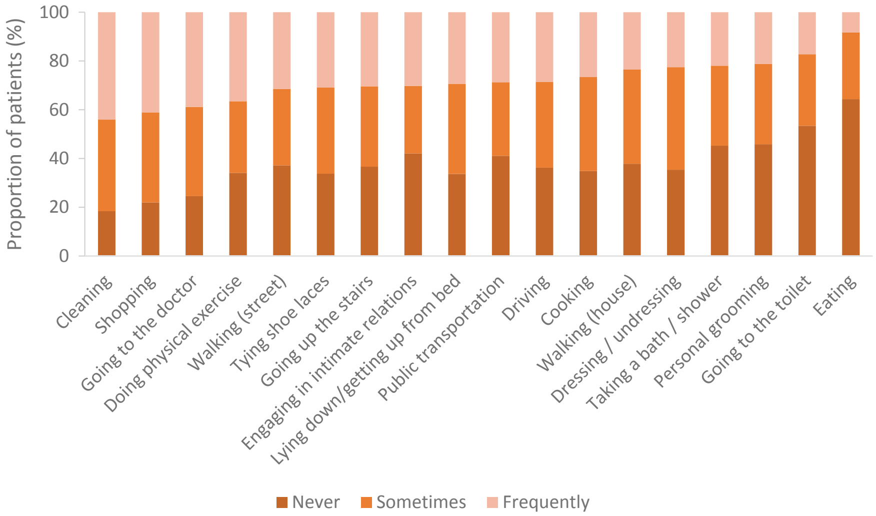

Fig. 6.5 Daily activities for which survey participants declared needing help (N = 664–1,969)

Table 6.1 Adaptations made/steps taken by participants to overcome difficulties

Activities	Yes		No	
	n	%	n	%
Customized shoes	1,525	55.5	1,223	44.5
Workplace adaptation	1,163	43.9	1,488	56.1
Moved to another job	751	28.2	1,911	71.8
Adapting home	861	31.7	1,855	68.3
Adapting car	614	22.6	2,099	77.4

The IMAS European survey also explored the presence of three key extra-articular manifestations: uveitis, ulcerative colitis, and Crohn's disease (the presence of psoriasis was not consistently captured across participating countries and is therefore not reported). These manifestations were reported by 22.4%, 8.4%, and 7.4% of participants, respectively, consistent with incidences reported in the literature (Winter et al. 2016).

These data support previous findings that extra-articular manifestations such as inflammatory bowel disease (IBD) and uveitis are common in axSpA and can increase the burden of disease and worsen overall health status by increasing functional limitation and occupational disability (Horst-Bruinsma et al. 2012; Molto and Nikiphorou 2018).

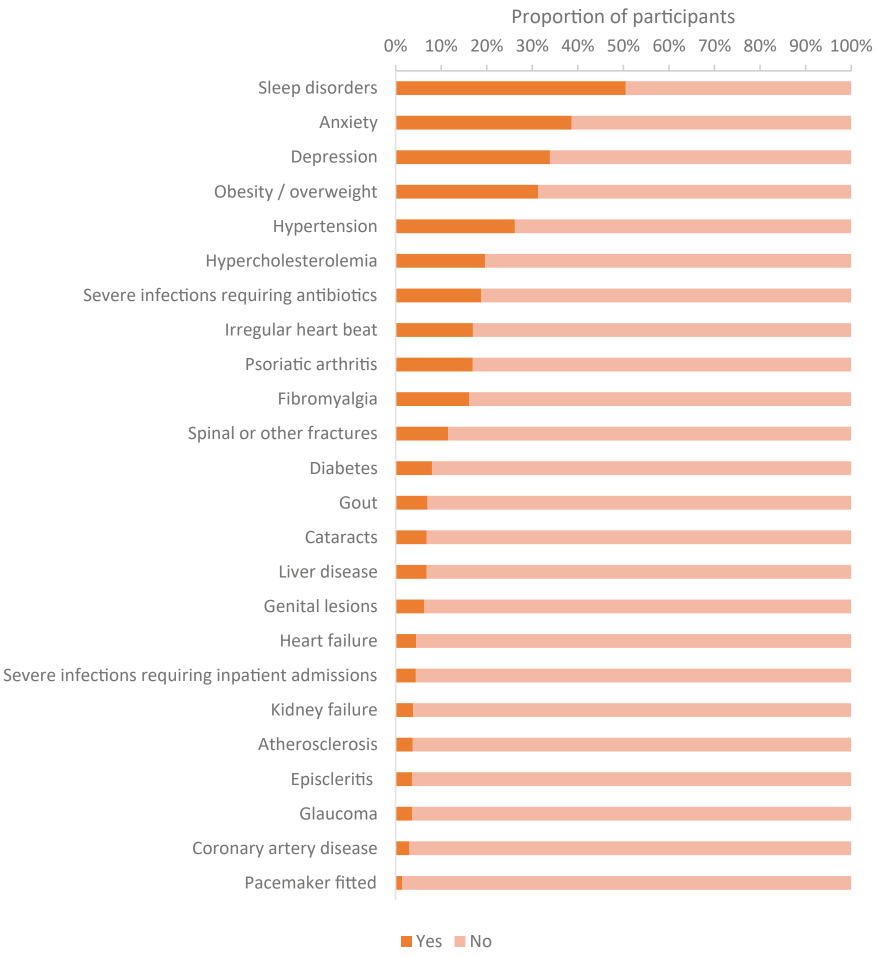

Fig. 6.6 Comorbidities reported by participants (N = 2,096)

6.4 Physical Health and Sociodemographic Characteristics

Understanding the links between sociodemographic characteristics and physical health may be useful for identifying groups at particular risk and tailoring disease management strategies accordingly.

A significant relationship was demonstrated between the BASDAI scores of European IMAS participants and age, gender, marital status, schooling, and income (Table 6.2; **Supplemental Fig. 6.1**). In agreement with previous studies, disease activity was generally higher in younger participants (those under 52 years old), females, those who were separated/divorced (relative to those who were single or married), those with a

Table 6.2 Mean BASDAI score of survey participants in subgroups stratified by age, gender, schooling, marital status, and income

	N	Median	Mean	SD
Overall	2,584	5.8	5.5	2.0
Age (years)[a]				
18–34	651	5.8	5.5	2.1
35–51	1,245	5.9	5.6	2.0
52–68	608	5.4	5.2	2.0
69–85	80	5.7	5.4	1.9
Gender[b]				
Male	985	5.3	5.1	2.0
Female	1,599	6.0	5.7	1.9
Schooling[c]				
No schooling completed	29	6.1	6.0	1.9
Primary school	217	5.9	5.7	1.9
High school	1,058	6.0	5.8	1.9
University	1,280	5.4	5.2	2.0
Marital status[d]				
Single	556	5.7	5.3	2.1
Married	1,745	5.7	5.5	2.0
Separated/divorced	250	6.2	5.9	1.9
Widowed	33	6.2	5.6	2.1
Income (monthly)[e]				
No income	42	6.4	5.8	2.6
€500 or less	548	6.1	5.8	2.0
€501–1,000	734	5.8	5.6	1.9
€1,001–1,500	436	5.8	5.4	1.8
€1,501–2,000	283	5.3	5.0	2.0
€2,001–3,000	150	4.8	4.7	2.0
€3,001–5,000	42	4.7	4.4	2.2
€5,001 or over	13	4.7	4.4	2.0

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *SD* standard deviation

[a] Kruskal-Wallis test p-value was 0.003 indicating an association between age and BASDAI score;

[b] Mann-Whitney test p-value was <0.001 indicating an association between gender and BASDAI score;

[c] Kruskal-Wallis test p-value was <0.001 indicating an association between schooling and BASDAI score;

[d] Kruskal-Wallis test p-value was 0.001 indicating an association between marital status and BASDAI score;

[e] Kruskal-Wallis test p-value was <0.001 indicating an association between monthly income per family member and the BASDAI score—the higher the income, the lower the BASDAI level

higher level of education, and those with higher income (Winter et al. 2016; Gran and Skomsvoll 1997; Roussou et al. 1997; Hart and Robinson 1959; McBryde and McCollum 1973; Braunstein et al. 1982; Lee et al. 2007; Daltroy et al. 1990).

Only age showed a significant relationship with spinal stiffness amongst European IMAS participants, with older participants being more likely to have spinal stiffness (**Supplemental Fig. 6.2**).

Gender was the only sociodemographic variable that showed a significant relationship with functional limitation, with female participants reporting significantly more functional limitation than male participants (mean Functional Limitation Index ± SD: 21.2 ± 16.0 vs. 19.1 ± 16.7; **Supplemental Table 6.2**).

Overall, there were no consistent sociodemographic predictors of physical health across disease activity, spinal stiffness, and functional limitation. Female participants reported higher disease activity and greater functional impairment than their male counterparts. Emerging evidence suggests that women with axSpA may experience more severe and widespread pain versus men (Calin et al. 1999; Slobodin et al. 2011), which may go some way to explaining these findings. Although older participants reported lower disease activity than younger participants, they also reported higher spinal stiffness. The reasons for this discrepancy remain unclear, but age-related stiffness may be a factor.

6.5 Physical Health and Diagnostic Delay

Participants who reported spinal stiffness had a significantly longer mean diagnostic delay than participants who did not report spinal stiffness (8.1 years vs. 5.6 years; χ^2 test $p < 0.001$). There was also a significant relationship between severity of spinal stiffness and diagnostic delay, with participants who reported severe spinal stiffness showing a longer mean diagnostic delay (Table 6.3). This highlights the importance of prompt diagnosis and treatment of axSpA to avoid the risk of further complications in affected patients.

No relationship was observed between disease activity and diagnostic delay (**Supplemental Table 6.3**).

Table 6.3 Mean diagnostic delay in participants by maximum degree of spinal stiffness

Maximum degree of spinal stiffness	Years of diagnostic delay[a]		
	N	Mean	SD
No restriction	185	4.3	5.8
Mild	451	5.5	7.2
Moderate	907	7.7	8.3
Severe	1,088	8.7	9.1
Total	2,631	7.5	8.5

SD standard deviation

[a] Kruskal-Wallis test p-value was <0.001 indicating an association between years of diagnostic delay and the maximum degree of spinal stiffness

6.6 Patients with axSpA Should Be Encouraged to Engage in Physical Activity

European IMAS participants who engaged in physical activities during the preceding 12 months reported statistically lower BASDAI scores than those who did not (Table 6.4) and were less likely to have active disease (BASDAI ≥ 4). However, this difference was not considered clinically relevant based on the minimal clinically important difference of 1.1 for BASDAI calculated in previous studies (Rusman et al. 2018).

A significantly higher proportion of participants who did not participate in physical activities reported severe spinal stiffness than those who did participate in physical activities (Table 6.5).

These results highlight the benefits of participating in exercise in axSpA and support previous findings on the positive impact of exercise on axSpA signs and symptoms (Kviatkovsky et al. 2016; Berg et al. 2012; Altan et al. 2012). Consistent with the ASAS-EULAR recommendations for the management of axSpA, exercise should be encouraged in all patients (Heijde et al. 2017).

Table 6.4 Participation in beneficial physical activities and BASDAI scores

Participation in physical activities	N	Mean BASDAI (SD)[a]	Participants (%)[b]	
			BASDAI < 4	BASDAI $\geq$ 4
No	552	5.8 (1.9)	16.7	83.3
Yes	2,032	5.3 (2.0)	23.3	76.7

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *SD* standard deviation

[a] Mann-Whitney test p-value was <0.001 indicating an association between participating in physical activities and BASDAI score;

[b] χ^2 test p-value was 0.001 indicating an association between participating in physical activities and having a BASDAI <4

Table 6.5 Participation in beneficial physical activities and degree of spinal stiffness

Participation in physical activities	Maximum degree of spinal stiffness[a]				Total
	None	Mild	Moderate	Severe	
No					
Frequency	45	77	148	292	562
%	8.0	13.7	26.3	52.0	100.0
Yes					
Frequency	142	394	786	823	2,145
%	6.6	18.4	36.6	38.4	100.0
Total					
Frequency	187	471	934	1,115	2,707
%	6.9	17.4	34.5	41.2	100.0

[a] χ^2 test p-value was <0.001 indicating an association between participating in physical activities and the maximum degree of spinal stiffness

6.7 BMI and Physical Health

BMI (a measure of body weight in relation to height) has been shown to affect numerous clinical aspects of axSpA, including response to therapy, symptom burden, ability to carry out daily activities, and quality of life (Durmus et al. 2009; Durcan et al. 2012; Toy et al. 2017; Rubio Vargas et al. 2016).

Although statistically significant relationships were observed between participants' BMI and BASDAI, Spinal Stiffness Index, and Functional Limitation Index, the small magnitudes of the differences between groups (0.2, 0.2 and 0.7, respectively) mean they are unlikely to have been clinically relevant in isolation (Table 6.6). However, together with healthy lifestyle habits such as increased physical activity and smoking cessation (see Sects. 6.6 and 10.2), such differences may influence the overall health of patients with axSpA.

The results of a study conducted using the Norwegian IMAS sample found that obesity was associated with higher BASDAI, and being overweight or obese was associated with a greater degree of spinal stiffness and a greater number of comorbidities (Bindesbøll et al. 2020).

6.8 Relationships Between Disease Activity, Spinal Stiffness, Inflammation, Physical Comorbidities, and Functional Limitations

The inter-relationships between BASDAI, Spinal Stiffness Index, inflammation, and Functional Limitation Index in European IMAS participants are summarized in Table 6.7 and **Supplemental Tables 6.4**, **6.5**, **6.6**, **6.7**, **6.8**, **6.9**, **6.10** and **6.11**.

Generally, participants with higher mean BASDAI scores had more severe spinal stiffness, more inflamed body areas, more physical comorbidities, and higher mean Functional Limitation Index values than those with lower BASDAI scores. Furthermore, those with more severe spinal stiffness had more inflamed body areas, more physical comorbidities, and higher mean Functional Limitation Index values. Since stiffness and joint pain/swelling are two components of BASDAI, these results are perhaps unsurprising. However, they do highlight that these aspects of physical health combined have a detrimental impact on the functional limitation of patients. Further research into the incidence of comorbidities in patients with axSpA and their association with BASDAI scores and spinal stiffness is warranted.

Table 6.6 Physical health of survey participants by BMI

BMI	BASDAI				Functional Limitation Index		Spinal Stiffness Index	
	N	Mean (SD)[a]	Participants (%)[b]		N	Mean (SD)[c]	N	Mean (SD)[d]
			BASDAI < 4	BASDAI ≥ 4				
Underweight/normal	1,243	5.4 (2.0)	23.4	76.6	1,330	20.3 (16.6)	1,277	7.4 (2.5)
Overweight/ obese	1,341	5.6 (2.0)	20.4	79.6	1,441	20.5 (16.0)	1,383	8.1 (2.4)

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *BMI* body mass index, *SD* standard deviation

[a] Mann-Whitney test p-value was 0.025 indicating a significant association

[b] χ^2 test p-value was 0.067 indicating no significant relationship

[c] Mann-Whitney test p-value was 0.356 indicating no relation between Functional Limitation Index and being overweight/obese

[d] Mann-Whitney test p-value was <0.001 indicating a significant association between Spinal Stiffness Index and being overweight/obese

Table 6.7 Correlation between measures of physical health in European IMAS participants

		BASDAI	Spinal Stiffness Index
Spinal Stiffness Index	Pearson's correlation	0.437[a]	–
	Significant (bilateral)	<0.001	–
	N	2,542	–
Number of body parts with inflammation	Pearson's correlation	0.319[a]	0.377[a]
	Significant (bilateral)	<0.001	<0.001
	N	2,582	2,657
Functional Limitation Index	Pearson's correlation	0.339[a]	0.230[a]
	Significant (bilateral)	<0.001	<0.001
	N	2,583	2,660
Number of physical comorbidities	Pearson's correlation	0.252	0.268
	Significant (bilateral)	<0.001	<0.001
	N	2,471	2,547

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *IMAS* International Map of Axial Spondyloarthritis

[a] Relationship significant at the 0.01 level (bilateral)

6.9 Conclusions

- The majority of European IMAS participants reported BASDAI scores consistent with active disease and some degree of spinal stiffness.
- Areas of the body that were reported to be affected by inflammation included those commonly associated with axSpA such as the lumbar region, sacroiliac joints, and hips, as well as peripheral joints such as the shoulders and knees.
- The vast majority of participants reported medium or high restriction in carrying out tasks of daily living and sometimes or frequently requiring assistance with these tasks; adaptations to overcome these difficulties were also frequently reported.
- The three most common comorbidities in participants were sleep disorders (50%), anxiety (39%), and depression (34%).
- Extra-articular manifestations (uveitis, ulcerative colitis, and Crohn's disease) were also relatively common.
- The data reported here serve to highlight the enormous impact that axSpA has on patients' lives. Minimizing disease activity and improving physical health should remain a key aim of disease management.

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Psychological Health

7

Psychological distress is frequently experienced by patients with axSpA, with some studies reporting that more than 50% of patients have concomitant depression or anxiety (Zou et al. 2016; Kilic et al. 2014; Shen et al. 2016; Hakkou et al. 2013; Meesters et al. 2014a). The exact mechanisms that lead to poor psychological status are not completely understood. It seems intuitive that the common symptoms of axSpA such as loss of mobility, stiffness, chronic pain, and fatigue, and their resultant interference with many aspects of daily functioning, including recreational activities, work, family life, and relationships are involved (Yang et al. 2016). Appreciation of the mental health of patients with axSpA is an important facet of their overall care as it can have a significant impact on response to treatment (Kilic et al. 2014).

In this chapter, the psychological health of the participants in IMAS will be described and the role of sociodemographic variables, clinical characteristics, and exercise in psychological health examined.

7.1 Overall Psychological Health

The psychological health of the European IMAS population was generally poor across the majority of participating countries (**Supplemental Fig. 7.1**). The mean (±SD) GHQ-12 score amongst 2,640 participants was 5.0 (±4.1) and 62% of survey participants declared a GHQ-12 higher than 3, signifying a risk of psychological distress (Banks 1983).

IMAS participants at risk of psychological distress also reported a higher mean (±SD) number of psychological comorbidities than those at lower risk (1.3 ± 1.2 vs. 0.5 ± 0.8; Mann–Whitney test p-value < 0.001). Many participants reported

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trouble sleeping (50.5%), anxiety (38.6%) and depression (33.9%), and the mean number of visits to a psychiatrist and/or psychologist over the past 12 months was 2.5 in the 1,235 participants who answered this question.

Given the high burden on mental health reported in this study, a mean of 2.5 visits to a psychiatrist and/or psychologist could be seen as being low. In general, psychotherapies based on cognitive-behavioral techniques for anxiety or depression would require between 8 and 20 sessions of individual therapy (Widnall et al. 2020). In this context, the findings of our survey suggest that either the psychological interventions being employed are too short to improve health outcomes, or that European axSpA patients are heavily relying on psychiatric care. As an effective psychiatric care would require at least three sessions a year (one for setting the treatment, one or two for short-term monitoring and one for long-term follow-up), one may hypothesize that European axSpA patients are not getting sufficient treatment for their psychological health.

Data on visits to mental health professionals of axSpA patients are scarce. A cross-sectional study in Spain reported that, in the 2-year period prior to the survey, only 2.1% of patients sought psychiatric care and only 0.9% sought psychological care (Jovani et al. 2012).

These findings highlight the significant toll of axSpA on psychological health. A holistic approach to care is therefore necessary when treating axSpA, taking into consideration psychological as well as physical symptoms (Packham 2018).

Poor sleep is a common complaint in patients with axSpA, with a recent systematic literature review indicating that 35–90% of patients experience this symptom (Leverment et al. 2017). Poor sleep in axSpA is associated with poorer quality of life, general health, mood, and work-related measures (Wadeley et al. 2018) and thus further efforts are required in clinical practice to assess and treat this common and often under-appreciated symptom. A meta-analysis of 16 axSpA studies found a prevalence of depression of 11–64% (Zhao et al. 2018), while anxiety was evident in 40% of patients with axSpA in a recent Chinese single-center study (Zou et al. 2016). These prevalence rates, like those reported in the IMAS survey, are in stark contrast to the background WHO prevalence rates in countries participating in IMAS, where anxiety ranged from 3.1–7.4% and depression from 4.5–5.5%. Recognizing and treating these common psychological comorbidities promptly in patients with axSpA is vital for ensuring an optimal outcome (Kilic et al. 2014).

7.2 Further Research is Required to Investigate the Link Between Sociodemographic Factors and Psychological Health in axSpA to Aid Identification of At-Risk Groups

The relationship between psychological health and a number of sociodemographic variables was assessed in IMAS, with significant associations identified between GHQ-12 score and age, gender, marital status, and income (Table 7.1;

Table 7.1 Mean General Health Questionnaire (GHQ)-12 score of survey participants in subgroups stratified by sociodemographic variables

	N	Median	Mean	SD
Overall	2,640	4.0	5.0	4.1
Age (years)[a]				
18–34	656	5.0	5.5	3.9
35–51	1,278	5.0	5.3	4.2
52–68	624	2.0	4.0	4.1
69–85	82	1.0	2.5	3.1
Gender[b]				
Male	1,018	3.0	4.2	4.2
Female	1,622	5.0	5.3	4.1
Schooling[c]				
No schooling completed	29	6.0	6.0	4.3
Primary school	226	5.0	5.3	4.3
High school	1,081	4.0	5.0	4.2
University	1,304	4.0	4.8	4.1
Marital status[d]				
Single	565	5.0	5.2	4.1
Married	1,786	4.0	4.8	4.1
Separated/divorced	255	5.0	5.6	4.3
Widowed	34	4.0	4.7	3.8
Income (monthly)[a]				
No income	43	8.0	6.7	3.7
€500 or less	559	6.0	6.1	4.3
€501–1,000	752	4.0	4.9	4.0
€1,001–1,500	441	4.0	4.6	4.1
€1,501–2,000	288	3.0	3.9	3.9
€2,001–3,000	151	2.0	3.3	3.5
€3,001–5,000	42	3.0	3.6	3.4
€5,001 or over	13	2.0	3.6	4.0
Patient organization membership[e]				
Yes	1,033	4.0	4.7	4.0
No	1,607	5.0	5.1	4.2

SD standard deviation, *GHQ-12* 12-item General Health Questionnaire

[a] Kruskal–Wallis test p-value was < 0.001 indicating an association between age categories and GHQ-12 score

[b] Mann–Whitney test p-value was < 0.001 indicating an association between gender and GHQ-12 score

[c] Kruskal–Wallis test p-value was 0.196 indicating no relation between level of schooling and GHQ-12 score

[d] Kruskal–Wallis test p-value was 0.006 indicating an association between marital status and GHQ-12 score

[e] Mann–Whitney test p-value was 0.036 indicating an association between being member of a patient organization and GHQ-12 score

Supplemental Fig. 7.2). Psychological health was worse in participants who were younger, female, single or separated/divorced, and those who had lower income. In a previously reported analysis among the subset of patients from Spain included in IMAS, bivariate analysis of sociodemographic factors similarly found an association between having no partner and worse mental health, but in contrast patients who were older or male had worse mental health (Garrido-Cumbrera et al. 2019).

While the relationship between sociodemographic factors and psychological health is well characterized in rheumatoid arthritis (Geenen et al. 2012), there is a relative lack of research on this in axSpA. A relationship between psychological health and income is in agreement with a recent German study that identified lower income as a significant risk factor for poorer psychological well-being in patients with axSpA (Redeker et al. 2018). However, previous studies have not shown a relationship between age and psychological health (Zou et al. 2016; Martindale et al. 2006), or between gender and psychological health (Webers et al. 2016). Furthermore, there is no other evidence linking marital status with psychological health. A previous study in 316 patients with axSpA identified lower education level as an independent risk factor for anxiety and depression, in contrast to the results presented here (Kilic et al. 2014). The reasons for these discrepancies are unclear but may be due to the use of GHQ-12 in the IMAS questionnaire as opposed to alternative measures of psychological health in other studies or due to the comparatively large sample size in IMAS versus previous studies.

7.3 Psychological Health and Clinical Characteristics

Significant relationships were observed between GHQ-12 score and BASDAI, Spinal Stiffness Index, Functional Limitation Index, and diagnostic delay (Table 7.2).

Generally, a higher GHQ-12 score was associated with higher disease activity and spinal stiffness, a greater degree of functional impairment (the limitation experienced in independently carrying out daily activities), and a longer diagnostic delay (Table 7.3). Furthermore, a higher proportion of participants with active disease (BASDAI $\geq$ 4) were at risk of psychological distress than those with inactive disease (BASDAI < 4; **Supplemental Table 7.1**), and GHQ-12 score was higher in patients with more severe spinal stiffness, regardless of the region of the spine affected (**Supplemental Table 7.2**).

Significant relationships were also observed between the number of psychological comorbidities (sleep disorders, anxiety, and depression) reported by participants and disease activity (BASDAI) and spinal stiffness (Spinal Stiffness Index) (Table 7.3). Participants with higher disease activity or more severe spinal stiffness had significantly higher numbers of psychological comorbidities than those with lower disease activity and less severe stiffness. This finding was confirmed in

Table 7.2 Disease activity (BASDAI), spinal stiffness (Spinal Stiffness Index), and function (Functional Limitation Index) by GHQ-12 cut-off

	Mean	SD	N
BASDAI[a]			
GHQ-12 < 3	4.6	2.0	986
GHQ-12 ≥ 3	6.0	1.8	1,598
Spinal Stiffness Index			
GHQ-12 < 3	7.3	2.5	1,016
GHQ-12 ≥ 3	8.1	2.4	1,624
Functional Limitation Index[a]			
GHQ-12 < 3	15.2	14.3	1,015
GHQ-12 ≥ 3	21.9	16.0	1,624
Diagnostic delay (years)[a]			
GHQ-12 < 3	7.1	8.7	989
GHQ-12 ≥ 3	7.7	8.4	1,576

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *GHQ-12* 12-item General Health Questionnaire, *SD* standard deviation

[a] Mann–Whitney test p-value was <0.001 indicating a relationship with GHQ-12 score

Table 7.3 Associations (Pearson's correlations) between GHQ-12 score or number of psychological comorbidities and select clinical characteristics

Relationship	r	p-value
GHQ-12 score		
BASDAI	0.405	<0.001
Spinal Stiffness Index	0.201	<0.001
Functional Limitation Index	0.268	<0.001
Diagnostic delay	0.053	0.007
Number of psychological comorbidities		
BASDAI	0.301	<0.001
Spinal Stiffness Index	0.253	<0.001

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *GHQ-12* 12-item General Health Questionnaire, *r* Pearson correlation coefficient

further analyses which showed that participants with active disease (BASDAI 4) had more psychological comorbidities than those with inactive disease (BASDAI < 4; **Supplemental Table 7.3**) and the number of psychological comorbidities was higher in patients with more severe spinal stiffness, regardless of the region of the spine affected (**Supplemental Table 7.4**).

These results highlight how various aspects of axSpA are interlinked. Impaired psychological well-being might affect a patient's perception of disease activity, stiffness, or function. Conversely, higher disease activity, more severe stiffness, or greater functional impairment might lead to the development of psychological distress.

Results from previous clinical studies corroborate the IMAS data. In a German survey of 1,736 patients with axSpA, psychological well-being (assessed using WHO-5) was associated with both disease activity (BASDAI) and function (Bath Ankylosing Spondylitis Functional Index [BASFI]) (Redeker et al. 2018). Several other studies have also established a link between disease activity and functional limitation with measures of psychological health such as anxiety and depression (Zhao et al. 2018; Martindale et al. 2006; Webers et al. 2016; Meesters et al. 2014b). Frequently associated with pain and limited function and mobility (Sieper and Poddubnyy 2017), spinal stiffness has also been linked to impaired psychological health, although it is potentially less important than disease activity and functioning (Zhao et al. 2018; Martindale et al. 2006).

It is clear that psychological therapy should be included as part of routine axSpA care and may help patients better manage their disease symptoms and improve outcomes.

7.4 Role of Physical Exercise in Symptomatic Relief and Mental Health Improvement of Patients with AxSpA

European IMAS participants who engaged in physical activity reported a modest but statistically significant reduction in GHQ-12 score compared with participants who were inactive (mean GHQ-12 4.8 vs. 5.6; Mann–Whitney test p-value < 0.001). Furthermore, participants who engaged in physical activity were at a decreased risk of psychological distress (Table 7.4).

All patients with axSpA should be encouraged to engage in exercise to help with symptomatic relief as well as for the well-documented beneficial effects on general mental health (Harvey et al. 2018; Heijde et al. 2017).

χ^2 test p-value was 0.002 indicating an association between participation in physical activities and scoring above the cut-off point of GHQ.

Table 7.4 Participation in physical activities and GHQ-12 cut-off point of survey participants

Participation in physical activities	GHQ-12 cut-off		Total
	<3	≥3	
No			
Frequency	182	375	557
%	32.7	67.3	100.0
Yes			
Frequency	834	1,249	2,083
%	40.0	60.0	100.0
Total			
Frequency	1,016	1,624	2,640
%	38.5	61.5	100.0

GHQ-12 12-item General Health Questionnaire

7.5 Conclusions

- A substantial proportion of European IMAS participants were at risk of psychological distress and had common psychological comorbidities such as sleep disorders, anxiety, and depression, highlighting the substantial negative impact of axSpA on psychological health.
- Participants who were younger, female, single or separated/divorced, and those who had lower income were most at risk of psychological distress.
- Psychological health was associated with disease activity, functional impairment, and spinal stiffness.
- Psychological care is an essential component of the holistic medical management of axSpA.

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Social Support

8

The key symptoms of axSpA such as pain, fatigue, and stiffness can combine to have a profound impact on a patient's ability to maintain a healthy social life (Doward et al. 2003; Hamilton-West and Quine 2009). Qualitative data capturing the perspectives of patients living with axSpA indicate that relationships with friends, family, and work colleagues can all become strained and participation in social events can become difficult (Doward et al. 2003; Hamilton-West and Quine 2009). Patients often report difficulties in their marital relationships, their relationships with other family members, and concerns regarding family planning (Doward et al. 2003; Hamilton-West and Quine 2009; Ward 1999).

A social support network is a crucial aspect of axSpA treatment and preservation of social function is one of the primary goals of axSpA treatment detailed in current ASAS-EULAR recommendations (Heijde et al. 2017). Indeed, a recent study found that having satisfactory social relationships was more important and contributed more to well-being in patients with AS than in a control population who did not have the disease (Genderen et al. 2018). However, supporting social participation, particularly in aspects such as intimate relationships and leisure activities, is often of lower priority than clinical factors when treating individuals with axSpA; this represents an important unmet need that needs to be addressed.

8.1 Impact of axSpA on Relationships

Almost half of the participants reported worsened relationships with work colleagues, and one-third reported worsened relationships with friends (Table 8.1). Due to the importance placed upon maintenance of social participation in current treatment recommendations (Heijde et al. 2017), this could have important implications for participants' quality of life and also the success of overall disease management.

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Table 8.1 Impact of axSpA on participants' relationships since disease onset (N = 1,037–2,649)

Relationships	Comparison with before disease onset										N
	Much better		Better		Same		Worse		Much worse		
	n	%	n	%	n	%	n	%	n	%	
Work colleagues	12	1.2	59	5.7	502	48.4	294	28.4	170	16.4	1,037
Friends	52	2.0	162	6.1	1,487	56.4	664	25.2	274	10.4	2,639
Spouse	109	4.6	203	8.6	1,330	56.3	482	20.4	237	10.0	2,361
Family	71	2.7	249	9.4	1,705	64.4	489	18.5	135	5.1	2,649
Neighbors	36	1.5	96	4.1	1,794	76.0	311	13.2	123	5.2	2,360

axSpA axial spondyloarthritis

Although the precise reasons for these worsened relationships were not collected in the IMAS European survey, previous qualitative studies in patients with axSpA have captured anecdotal reports that physical changes were 'off-putting at meetings' and that 'bullying and harassment… by an intimidating workplace' was experienced (Hamilton-West and Quine 2009). The worsened relationships with work colleagues may also be a result of actual or perceived problems with presenteeism and/or absenteeism (as discussed in Chap. 10). For example, patients with axSpA may be unable to perform certain aspects of their work due to fatigue or loss of mobility and colleagues may feel unhappy that they are having to take on extra work as a result (or be worried that this may happen in future). Furthermore, an association between presenteeism and poor relationships with colleagues has been reported (Boonen et al. 2015), including conflicts with colleagues and employers during painful episodes that affect speed or quality of work (Bagcivan et al. 2015).

Worsened relationships with friends may be due to patients with axSpA being unable to participate in certain social events, concerns about dependence on other people, or a lack of understanding of how axSpA affects individuals (Hamilton-West and Quine 2009). Patients with axSpA who have a worse health state have been reported to be more likely to have reduced productivity, both within and outside the workplace, and to miss family, social, and leisure activities more often than those with a better health state (Osterhaus and Purcaru 2014). Patients with AS have also reported logistical problems, such as with scheduling activities/having to change plans due to the unpredictable fluctuating nature of the disease or inability to stay at a friend's house due to an unsuitable mattress (Mengshoel 2008). Nevertheless, some IMAS participants reported that relationships changed for the better, with one out of 10 participants improving their relationships with their spouse or family.

Table 8.2 Effect of axSpA on levels of social activities in participants (N = 2,515–2,685)

Social activities	Comparison with before disease onset										N
	Much more		More		Same		Less		Much less		
	n	%	n	%	n	%	n	%	n	%	
Sports	138	5.1	348	12.9	481	17.8	709	26.2	1,029	38.0	2,705
Travel/excursions	39	1.5	166	6.2	941	35.0	804	29.9	735	27.4	2,685
Intimate relations	28	1.1	51	2.0	1,017	40.4	835	33.2	584	23.2	2,515
Cinemas/theaters/museums	29	1.1	107	4.0	1,188	44.4	722	27.0	631	23.6	2,677
Bars/restaurants	55	2.1	107	4.0	1,166	43.6	727	27.2	618	23.1	2,673

axSpA axial spondyloarthritis

8.2 Impact of axSpA on Social Activities

Participants reported that axSpA had the greatest impact on their ability to socialize through sports, with two-thirds of respondents participating in sports less than before (Table 8.2). Conversely, after disease onset, one-fifth of participants socialized more through sports, and were perhaps motivated by the dual benefit to their physical and social health gained through sporting activities.

axSpA had an overall negative impact on social activities, with approximately half of participants reporting that they were traveling, engaging in intimate relations, going to the cinema, or visiting museums and bars less or much less than before (Table 8.2).

As missing social events has previously been associated with a worse health state in axSpA (Osterhaus and Purcaru 2014), and as patients with AS have reported having to stay at home during episodes of pain (Bagcivan et al. 2015), it is possible that the negative impact on social participation found in the IMAS survey could be explained by the high disease activity and physical limitations experienced by participants (Chap. 6).

Engaging in social activities has been associated with a higher satisfaction with life in patients with AS, although this aspect has typically not been prioritized by HCPs involved in managing the disease (Genderen et al. 2018). This concept, along with the data reported from the IMAS survey, highlights the importance of supporting patients with axSpA to maintain their social roles.

8.3 Patient Organizations Provide an Important Support Network

Approximately 70% of IMAS participants were recruited through patient organizations, and the majority of countries participating in IMAS had at least one of these groups.

Patient organizations play an integral role in providing patients and their families with the tools and resources they need to face the challenges of living with a serious and chronic disease such as axSpA. Support is offered in several different ways, including patient education, disease-specific group physiotherapy, disease-adapted sport, legal advice, and scientific research. Such materials are usually offered freely through online channels, extending access to as wide an audience as possible.

There is increasing appreciation of the key role played by patient organizations in offering support to patients (Strand and Singh 2017), with evidence to suggest that joining a support group can improve some of the signs and symptoms of axSpA (Barlow et al. 1992).

The majority of survey participants reported that they were not members of a patient organization (in response to a question asking ‘Are you a member of any Spondylitis Support Group or Association?’; Fig. 8.1), which is somewhat surprising given that most participants were recruited for the survey through these groups. However, much of the support and information provided is freely available to people who are not full members through websites and social media. The ability of patient organizations to encourage large numbers of patients to participate in the IMAS survey, even though many were not members, suggests that patients are accessing freely available material and engaging with these services regardless of membership. The nature of patient organizations varies across Europe and they may be a particularly useful source of information where patients have limited access to specialist rheumatology centers.

In a previously reported analysis of the subset of patients from Spain included in IMAS, membership of a patient organization was linked with greater engagement in physical activities considered beneficial for axSpA and lower likelihood of smoking (Garrido-Cumbrera et al. 2020). Despite being older and having longer disease duration, membership was also linked with lower BASDAI, lower Functional Limitation Index, and less risk of psychological distress compared with

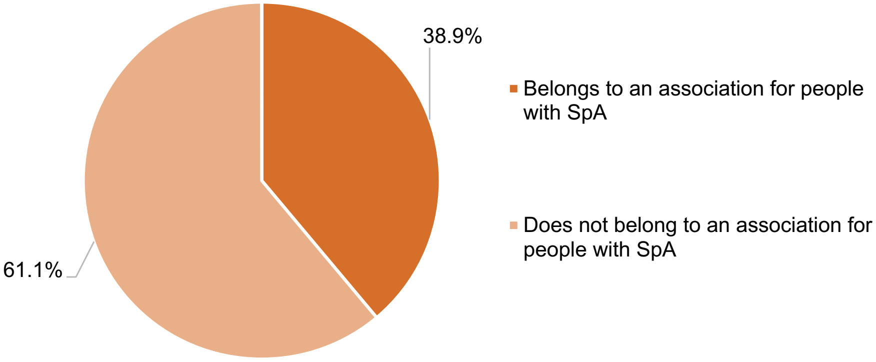

Fig. 8.1 Membership of patient organizations among participants (N = 2,846). *SpA* spondyloarthritis

non-members, but conversely (like in the overall IMAS population) higher Spinal Stiffness Index scores, potentially reflecting the older age of those who were members.

8.4 Conclusions

- Substantial proportions of participants reported worsened relationships with work colleagues, spouses, family, and friends.
- axSpA had a significant impact on participants' ability to participate in social activities, particularly those of a sporting nature and travel.
- Patient organizations recruited 70% of the participants to the IMAS survey; these groups offer an important support network and reach audiences beyond their membership, for example by providing freely accessible educational material.
- The results serve to highlight the significant impact of axSpA on the social lives of individuals with the disease.
- Maximizing health-related quality of life through preservation of social engagement is recognized in treatment guidelines as a key goal of axSpA management.

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Healthcare

9

axSpA has a considerable impact on healthcare systems, both in terms of absolute monetary costs and healthcare resource utilization (Heijde et al. 2017; Harvard et al. 2016). An analysis of 216 patients with AS from the Netherlands, France, and Belgium showed that mean direct annual societal costs per patient were €2,640, of which 82% were direct healthcare costs (Boonen et al. 2003). Data from the Atlas of Ankylosing Spondylitis in Spain 2017 study among 578 patients with AS reported that the estimated median annual cost per patient was €5,402, with the majority again accounted for by direct healthcare costs (Merino et al. 2021). The impact of axSpA on healthcare resources is driven by several factors, including the need for multidisciplinary management of the disease and regular follow-up, which is typically coordinated by a rheumatologist but also involves rehabilitation specialists, occupational therapists, physiotherapists, social workers, nurses, manual therapists, podiatrists, dieticians, psychologists, ophthalmologists, and vocational counsellors (Heijde et al. 2017).

9.1 Health Coverage for European IMAS Participants

Healthcare in European countries is provided through a range of different systems, all run at a national level. Generally, these systems are funded primarily through public taxation (universal healthcare); private contributions towards meeting the non-taxpayer refunded portion of costs are necessary in some countries or healthcare may be funded entirely privately (non-subsidized) either out of pocket or through personal or employer-funded insurance. Healthcare systems in the countries participating in IMAS are summarized in **Supplemental Table 9.1**.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_9.

M. Garrido-Cumbrera et al., *Axial Spondyloarthritis: Patient-Reported Impact in Europe*, https://doi.org/10.1007/978-3-030-97606-4_9

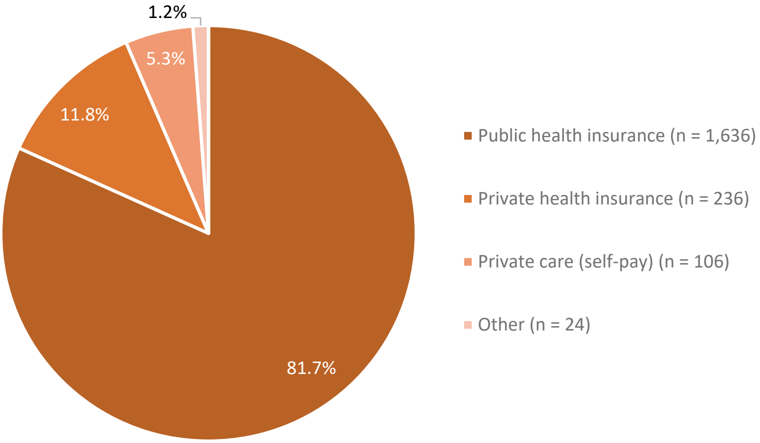

Fig. 9.1 Main healthcare funding source for axSpA in the past 12 months per participant (N = 2,002). *axSpA* axial spondyloarthritis. No data were obtained for Belgium or France as related items were removed from the survey for these countries

The vast majority of survey participants reported that their main health coverage was public health insurance (Fig. 9.1), which reflects the use of public universal healthcare in most countries participating in the IMAS European survey. More than 15% had private insurance or paid for their healthcare directly. The benefits of private healthcare include reduced waiting times, more regular follow up, and access to the most effective and newest therapies. The reasons why participants sought private treatment were not captured in the IMAS report.

9.2 Management of axSpA

The majority (88.6%) of European IMAS survey participants reported that their axSpA was being managed by a rheumatologist. This is in accordance with current ASAS-EULAR management recommendations (Heijde et al. 2017). The benefits of a rheumatologist managing a patient's axSpA are obvious; rheumatologists are experienced in treating the signs and symptoms of axSpA while recognizing and managing its extra-articular manifestations and comorbidities (Heijde et al. 2017). Furthermore, treatment by a specialist multi-disciplinary team allows ready access to ancillary services (such as psychology and physiotherapy) and links to patient support groups (Heijde et al. 2017).

In the 11.4% of participants who were not managed by a rheumatologist, data were not collected on which specialty managed their disease. Nevertheless, this represents a relatively large proportion of the IMAS population who were not being managed according to current recommendations.

Table 9.1 Frequency of appointments with a rheumatologist in the prior 12 months per participant (N = 2,628)

Frequency	N	%
None	234	8.9
Once	524	19.9
Every 6 months	576	21.9
Every 3 or 4 months	677	25.8
Every 2 months	349	13.3
Monthly or more regularly	268	10.2

Over 90% of participants reported having an appointment with a rheumatologist in the 12 months prior to the survey (Table 9.1). The majority of respondents had visits every 2–6 months, which highlights the relatively frequent follow-up required for axSpA patients. The number of visits to a rheumatologist reported here was similar to the rate reported in a previous study of the management of SpA conducted in Spain (Jovani et al. 2017). These data may aid understanding of the impact of axSpA on healthcare providers and inform organizational aspects of its management.

Of all axSpA-related healthcare appointments in the prior 12 months, survey participants reported visiting a physiotherapist most frequently (Fig. 9.2). This result is consistent with the needs of patients with axSpA, since a predominant problem is stiffness. Physical therapy is encouraged in current ASAS-EULAR

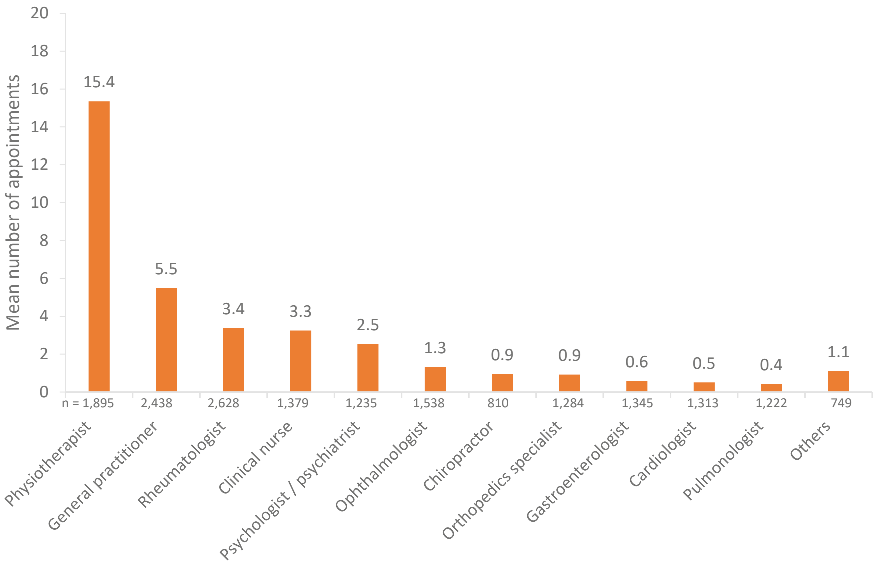

Fig. 9.2 Mean number of axSpA-related healthcare appointments in the prior 12 months per participant (N = 749–2,628). Data are presented as means for the overall survey population, including those with no appointments. *axSpA* axial spondyloarthritis

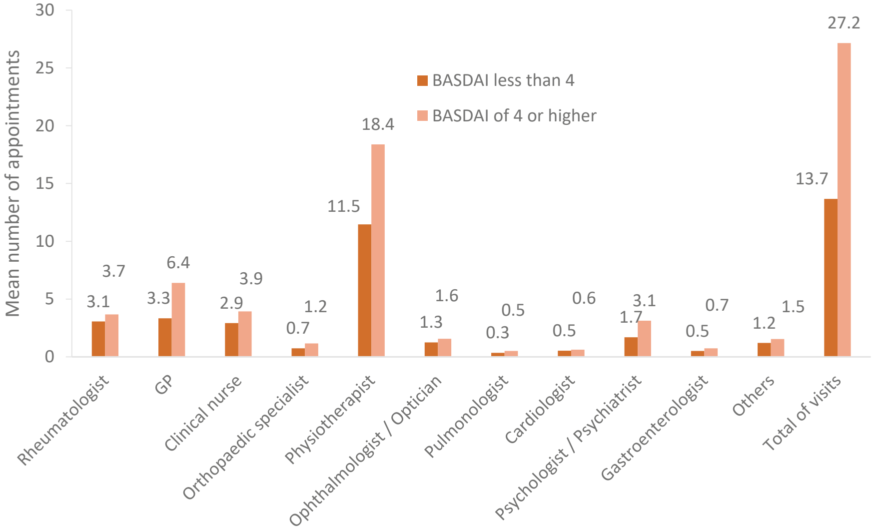

Fig. 9.3 Mean number of axSpA-related healthcare appointments in the prior 12 months by level of disease activity (high: BASDAI $\geq$ 4; low: BASDAI < 4; N = 96–1,860). Data are presented as means for the overall survey population, including those with no appointments. *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index, *axSpA* axial spondyloarthritis, *GP* general practitioner

treatment recommendations (Heijde et al. 2017), and usually includes stretching, exercise, improving posture, and even strategies such as selecting the right mattress and workplace chair (Linden et al. 2002; Passalent 2011; Elyan and Khan 2008). Physical therapy can help to relieve pain and stiffness and improve mobility, key aspects for maintaining long-term mobility and health in patients with axSpA (Linden et al. 2002; Passalent 2011; Elyan and Khan 2008).

Patients with more active disease (those patients with a BASDAI of 4 or greater) made more visits to HCPs than those with lower disease activity/inactive disease (BASDAI less than 4; Fig. 9.3). This increased healthcare use amongst patients with high disease activity was consistent across all HCP specialties; every specialist, except pulmonologists, cardiologists (and others), received significantly more visits from patients with high disease activity than visits from patients with lower disease activity.

9.3 Medical Tests

Patients with axSpA generally require more frequent medical testing than healthy individuals. Among the survey participants, blood and urine tests were the most frequently administered medical tests in the prior 12 months, followed by X-rays,

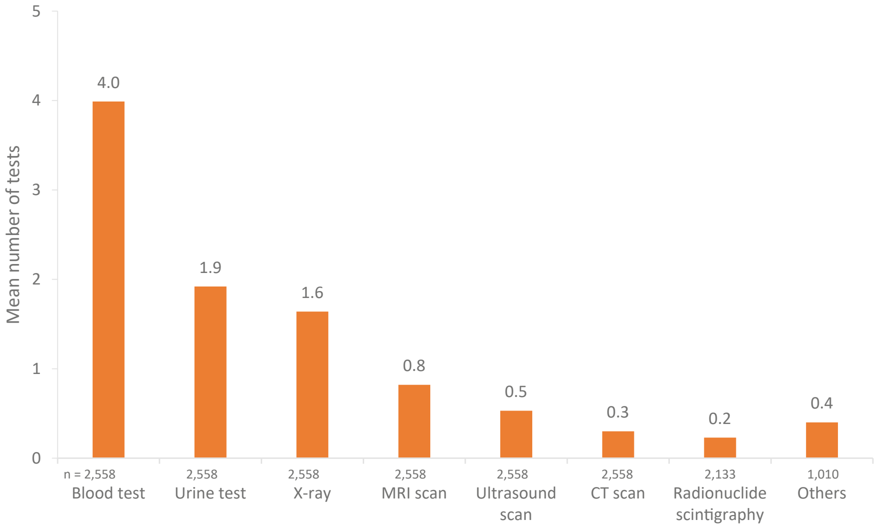

Fig. 9.4 Mean number of axSpA-related medical tests in the prior 12 months per participant (N = 1,010–2,558). *axSpA* axial spondyloarthritis, *CT* computerized tomography, *MRI* magnetic resonance imaging. Data are presented as means for the overall survey population, including those with no appointments; the survey in Norway did not collect data regarding radionuclide scintigraphy

MRI, and ultrasound scans (Fig. 9.4). This finding is as expected and reflects the routine management of individuals with axSpA.

Laboratory testing of blood and urine is often employed to assess general health as well as to measure levels of certain inflammatory markers, while imaging is essential for diagnosis and the assessment of structural damage progression and inflammation in the spine, sacroiliac joints, and any affected peripheral sites (Heijde et al. 2017; Mandl et al. 2015; Birtane et al. 2017; Shaikh and Raftery 2014). The majority of the medical tests reported by the participants were covered by public insurance schemes (**Supplemental Fig. 9.1**).

X-rays were the most frequent imaging modality reported by the participants, reflecting their recommended use for detecting sacroiliitis (inflammation of the sacroiliac joints) and structural damage in the spine and sacroiliac joints in axSpA (Mandl et al. 2015). Indeed, participants reported X-rays most commonly being performed in lumbar, pelvic, and spinal regions (**Supplemental Tables 9.2** and **9.3**).

9.4 Impact of Diagnostic Delay on Number of Visits

- Among patients diagnosed at least 1 year before participating in the survey, those who experienced a diagnostic delay of more than a year (n = 2,208) undertook a considerable number of visits to specialists and medical tests in the year prior to participating in the IMAS European project, which increased with disease activity.

- Patients with active disease (BASDAI greater than 4) reported a higher number of visits to rheumatologists (3.7 ± 3.5 vs. 2.9 ± 2.6), general practitioners (6.6 ± 10.0 vs. 3.5 ± 4.1), physiotherapists (19.3 ± 25.0 vs. 11.7 ± 17.0), and psychologists/psychiatrists (3.4 ± 10.7 vs. 1.9 ± 7.7) than those patients with inactive disease (BASDAI less than 4).
- Regarding follow-up tests, patients with active disease also undertook more X-rays (1.8 ± 2.8 vs. 1.3 ± 1.9), MRI scans (0.9 ± 1.2 vs. 0.6 ± 1.1), and blood tests (4.7 ± 4.4 vs. 3.6 ± 3.2) compared with patients with inactive disease.
- However, one in five patients visited the rheumatologist only once in the year prior to IMAS (21.1%).

9.5 Hospital Admissions, Use of Emergency Services, and Other Healthcare Centers

Overall, the mean (±SD) number of axSpA-related inpatient hospital admissions among survey participants in the prior 12 months was 1.1 ± 2.1. Half the European IMAS participants reported no hospital admissions during this time, while a quarter had one hospital admission and the remaining quarter more than one (Fig. 9.5).

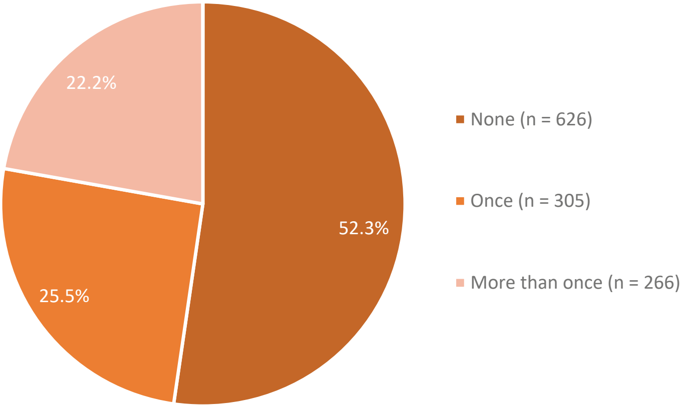

Fig. 9.5 Number of axSpA-related inpatient hospital admissions in the past 12 months per participant (N = 1,197)[a]. *axSpA* axial spondyloarthritis. [a]No data were obtained for Austria or the Netherlands as related items were removed from the survey for these countries

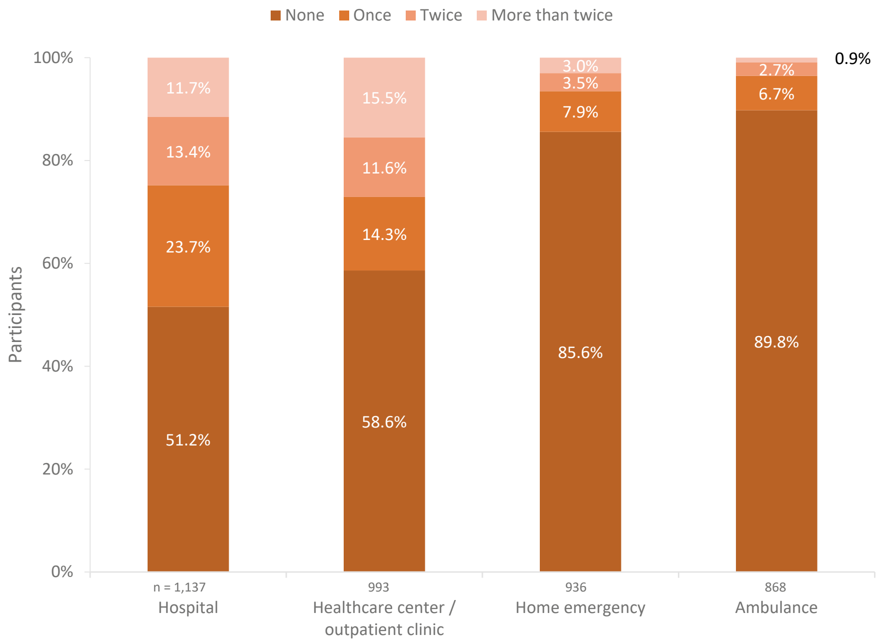

Fig. 9.6 Number of axSpA-related emergency uses of healthcare services in the prior 12 months per participant (N = 868–1,137). *axSpA* axial spondyloarthritis

Fewer than half of the participants reported emergency hospital or outpatient clinic visits in the year prior to the survey, and only one in 10 used other emergency services or ambulance services (Fig. 9.6). Although the majority of inpatient admissions and outpatient visits were covered by public health insurance (**Supplemental Fig. 9.2**), more than half of emergency services used by survey participants were paid for personally or covered by private schemes.

Previous studies have shown higher rates of inpatient admission, emergency department visits, non-hospital-based outpatient visits, hospital-based outpatient visits, and other outpatient services in patients with axSpA compared with matched controls (Walsh et al. 2018). The reasons for hospital admission or emergency services use were not captured in the IMAS survey but the high prevalence of comorbidities in patients with axSpA has been highlighted as a contributing factor in previous studies (Walsh et al. 2018). Nevertheless, the IMAS data aid our understanding of the impact of axSpA on healthcare providers, which may be useful for improving organizational aspects of disease management in the future.

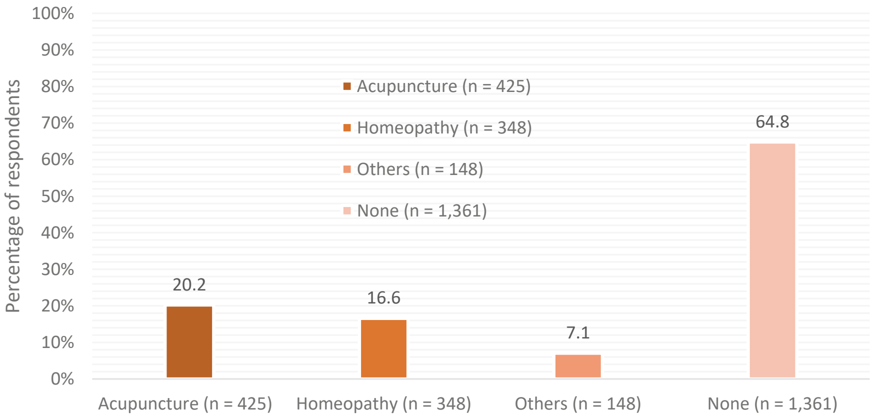

Fig. 9.7 Percentage of participants reporting use of alternative therapies for axSpA (N = 2,100). *axSpA* axial spondyloarthritis

9.6 Use of Alternative Therapies

Alternative therapies such as acupuncture, homeopathy, and aromatherapy were frequently used by the survey participants (Fig. 9.7). More than one-third of survey participants reported using an alternative therapy of some kind, mostly acupuncture. Those who used these therapies did so regularly, between two and three times per month. Although the reasons for using alternative therapies were not captured, this finding may reflect the relatively high disease activity in the participants despite treatment with conventional therapy.

A previous study that surveyed the beliefs of patients with spondyloarthritis found that some patients believe that alternative therapies can help prevent the exacerbation of pain and flares (Berenbaum et al. 2014). However, it is important to note that such therapies are usually started without consulting the managing physician (Berenbaum et al. 2014), and despite anecdotal evidence of modest benefits with some alternative therapies, there is currently a lack of robust evidence for the benefits of complementary medicines in axSpA (Danve and Deodhar 2018; Phang et al. 2018; Chatfield et al. 2009). Further research into such therapies and the rationale for why patients chose to use them is warranted.

9.7 Conclusions

- Patients with more active disease (those patients with a BASDAI of 4 or greater) made more visits to healthcare professionals than those with lower disease activity/inactive disease (BASDAI less than 4).

- Nine out of 10 IMAS European survey participants reported that their axSpA was being managed by a rheumatologist with most seeing their rheumatologist every 2–6 months.
- One in 10 participants were not treated by a rheumatologist, indicating that a relatively large proportion were not having their disease managed according to current treatment recommendations.
- The most visited HCPs were physiotherapists, which highlights the vital role they play in treating the pain and stiffness associated with axSpA with stretching and exercises.
- A significant proportion of participants ($\sim 35\%$) reported use of alternative therapies, despite the lack of robust evidence for complementary medicine in axSpA.

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Habits and Lifestyle

10

Various aspects of the habits and lifestyle of patients with axSpA can affect their physical health, mental health, and indeed response to therapy. A multifaceted, individualized physical activity program is recommended in order to preserve/improve spinal mobility, maintain functional capacity, and reduce stiffness and pain (Gyurcsik et al. 2012; Elyan and Khan 2008). This recommendation is supported by evidence showing that individual exercise programs reduce pain and enhance physical function in patients with axSpA, especially in those with severe disease (Dagfinrud et al. 2005; Ince et al. 2006; Karapolat et al. 2009; Kisacik et al. 2016; O'Dwyer et al. 2015; Santos et al. 1998; Tubergen and Hidding 2002).

Unhealthy lifestyle habits can have a negative effect on the course of axSpA (Averns et al. 1996). Patients with axSpA who are smokers experience higher disease activity than those who never smoke (Chung et al. 2012; Kaut et al. 2017; Zhao et al. 2017; Zhang et al. 2015). Stopping smoking is associated with reduced disease activity and improved physical function and quality of life (Jones et al. 2017), and should therefore be recommended as part of the treatment strategy for patients with axSpA (Chung et al. 2012; Zhao et al. 2017; Jones et al. 2017).

The impact of alcohol consumption in axSpA is less clearly understood. While some studies suggest that heavy alcohol consumption may be linked with impaired physical functioning in patients with axSpA (Zhang et al. 2015), others have reported benefits of moderate alcohol consumption. Further research is required to establish if this is due to biological effects of alcohol on inflammation or disease-associated behavior modification (Rohde et al. 2017; Zhao et al. 2018).

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_10.

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10.1 Physical or Sporting Activity

Walking was the most frequently reported activity, which may be due to the fact that it is free, accessible, and relatively easy (Fig. 10.1). Stretching, swimming, hiking, and cycling were the next most commonly performed physical activities, with dancing, tennis, and aquatic therapy least frequently reported.

Previous studies in patients with axSpA have demonstrated that exercise is associated with improvements in health status (Sveaas et al. 2020; Sveaas et al. 2014; Heijde et al. 2017a). European IMAS participants who engaged in physical activity spent from approximately 2–6 h per week on an activity. The greatest amount of time each week was spent on walking (**Supplemental Table 10.1**). In total, the mean (SD) number of hours respondents spent on all physical activity was 8.9 (7.3) per week.

The WHO states that physical activity has multiple benefits for both physical and psychological health. The WHO recommendation for adults aged from 18 to 64 years old is to perform at least 150 min of physical activity per week to achieve these benefits (Mengshoel 2008). Most IMAS survey participants (84.5%) did sufficient physical activity to comply with the WHO recommendation (Table 10.1).

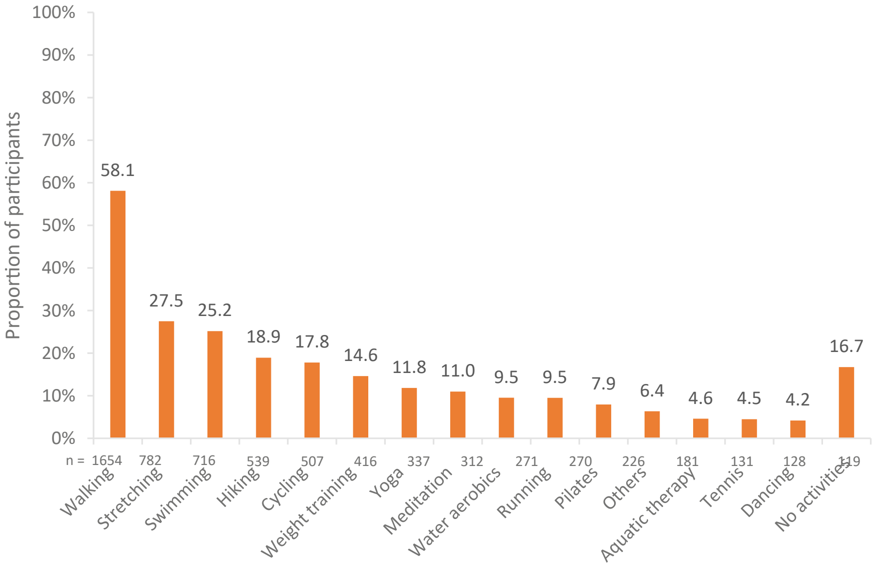

Fig. 10.1 Participation in physical or sporting activity reported by respondents (N = 2,846)

Table 10.1 Distribution of survey participants according to compliance with the WHO physical activity recommendation (N = 2,286)

Followed WHO recommendations?	N	%
Yes	1,931	84.5
No	355	15.5

WHO World Health Organization

10.1.1 Association Between Physical Activity and Physical Health

Survey participants who reported practicing any type of physical activity presented with statistically lower levels of disease activity (BASDAI), Functional Limitation Index, and Spinal Stiffness Index than those who did not partake in such activity (Table 10.2). Respondents with BASDAI < 4 participated in more physical activities and for a longer period of time than those with BASDAI $\geq$ 4 (**Supplemental Tables 10.2** and **10.3**), while spinal stiffness was less severe in participants who engaged in physical activity (**Supplemental Fig. 10.1**; **Supplemental Tables 10.4** and **10.5**). Both disease activity (BASDAI) and spinal stiffness were also lower in participants who met WHO recommendations for physical activity than in those who did not (**Supplemental Tables 10.6** and **10.7**. The differences between groups in these comparisons are relatively small in magnitude and as such physical activity alone may not be sufficient for clinically-relevant improvements in outcomes. However, together with other healthy lifestyle habits such as smoking cessation

Table 10.2 Mean BASDAI score, Functional Limitation Index, and Spinal Stiffness Index of survey participants by physical activity status

Physical activity	BASDAI	Functional Limitation Index	Spinal Stiffness Index
No			
Mean	6.0	21.6	8.3
SD	1.9	15.0	2.6
N	411	442	414
Yes			
Mean	5.4	20.2	7.6
SD	2.0	16.5	2.5
N	2,173	2,329	2,246
Total			
Mean	5.5	20.4	7.7
SD	2.0	16.3	2.5
N	2,584	2,771	2,660
Mann–Whitney test p-value	<0.001	0.010	<0.001

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *SD* standard deviation (see Sect. 10.2), such differences may contribute to improvements in the overall health of patients with axSpA.

The reasons for respondents' non-participation in sports was not collected in the IMAS survey so it is unclear if this was due to choice or an inability to take part due to their disease. It should be noted, however, that a number of participants in the survey reported difficulties doing exercise as a result of their disease.

In previous studies, patients with axSpA have highlighted having to give up certain sports due to their disease (World Health Organization (WHO). Recommended levels of physical activity for adults aged 18–64 years 2019); conversely, patients in other studies have suggested that axSpA has actually forced them to increase their levels of exercise above levels pre-diagnosis (Hamilton-West and Quine 2009). Regardless, the benefits of exercise in the management of axSpA are well characterized (Ince et al. 2006; Karapolat et al. 2009; Kisacik et al. 2016; O'Dwyer et al. 2015; Santos et al. 1998; Tubergen and Hidding 2002) and patients should be encouraged to discuss their exercise regime with their HCP to find a level and activity that best suits their needs.

10.2 Lifestyle Habits

While the majority of survey participants reported that they were non-smokers, almost one-third were smokers (Fig. 10.2).

Approximately two out of five survey participants reported occasional consumption of alcohol (no specific definition of 'occasional' was stated in the survey), with just over a quarter of respondents indicating that they never consumed alcohol (Fig. 10.3). Few participants (2.7%) reported daily alcohol consumption.

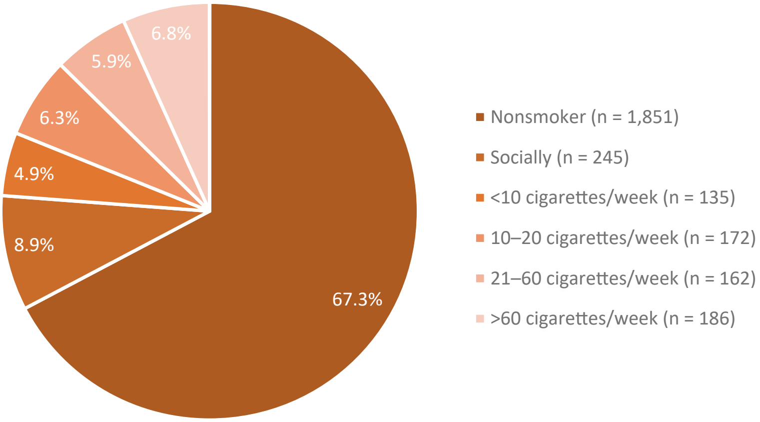

Fig. 10.2 Smoking status of survey participants (N = 2,751)

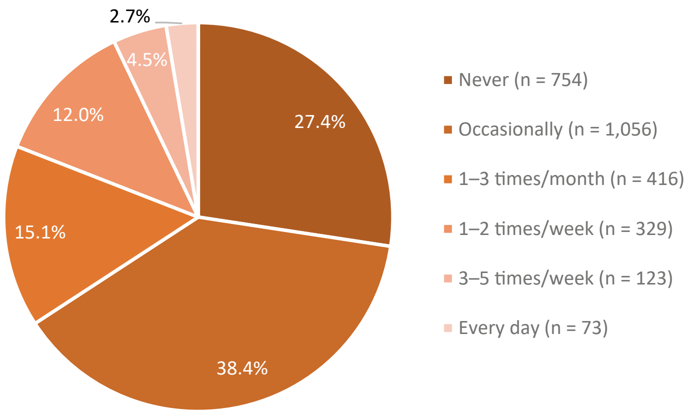

Fig. 10.3 Frequency of alcohol consumption by survey participants (N = 2,751)

10.2.1 Smoking and Physical Health

Survey participants who were smokers presented with statistically higher mean BASDAI, Spinal Stiffness Index, and Functional Limitation Index scores than non-smokers (Table 10.3). While the magnitude of the differences between groups in these indices is relatively small (0.4, 0.4, and 0.8, respectively) and therefore unlikely to be clinically relevant in isolation, they may contribute to improvements in patient outcomes when taken together with other healthy lifestyle habits.

Previous survey data have linked smoking with greater disease activity, spinal stiffness, and physical limitations (Zhang et al. 2015). Furthermore, data from the German Spondyloarthritis Inception Cohort (GESPIC) study, a longitudinal study conducted in Germany, found that heavy smokers had increased structural damage to the spine, while occasional smokers had the same health outcomes as

Table 10.3 Mean BASDAI, Spinal Stiffness Index, and Functional Limitation Index scores of survey participants by smoking status[a]

Smoking status	BASDAI			Spinal Stiffness Index			Functional Limitation Index		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
Non-smoker	5.4	2.0	1,736	7.6	2.5	1,789	19.3	15.8	1,851
Smoker	5.8	1.9	846	8.0	2.4	870	22.1	16.8	900
Total	5.5	2.0	2,582	7.7	2.5	2,659	20.2	16.2	2,751

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *SD* standard deviation

[a] Mann–Whitney test p-value were below 0.001 indicating an association between smoking and BASDAI, Spinal Stiffness Index, and Functional Limitation Index scores

non-smokers (Poddubnyy et al. 2013). Although a topic of ongoing research, smoking is thought to influence the disease course of axSpA by altering gene expression linked to immune function (O'Rielly et al. 2015). Consequently, current ASAS-EULAR treatment guidelines for axSpA state that all patients should be encouraged to stop smoking (Heijde et al. 2017b).

10.2.2 Alcohol Consumption and Physical Health

Participants who never consumed alcohol presented with higher mean BASDAI scores and higher Functional Limitation Index scores compared with those who drank alcohol either daily or occasionally (Table 10.4). Although the small differences in BASDAI score between groups are unlikely to be clinically relevant, differences in Functional Limitation Index were up to 7, which suggests they may have some clinical relevance despite the disparity in sample sizes between groups.

The effects of alcohol consumption on axSpA remain unclear. A Chinese study of 425 patients with AS treated at a single center showed that moderate alcohol consumption was associated with higher disease activity (Zhang et al. 2015); however, several other studies have suggested potential benefits of moderate alcohol consumption in axSpA, potentially due to an anti-inflammatory effect (Rohde et al. 2017; Zhao et al. 2018). Although the results of the IMAS survey support the latter conclusion, further research is needed to investigate the effects of alcohol in patients with axSpA.

Table 10.4 Mean BASDAI and Functional Limitation Index scores of survey participants by alcohol consumption[a]

Alcohol consumption	BASDAI[a]			Functional Limitation Index[a]		
	Mean	SD	N	Mean	SD	N
Never	5.8	2	696	23.4	17.3	754
Occasionally	5.6	2	979	21.2	16.2	1,056
1–3 times per month	5.4	1.8	406	16	14	416
1–2 times per week	4.9	2.1	318	16	14	329
3–5 days per week	5	2.1	114	17.9	15.1	123
Every day	5.1	2.4	69	19.8	17	73
Total	5.5	2	2,582	20.2	16.2	2,751

BASDAI Bath Ankylosing Spondylitis Disease Activity Index, *SD* standard deviation

[a] Kruskal-Wallis test p-value was <0.001 indicating an association between alcohol consumption and BASDAI score

10.3 Conclusions

- Walking was the most common physical activity reported by participants; other common activities included stretching, swimming, hiking, and cycling.
- Most participants (84%) did sufficient physical activity to comply with the WHO recommendation of 150 min per week.
- Exercise forms an integral part of the management of axSpA and, therefore, all patients should be encouraged to discuss their exercise regime with their HCP to find a level and activity that best suits their needs.
- While the majority of participants reported that they did not smoke, almost one-third were smokers.
  - In accordance with current treatment recommendations, all patients with axSpA should be encouraged to stop smoking.
- Although moderate alcohol consumption (one to three times a month) was associated with a lower degree of functional limitation compared with drinking every day or not drinking at all, further research is required on the effect of alcohol on axSpA based on the relatively scant evidence published on this topic to date.

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Employment Status and Productivity

11

Due to the pain, fatigue, and loss of mobility associated with their disease, patients with axSpA often struggle to meet the demands of employment, which can lead to higher rates of unemployment, sick leave (absenteeism), and impairment while at work (presenteeism) compared with the general population (Boonen et al. 2010, 2001; Mau et al. 2005; Healey et al. 2011). As disease symptoms often begin in the third decade of life and axSpA is a chronic life-long illness, restrictions in work participation can have substantial short- and long-term implications for both patients and society as a whole (Sieper and Poddubnyy 2017; Castillo-Ortiz et al. 2016; Boonen 2002).

Age, disease duration, structural damage, and physical functioning have been shown to be contributing factors to work disability in patients with axSpA (Boonen et al. 2010, 2001; Macfarlane et al. 2018). Understanding what drives reductions in work productivity in patients with axSpA allows patients at risk to be identified and managed accordingly.

11.1 Employment Rates in European IMAS Participants Compared with the European General Population

While more than half of participants were employed at the time of the survey, one out of five survey participants were on sick leave (n = 596) (Fig. 11.1).

Both male and female participants had lower employment rates than the overall European Union population (as reported in the Eurostat database) (Eurostat 2018) (Table 11.1). This highlights the significant negative impact of axSpA on employment prospects.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_11.

M. Garrido-Cumbrera et al., *Axial Spondyloarthritis: Patient-Reported Impact in Europe*, https://doi.org/10.1007/978-3-030-97606-4_11

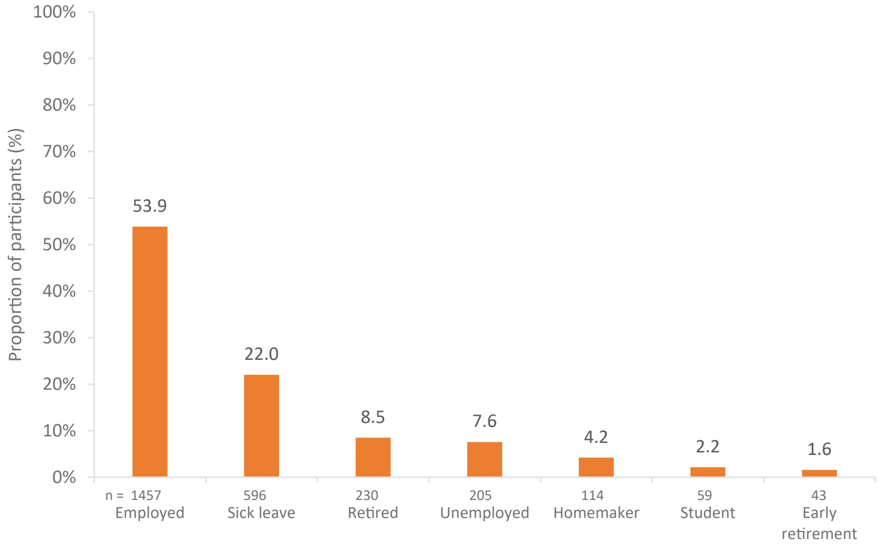

Fig. 11.1 Employment status of participants (N = 2,704). Data are based on responses to the question 'What is your current employment status?'; options were: 'employed', 'temporary sick leave', 'permanent sick leave', 'retired', 'early retirement', 'unemployed', 'homemaker', 'student', 'other', 'do not know'.

Table 11.1 Employment rate by sex compared with European general population (N = 2,704)

	n	IMAS employment rate (%)	European employment rate (%)[a]
Men	603	56.4	78.0
Women	854	52.3	66.5
Total	1,457	53.9	72.2

IMAS International Map of Axial Spondyloarthritis

[a] Data from EUROSTAT, 2017 (Eurostat 2018)

These results contrast in part with those of a prior review of European studies in patients with AS, which suggested that employment rates were significantly lower for men with AS, but not for women, when compared with the general population (Boonen 2006). Variations in the impact of social security provision and labor market conditions on men and women were noted as potential reasons for discrepancies in how AS impacts employment between sexes. Nevertheless, the employment rates of men and women with axSpA were affected equally in the IMAS survey.

The most common occupations of employed survey participants were jobs requiring university qualifications, and skilled non-manual and executive positions (Fig. 11.2). Professions requiring manual labor were less frequently reported, as would be anticipated given the nature of the disease and its associated limitations.

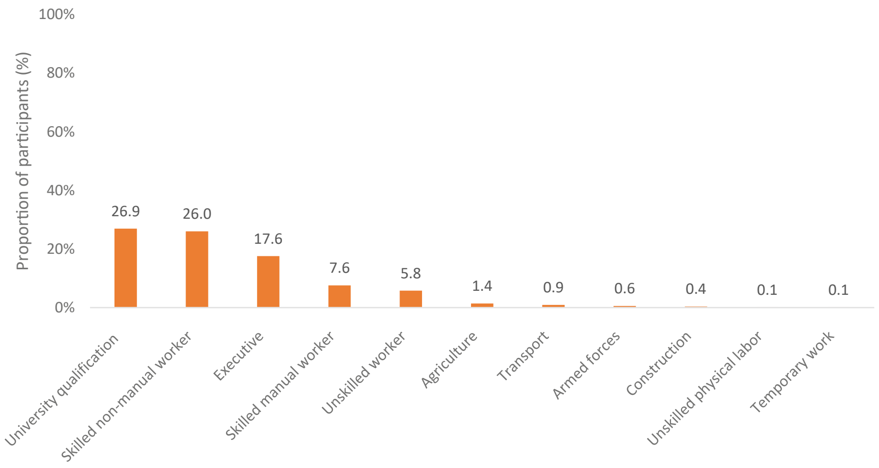

Fig. 11.2 Distribution of employed survey participants by type of occupation (N = 1,070). Data from France are not included in this figure as different categories were used for 'occupation' in France

Common symptoms of axSpA (pain, fatigue, reduced physical function and mobility) impact an individual's ability to undertake physical activity (Strand and Singh 2017), and physically demanding jobs have been linked to worse progression of axSpA (Ramiro et al. 2015).

Almost half (45.8%) of the survey participants reported that axSpA had influenced their job choice in some respect, illustrating the profound cumulative impact that axSpA can have on an individual's life and over their ability to have control over their future career options.

11.2 Work-Related Issues as a Result of axSpA

Two-thirds (67.8%) of employed survey participants indicated that they had suffered issues with work related to axSpA in the prior 12 months (Garrido-Cumbrera et al. 2020). Work-related issues were defined as the following: 'I asked for some days off/leave of absence'; 'I took sick leave'; 'I reduced my working hours'; 'I missed work only for the time my doctor's appointment took'; 'it has been difficult for me to fulfil my working hours'; 'I have occasionally changed my work shift'; 'my professional life has suffered (e.g. missed promotion)'; 'I had to give up my previous job'; and 'other'.

The most common work-related issue as a result of axSpA was the need to take sick leave, followed by difficulty in fulfilling working hours and missing work for doctor's appointments (Table 11.2). These data illustrate that both absenteeism

Table 11.2 Work-related issues as a result of axSpA reported by survey participants with a work-related issue in the prior 12 months (N = 555–870)

	n	%
I took sick leave	483	56.3
It has been difficult for me to fulfill my working hours	386	44.4
I missed work only for the time my doctor's appointment took	298	34.4
I asked for some days off	258	31.6
I reduced my working hours	211	25.8
I have occasionally changed my work shift	154	18.9
My professional life has suffered	138	16.7
I had to give up my previous job	71	8.8
Other	45	8.1

(absence from work due to sick leave) and presenteeism (impairment while at work) were common in participants.

BASDAI scores were statistically significantly higher in participants with versus without the work-related issues surveyed, except for missing work for doctor's appointments (**Supplemental Fig. 11.1**), but none of the differences were large enough to be clinically significant (Pavy et al. 2005). These results are consistent with those from previous studies in patients with axSpA linking disease activity with absenteeism, presenteeism, and work productivity loss (Lunteren et al. 2017; Hooge et al. 2016).

In addition, the level of functional limitation (limitation in independently performing the routine activities of daily living) on daily activities was higher in those participants who faced work-related issues than in those who did not, even for missing work for doctor's appointments (**Supplemental Fig. 11.2**). Thus, participants with higher functional limitation experienced more issues at work. These observations are consistent with those in previous studies that have shown a relationship between loss of work productivity and decreased physical functioning (Hooge et al. 2016; Boonen et al. 2002; Ward and Kuzis 2001; Haglund et al. 2015; Espahbodi et al. 2017).

Participants experiencing work issues also scored higher in GHQ-12 compared with those not suffering from these issues, except for missing work for doctors' appointments and changing work shifts (**Supplemental Fig. 11.3**). In previous research, both absenteeism and presenteeism have been associated with higher levels of anxiety and depression in work environments (Espahbodi et al. 2017). The association between work issues and psychological distress identified here emphasizes the need to measure and better understand the psychological impact of work issues in axSpA.

11.3 Relationship Between axSpA and Sick Leave

In total, 304 participants were on temporary sick leave at the time of the survey. The proportions of participants in a particular occupation that were on temporary sick leave were generally higher for unskilled workers and positions requiring manual work (Table 11.3). Although working in the armed forces or construction would generally require physical labor, no participants in these occupations were on temporary sick leave and only one of the 16 participants working in agriculture was on temporary sick leave; however, as only a small number of participants were in these positions it is possible that they were patients with less severe disease or that they were working in office-based positions. On average, survey respondents on temporary sick leave spent 7 months out of work (mean length of temporary sick leave in prior 12 months = 6.98 months; SD = 4.13; N = 255).

Nine out of 10 survey participants who were on temporary sick leave declared that their absence was a consequence of axSpA (Fig. 11.3).

In total, 292 participants were on permanent sick leave at the time of the survey. Seven out of eight survey participants considered their permanent sick leave to be a consequence of having axSpA (Fig. 11.4). As both temporary and permanent sick leave were self-reported (with no definition of each term provided) it is possible that participants differed in their interpretation of these terms. However, of the 167 participants who stated their duration of permanent sick leave, 136 (81.4%) had been on sick leave for the full 12-month period surveyed.

These results illustrate the substantial impact that axSpA places on the ability of an individual to attend work (absenteeism). A previous study conducted in 72 patients with AS in the Netherlands found that 73% of all episodes of sick leave and

Table 11.3 Distribution of survey participants who were employed or on temporary sick leave by type of occupation (N = 1,283)

	Employed		Temporary sick leave	
	n	%	n	%
Armed forces	6	100.0	0	0.0
Construction	4	100.0	0	0.0
Temporary work	1	100.0	0	0.0
Agriculture	15	93.8	1	6.3
University qualification	288	92.3	24	7.7
Executive	188	89.5	22	10.5
Skilled non manual worker	278	85.3	48	14.7
Unskilled worker	62	80.5	15	19.5
Transport	10	76.9	3	23.1
Skilled manual worker	81	71.7	32	28.3
Other	136	68.0	64	32.0
Unskilled physical labor	1	20.0	4	80.0

Only those who were working or on temporary sick leave were asked for this information

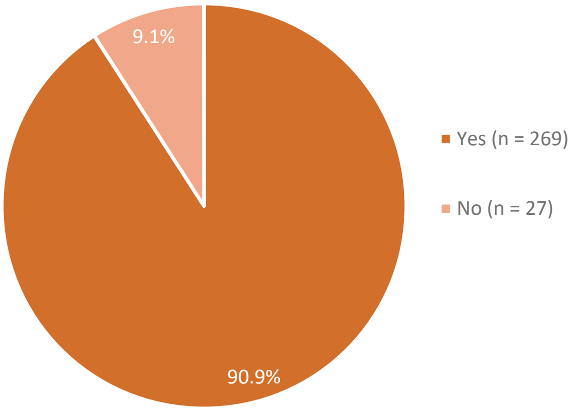

Fig. 11.3 Participants whose temporary sick leave was due to axSpA (N = 296). *axSpA* axial spondyloarthritis

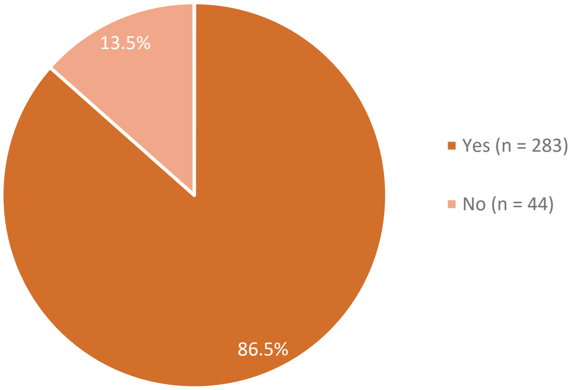

Fig. 11.4 Participants whose permanent sick leave was due to axSpA (N = 327). *axSpA* axial spondyloarthritis

80% of all days of sick leave were attributable to AS, which is in broad agreement with the data presented here (Boonen et al. 2010). In the same study, 7.2% of official working hours were lost due to AS-related sick leave, at an estimated cost of €2,923 per patient per year, highlighting the personal and societal impact of the disease (Boonen et al. 2010).

11.4 Relationship Between axSpA and Unemployment

In total, 205 participants were unemployed at the time of the survey. Two-thirds of the participants who were unemployed declared that axSpA was the cause of their unemployment (Fig. 11.5). On average, unemployed survey participants had been without work for more than 10 months in the last year (mean length of unemployment in prior 12 months = 10.10 months; SD = 3.58; N = 121).

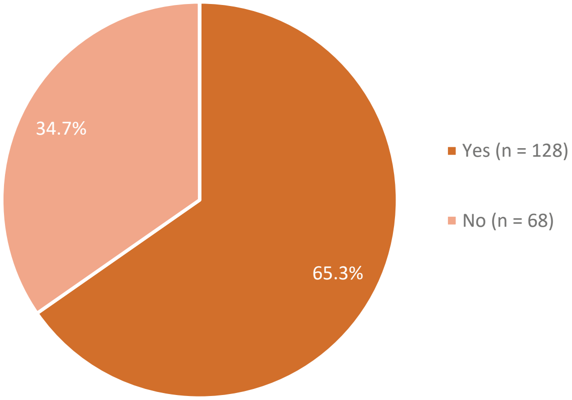

Fig. 11.5 Participants who reported being unemployed due to leaving or losing their jobs because of axSpA (N = 196). *axSpA* axial spondyloarthritis

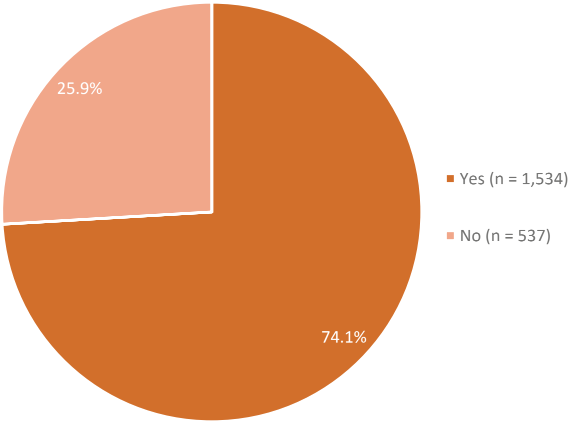

Fig. 11.6 Participants who experienced difficulties finding a job due to axSpA (N = 2,071). *axSpA* axial spondyloarthritis

Three out of four participants declared that axSpA was an obstacle when looking and applying for a job (Fig. 11.6). Specific reasons for this were not captured in the IMAS survey, representing an important avenue of future research.

A previous study conducted in 570 patients with AS in the UK found that 43% of patients who were of working age were unemployed (Cooksey et al. 2015). AS patients retired 9.5 years earlier than the general population and 10.2 years earlier than the usual retirement age for their specific occupation, with 74% citing AS as the main reason for early retirement (Cooksey et al. 2015). A greater appreciation of the impact of unemployment in axSpA and development of interventions to help keep individuals with axSpA in productive work are therefore vital for reducing the costs of the disease to both patients and society as a whole.

Participants who were unemployed or faced difficulties gaining employment reported significantly higher disease activity (BASDAI; $p < 0.001$ for both), functional limitation (Functional Limitation Index; $p = 0.007$ and $p < 0.001$, respectively), and psychological distress (GHQ score; $p < 0.001$ for both) compared with those participants without such challenges (**Supplemental Figs. 11.4, 11.5**, and **11.6**).

These results are consistent with previous studies on this topic. In a UK study, poor function and depression, although not disease activity, were associated with unemployment in patients with AS (Healey et al. 2011), while in a separate Dutch study, both disease activity (BASDAI) and function (BASFI) were predictors of adverse work outcome over a period of 12 years (Castillo-Ortiz et al. 2016). Aside from the impact of axSpA on mental health and the resultant potential difficulties in finding and retaining work for affected individuals, not being in work has a relatively well characterized detrimental effect on mental health itself (Breslin and Mustard 2003). This further highlights the burden of disease in axSpA and the importance of devising steps to ensure that affected individuals find and remain in work.

11.5 Conclusions

- Employment rates were lower in European IMAS participants than those expected in the European general population.
- Both absenteeism (absence from work due to sick leave) and presenteeism (impairment while at work) were common.
- Almost all participants on temporary or permanent sick leave reported that their sick leave was related to axSpA; most also felt that axSpA was an obstacle when looking for and applying for work.
- Disease activity (BASDAI), functional limitation (Functional Limitation Index), and psychological distress (GHQ score) were higher in participants who were unemployed or faced difficulty gaining employment.
- A greater appreciation of the impact of axSpA on work productivity and development of interventions to help individuals with axSpA remain in productive work are vital for reducing the costs of the disease to both patients and society as a whole.

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Fears and Hopes

12

Patients with axSpA are likely to live with a range of hopes, such as retaining a good quality of life and normal social and physical functioning, and fears, including a fear of suffering, losing autonomy, and being a burden on relatives, relating to their disease (Garrido-Cumbrera et al. 2017; Gossec et al. 2015). Addressing these needs is an important consideration when designing appropriate treatment strategies for axSpA, particularly in light of the latest treatment recommendations, which advocate a shared decision-making process between patients and clinicians, including co-defining treatment goals (Heijde et al. 2017; Smolen et al. 2018).

12.1 Fears Reported by European IMAS Participants

The most frequently reported fears among survey participants were disease progression (32.9%), suffering pain (30.5%), loss of mobility (30.0%), and loss of independence/disability (29.2%) (Fig. 12.1). These findings are similar to those reported in another qualitative study in France which found that patients with axSpA most commonly feared suffering loss of autonomy and mobility and becoming a burden for relatives (Gossec et al. 2015).

Accordingly, the two most frequently reported hopes, halting disease progression (32.5%) and eliminating pain (30.7%), mirrored the most common fears (Fig. 12.2). Participants also expressed their hopes to obtain effective treatment (23.3%) and improve quality of life (22.0%). These findings are broadly in agreement with those reported in previous studies (Kiltz et al. 2016; Berenbaum et al. 2014), although it is notable that certain hopes reported previously, such as improving sleep quality, reducing fatigue, and improving motivation, were not frequently reported in the IMAS European survey (Kiltz et al. 2016; Berenbaum et al. 2014). The reason for this discrepancy is unclear but may be due to differences in study design, specifically the use of free text responses versus established multiple choice categories.

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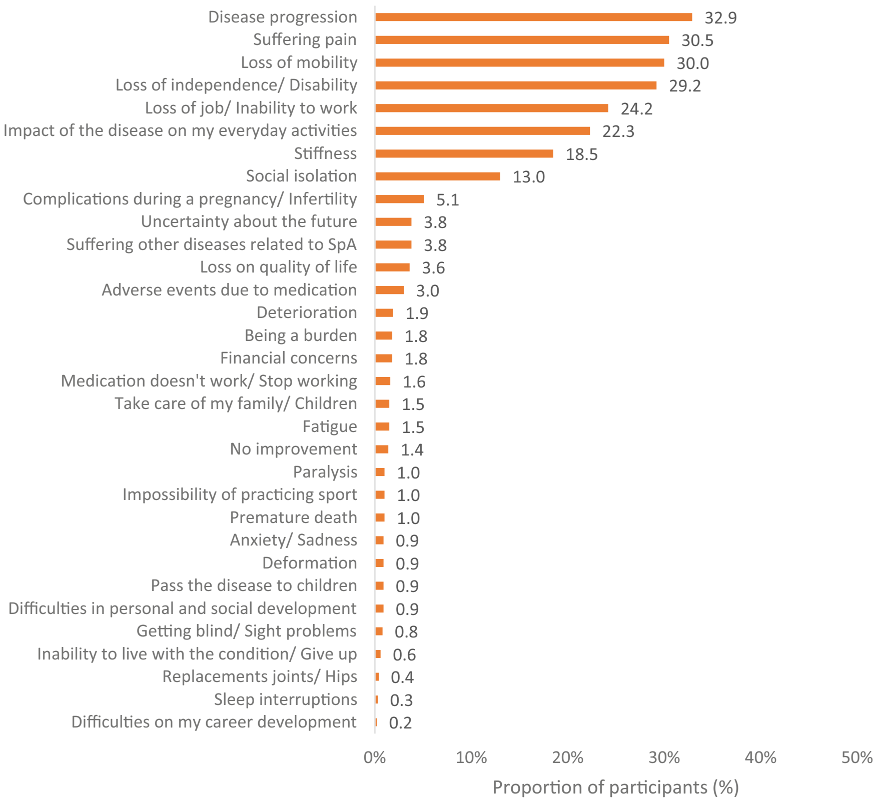

Fig. 12.1 Participant fears related to axSpA[a] (N = 2,435). *axSpA* axial spondyloarthritis, *SpA* spondyloarthritis. [a]In all countries except France, fears were collected as free text responses

The core set of fears and hopes reported in the IMAS survey and previous studies may reflect unmet needs and key gaps in the information given to patients about their disease, its outlook, and its management. Optimal axSpA management should incorporate education for patients to minimize misconceptions, clarify treatment expectations, ensure patients feel supported, and ultimately improve health outcomes. As several factors, including the patient–physician relationship and treatment adherence, may affect axSpA-related hopes and fears (Gossec et al. 2018), it is critical for patients to share their thoughts with their physician to ensure the best possible management of their disease.

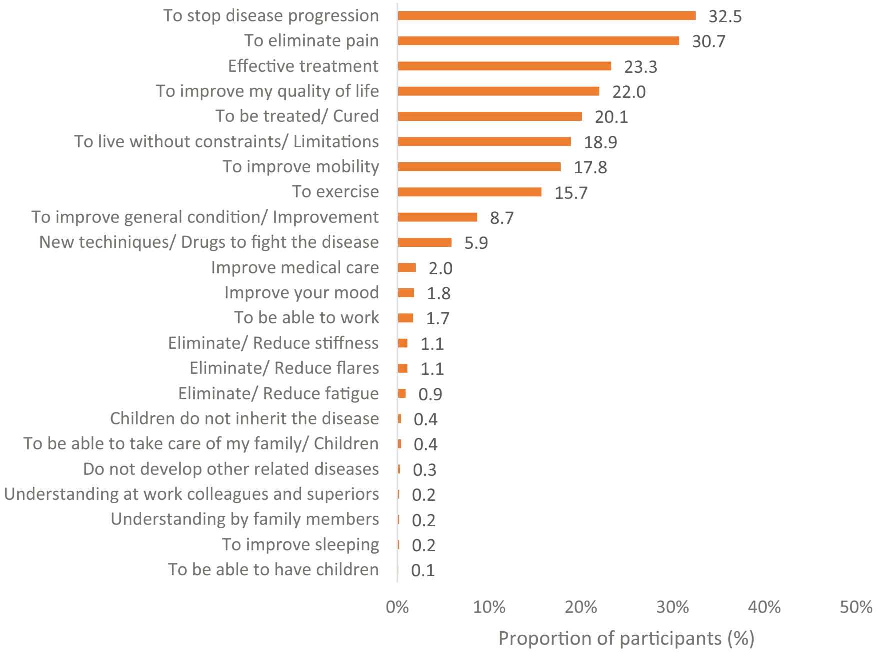

Fig. 12.2 Participants' Hopes About axSpA[a] (N = 2,435). *axSpA* axial spondyloarthritis. [a]In all countries except France, hopes were collected as free text responses

12.2 Treatment Goals for Patients with axSpA

The treatment goals most commonly reported by the European IMAS survey participants were to eliminate or reduce pain (28.6%) and improve mobility (19.3%; Fig. 12.3). Improved management of pain has previously been highlighted as a key treatment priority of patients with axSpA (Kiltz et al. 2016; Berenbaum et al. 2014). Given that improved mobility (a treatment goal for nearly one in five patients) correlates with improved quality of life (Huang et al. 2017), it is interesting that the proportion of participants who stated that improving quality of life was a treatment goal was relatively low. This may reflect variation between participants in their interpretation of the term 'quality of life'.

Some of the treatment goals reported by participants were inconsistent with their hopes and fears. There are several possible explanations for this. For example, some participants may not have considered their hopes as being realistic treatment goals; this highlights the importance of patient–clinician discussions of fears, hopes, and treatment goals in order to improve education and facilitate shared decision making (Heijde et al. 2017). Accordingly, participants may also have reported their treatment goals as being those suggested by their clinician rather than what they

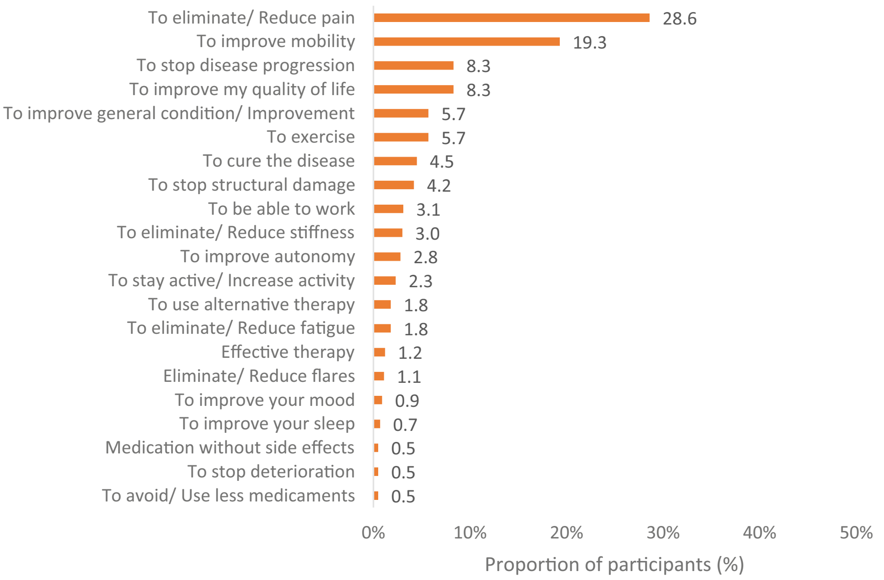

Fig. 12.3 Participant treatment goals relating to axSpA[a] (N = 1,927). *axSpA* axial spondyloarthritis. [a]Treatment goals were not collected in the survey for France

personally believed. The results may also have been affected by ‘respondent fatigue’, a term used to describe a situation where survey respondents become ‘tired’ of answering questions, particularly when they appear to be asking the same thing several times; some participants may therefore have reported something as a treatment goal then not thought it necessary to state it again when reporting fears or hopes later in the survey. Finally, the use of open versus closed questions in the study design allowed discrepancies such as these to arise.

12.3 Patient–Clinician Communication is Important for Optimal Disease Management

As indicated in the ASAS-EULAR recommendations for axSpA management, shared decision-making requires patients to be educated about their disease and treatment options to enable a collaborative approach to defining an appropriate treatment goal (Heijde et al. 2017; Smolen et al. 2018). However, more than one-third of IMAS participants (36.8%) had not talked with their managing physician about their personal treatment goals (Fig. 12.4). This represents a key area where improvement is required.

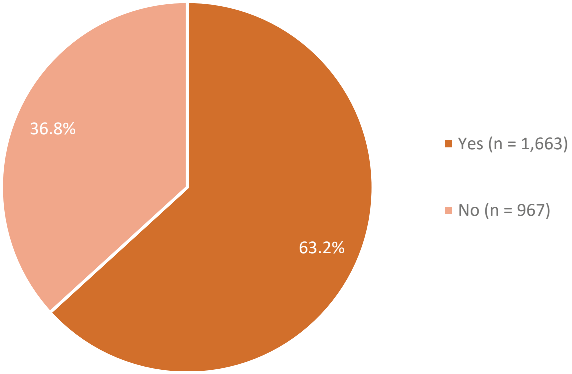

Fig. 12.4 Communication of personal goals to physician (N = 2,630)

The hopes and fears reported by European IMAS participants were generally aligned with medical priorities and guidelines highlighting the importance of maximizing health-related quality of life (Heijde et al. 2017). Current guidelines recommend that axSpA treatment should be individualized according to the current signs and symptoms along with characteristics such as comorbidities and psychosocial factors (Heijde et al. 2017). As many of these factors are only known to the patient, improvements in patient–clinician discussions may allow the clinician to offer the most appropriate education/advice and potentially treatment adjustment. Clinicians also need to be encouraged to be transparent with patients and acknowledge areas of uncertainty within axSpA management due to lack of evidence.

12.4 Conclusions

- Survey participants' most common disease-related fears were disease progression, suffering pain, and loss of mobility. Nevertheless, they hoped to halt disease progression, eliminate pain, obtain effective treatments, and improve quality of life.
- These insights into what is relevant for patients may reflect unmet treatment needs and key gaps in the information given about their disease, its outlook, and its management that could be addressed through improved education.
- One out of three participants reported that they had not talked to their clinician about their personal treatment goals.
- Patients with axSpA may achieve better health outcomes through adjusting therapy with an aim of achieving a specific treatment goal (Smolen et al. 2018); proactive and transparent discussions of expectations and treatment goals between HCPs and patients should be encouraged to enable effective shared-decision making and the design of individualized treatment strategies that provide optimal management of the disease.

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IMAS European Survey Strengths and Limitations

The IMAS European survey was a large survey that provided a valuable insight into the many aspects of axSpA from the perspective of patients across Europe. Like all studies, it has both strengths and weaknesses.

Strengths

- The IMAS European survey included a relatively large sample size (2,846 participants).
- Covering 13 European countries with different cultures, economies, and healthcare systems, the survey provides a wide range of perspectives from participants across Europe and highlights some important differences between the countries. In contrast, studies carried out in a single center, country or a smaller number of countries sometimes assume that data from one European country are representative of neighboring countries.
- The IMAS project was developed and overseen by a multi-disciplinary team of axSpA experts that included rheumatologists, psychologists, researchers, and patient representatives. The collaboration between people with different expertise and perspectives enabled the survey to investigate as many potentially important points as possible while greatly enhancing the interpretation of the data.
- The IMAS project provided a voice to patients in a sphere dominated by clinical data and the perspectives of physicians. The survey collected information in a range of different formats, which included scores from patient-reported outcome measures about the disease itself, along with data regarding treatments, comorbidities, and healthcare usage, and, uniquely, a large focus on how the disease affects the day-to-day lives of affected patients, physically, emotionally and economically. Too often studies in axSpA are focused on the physician's perspective and assume that the factors important medically are those most important to the patient. By asking for patients' opinions and providing the opportunity to give free-text responses as well as just a grading or 'yes/no' type answer, we identified that many aspects important to the patient align with medical priorities, such as reducing pain and halting disease progression, but also that the overall impact of disease is broader.

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- By performing a literature review alongside the survey we could assess how our data compared with the results from other studies, providing the context in which to interpret the data and identify trends and novel findings worthy of further discussion.

Limitations

- Although the overall sample size was large, participant numbers were small for some countries which prevented meaningful analysis of some of the data.
- The sample was also predominantly female (61% female, 39% male), whereas recent data suggest the prevalence of axSpA is similar for both genders. Males were therefore under-represented in the survey, which may limit the conclusions that can be drawn as there is a growing evidence of differences in symptoms and their severity in men versus women.
- Three-quarters of participants surveyed were aged under 52 years, which may be a result of the online nature of the survey; although online surveys offer convenience they may also restrict participation to patients with more technical/computer skills, who are often younger. However, it may also reflect that most cases of axSpA are diagnosed before the age of 45 years and patients with a more recent diagnosis may be more inclined to participate in research.
- Around 70% of participants in the IMAS survey were recruited through patient organizations. While patient organizations offer valuable support to patients, this may represent a potential bias as patients more likely to join or engage with a patient organization may also be more likely to want to participate in surveys such as this.
- The reporting of data from the patient’s perspective was a key strength of our study, but it may have led to some inaccuracies in the reporting of some of the more medically focused information, as, for example, patients may be unsure which class of medication their particular treatment belongs to or what their specific diagnosis was. Furthermore, as patients were on a range of different treatments, including NSAIDs, csDMARDS, biologics, and every combination therein, we were also unable to perform any meaningful analyses on outcomes by therapy class. The clinical data therefore must also be viewed in the context of the myriad of different treatments the participants received.
- Finally, the survey relied on self-reported data and did not attempt to confirm participant diagnosis nor support participant responses with clinician-reported assessments. As a result, lab markers of disease activity were not available, and HLA-B27 status was reported for a relatively small proportion of patients and could not be verified. The same is also true for the classification status (radiographic or non-radiographic), which cannot be verified; therefore, we focused on the analysis of the entire axSpA population.

Summary

The IMAS European data build on previous knowledge and have identified a number of findings that may be helpful in informing long-term plans and treatment goals. The hope is that ultimately this will help to improve the quality of life and optimize clinical outcomes for patients in the future, while fostering closer relationships between patient organizations, HCPs, and policy makers across Europe. The IMAS European survey provides an invaluable snapshot of the status of axSpA in Europe from the perspective of patients that is a valuable addition to the studies of this nature published previously.

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Appendix

Glossary of Terms

Within any given definition, terms highlighted in **bold type** have their own definition elsewhere in the glossary.

Active disease: When **axSpA** is 'biologically active', i.e. there is active inflammation (see also **BASDAI**, **disease activity**). An important principal of **axSpA** therapy is minimizing disease activity to provide symptomatic relief to patients and prevent progression of structural damage.

Acupuncture: Where needles are inserted at particular sites in the body for therapeutic or preventive purposes. Acupuncture is generally considered to be an **alternative/complementary therapy**.

Acute phase reactants: Proteins that are present at increased levels in acute (short term/transient) inflammation. Your doctor may do a blood test to check the levels of these proteins (along with other factors) either when diagnosing or monitoring **axSpA**.

Adverse event: Any unexpected medical event that occurs while you are taking a medicine. The European Medicines Agency defines an adverse event as 'an untoward medical occurrence after exposure to a medicine, which is not necessarily caused by that medicine'.

Alternative therapy/medicine: A treatment that differs from that given in typical mainstream healthcare. The term 'alternative therapy' is also sometimes used interchangeably with '**complementary therapy**' although they are actually slightly different. Alternative therapy is the use of a non-mainstream practice *instead of* conventional medicine, whereas complementary therapy actually refers to the use a non-mainstream practice *together with* conventional medicine. Examples of treatments that may be alternative or complementary include **acupuncture** and **aromatherapy**.

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Aromatherapy: An **alternative/complementary therapy** that uses aromatic oils to try to improve physical health or general well-being.

AS (ankylosing spondylitis): The ‘radiographic stage’ of **axSpA** which can follow the **nr-axSpA** stage. The term ‘radiographic’ in this context means that **sacroiliitis** can be seen on an **X-ray** of an affected person.

ASAS (Assessment of SpondyloArthritis international Society): An international group of experts that aims to increase awareness and promote the study of **spondyloarthritis**. ASAS also evaluates treatments, develops new ways of assessing **spondyloarthritis**, and may issue guidelines and recommendations (often in collaboration with **EULAR**).

axSpA (axial spondyloarthritis): A **chronic** inflammatory condition that can lead to **chronic** pain, structural damage, and disability. axSpA primarily affects the ‘axial skeleton’, i.e. the spine and/or **sacroiliac joints**, but can also affect other parts of the body (see **extra-articular manifestations**, **peripheral manifestations**). axSpA exists in two stages, **nr-axSpA** and **AS**.

BASDAI (Bath Ankylosing Spondylitis Disease Activity Index): A questionnaire that evaluates **disease activity** in patients with **axSpA**. 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 touch; and the level of stiffness in the morning. Patients respond using a scale ranging from 0 (no activity) to 10 (maximum activity), so a higher score indicates higher disease activity. BASDAI scores can be divided into high (patients who score 4 or higher) and low (patients who score less than 4) scores to allow the assessment of the distribution of patients according to disease activity.

Biologic therapy: A medicine that uses a biological substance, e.g. an antibody, to target a specific process (e.g. inflammation) involved in a particular condition.

BMI (body mass index): A measure used to determine whether someone is considered to be within a medically normal weight range depending on their height, according to World Health Organization criteria. Individuals are categorized as underweight (<18.50 kg/m^2), within the normal range (18.50–24.99 kg/m^2), overweight (25.00–29.99 kg/m^2), or obese (≥ 30 kg/m^2).

Cervical (region, spine): The neck (top) region of the spine.

Chiropractor: A chiropractor uses their hands to help relieve problems with the bones, muscles, and joints. Chiropractic treatment is classed as a **complementary/alternative medicine**.

Chronic: Long-term/ongoing. In **axSpA** the word chronic is often used to refer to the ongoing pain ('chronic pain') associated with this long-term (chronic) condition. Chronic pain, for example, differs from 'acute pain' which is the term used to refer to short-term pain often resulting from an injury (such as the short-term pain you experience after stubbing your toe).

Clinical features: This term is generally used to refer to signs (observed by a doctor or other healthcare professional) and symptoms (experienced by the patient, such as pain) of a condition. Clinical features are those that give rise to observed/ experienced changes from the norm rather than only being apparent when laboratory (e.g. blood or urine analysis) or imaging (such as **X-ray**) tests are carried out. Different types of information, including clinical features, laboratory tests, and imaging are used in the diagnosis and monitoring of **axSpA**.

Cohort study: A type of **longitudinal study** where a defined subset of people (a cohort) are followed over a period of time.

Comorbidities: A term used to refer to medical conditions other than the one being focused on; comorbidities may be related or unrelated to the condition of interest. For example, in a study of people with **axSpA**, some people may also have Type 2 diabetes (a comorbidity unlikely to be related to axSpA) or **psoriasis** (which may be related to axSpA; see **extra-articular manifestations**). Information on comorbidities may be important in determining the treatment a person receives or when scientists are evaluating data from a study of a particular medical condition.

Complementary therapy/medicine: A non-mainstream practice (i.e. one not usually given in typical mainstream healthcare) that is used together with conventional medicine. The term 'complementary therapy' is also sometimes used interchangeably with '**alternative therapy**' although they are actually slightly different as alternative therapy is the use of non-mainstream practice *instead of* (rather than *as well as*) conventional medicine. Examples of treatments that may be alternative or complementary include **acupuncture** and **aromatherapy**.

Conventional radiography: Radiography that uses **X-rays**.

Correlation coefficient: A number given to illustrate the strength of a statistical correlation (i.e. an association) between two things. The closer the number is to 1, the stronger the correlation. A correlation coefficient can also be positive or negative (preceded by a minus sign). A positive correlation coefficient means that there is a direct correlation between two things, e.g. a positive coefficient of 0.950 between age and frequency of travel would strongly indicate that older people travel more often than younger people. A negative correlation coefficient of –0.950 would strongly indicate that older people travel less often than younger people. Correlations are sometimes presented using a **scatter diagram**. The correlation coefficient will normally be accompanied by a '**p-value**' (e.g. $p = 0.12$ or

$p < 0.001$); the p value is used to indicate if the result is statistically significant and p-values below 0.05 were considered statistically significant in the European IMAS survey. It is important to note that a statistically significant result may not be clinically significant or meaningful to the patient/doctor as it may sometimes just be a pattern observed in the numbers. Many different statistical methods are used to generate correlation coefficients and p-values (technical details of those used in the European IMAS survey report can be found in Chap. 3).

Crohn's disease: A type of **inflammatory bowel disease (IBD)** that can affect any part of the gastrointestinal tract, from the mouth to the anus. Crohn's disease is a potential **extra-articular manifestation** of **axSpA**.

Cross-sectional study: A study carried out on a group of people at a set point in time (e.g. by asking people to complete a single survey about their current situation/treatment). This differs from a **longitudinal study** where people may be followed up over a period of time (e.g. every 6 months).

csDMARD (conventional synthetic disease-modifying anti-rheumatic drug): The name given to a group of drugs conventionally used to treat rheumatoid and psoriatic arthritis, which includes drugs such as sulfasalazine, leflunomide, and methotrexate. csDMARDS are not normally effective for **axSpA** itself but are sometimes used to treat **peripheral manifestations**.

CT (computerized tomography) scan: A scan that uses **X-rays** and a computer to produce detailed images of structures inside the body, including internal organs, blood vessels, and bones. The patient normally lies on their back on a flat bed that passes into the CT scanner.

Dactylitis: Inflammation of a finger or toe. Dactylitis is sometimes referred to as 'sausage fingers'. Dactylitis is a possible **peripheral manifestation** of **axSpA**.

Disease activity: Disease activity in the European IMAS survey report is based on the **BASDAI** score (see **BASDAI** for further details). An important principal of **axSpA** therapy is minimizing disease activity to provide symptomatic relief to patients and prevent progression of structural damage.

DMARD (disease-modifying anti-rheumatic drug): An overarching name given to the group of drugs that may be used to treat rheumatic diseases. DMARDs may be categorized as **csDMARDs** or biologic DMARDs (a type of **biologic therapy**).

Dorsal (region, spine): The central region of the spine, sometimes referred to as the thoracic spine.

Efficacy: How well a treatment works. Strictly speaking, this term should be used when referring to results from a clinical trial (i.e. how well a treatment works under ideal controlled conditions) but it is sometimes also used when talking about the effectiveness of a drug in general use. Doctors need to consider both the potential effectiveness of a drug and potential **adverse events** as well as other factors (such as **comorbidities**) when selecting treatment options for a patient.

Enthesitis: Inflammation where a **tendon** or **ligament** joins a bone. Enthesitis is a possible **peripheral manifestation** of **axSpA**.

EULAR (European League Against Rheumatism): An organization that represents people with arthritis/rheumatism and associated healthcare professionals. EULAR may make recommendations or issue recommendations for **axSpA** treatment alongside other organizations such as **ASAS**.

Extra-articular manifestation: When axSpA involves another area of the body (outside of the spine and joints). Examples of possible extra-articular manifestations are **Crohn's disease**, **ulcerative colitis**, **uveitis**, and **psoriasis**.

GHQ-12 (General Health Questionnaire-12): A questionnaire used to measure psychological distress. This questionnaire evaluates the severity of mental health problems using 12 rapid questions, with the answers used to calculate a score. Higher scores indicate higher levels of psychological distress. The European IMAS survey used a validated cut-off point of 3, implying that individuals with a score of 3 or more were at higher levels of psychological distress and may have a psychiatric disorder.

Global Limitation Index: A score generated by adding together 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). A score of 0 refers to no limitation; 1, low limitation; 2, medium limitation; and 3, high limitations for each of the 18 different daily activities. Thus, a value between 0 and 18 implies low limitation; between 18 and 36, medium limitation; and between 36 and 54, high limitation.

Global Stiffness Index: A method used to assess the degree of stiffness experienced by patients in the spinal column, distinguishing between the **cervical**, **dorsal**, and **lumbar** areas. The degree of stiffness is measured based on patient's responses regarding the areas affected (without limitation, mild limitation, moderate limitation, and significant limitation). A score is obtained by adding together the responses for the degree of stiffness in each of the areas of the spine; higher scores indicate higher levels of stiffness.

HLA-B27 (Human Leukocyte Antigen-B27): A genetic marker that is present in the blood of many people with **axSpA**. The presence of HLA-B27 alone does not necessarily mean someone has axSpA, and some people with axSpA test negative for HLA-B27. HLA-B27 is therefore assessed among other factors when considering a diagnosis of axSpA.

Homeopathy: An **alternative/complementary therapy** that is based on the use of diluted substances which practitioners claim help the body to heal itself. There is currently no good-quality evidence to suggest that homeopathy is effective for any health condition.

IBD (inflammatory bowel disease): An overarching term given to inflammatory diseases of the gut, mainly **Crohn's disease** and **ulcerative colitis**. IBD is a potential **extra-articular manifestation** of **axSpA**.

Inactive disease: In the context of **axSpA**, inactive disease refers to a state where the disease is not showing biological activity (e.g. inflammation; see also **active disease**). An important principal of **axSpA** therapy is minimizing disease activity to provide symptomatic relief to patients and prevent progression of structural damage.

Inflammatory markers: Markers that increase in the blood according to the level of inflammation present. Your doctor may perform blood tests so that these markers can be used to monitor your overall levels of inflammation and assess whether you are receiving the most suitable medication.

Kruskal–Wallis test: A type of statistical test. Many different statistical methods are used to assess whether or not results are statistically significant (see also **p-values**) and the most appropriate type of test used is carefully determined by a statistician. Further details of the statistical tests used in the European IMAS survey can be found in Chap. 3.

Ligament: A tissue that connects bones to other bones.

Longitudinal study: A study often performed in a '**real-world setting**' to gain information about a group of patients over a period of time. For example, a study in **axSpA** might examine how patients' levels of pain or stiffness change over a period of time than might be used in a typical clinical trial.

Lumbar (region, spine): The lower part of the spine.

Mann–Whitney (test): A type of statistical test. Many different statistical methods are used to assess whether or not results are statistically significant (see also **p-values**) and the most appropriate type of test used is carefully determined by a statistician. Further details of the statistical tests used in the European IMAS survey can be found in Chap. 3.

Manual therapist: Someone who performs manual therapy on patients using their hands, e.g. a **physiotherapist**, **osteopath**, or **chiropractor**.

Mean: Informally known as the average of a set of values (e.g. the ages of the patients included in a study), typically calculated as the sum of the values divided by the number of values.

Median: The middle value among a set of values (e.g. the ages of the patients included in a study) when ordered in ascending order. As such, 50% of the values will be below the median, and 50% will be above the median.

Meta-analysis: A statistical analysis performed on data gained from several studies (e.g. clinical trials). A systematic search (see **systematic review**) is performed to identify published scientific articles on a particular topic and then the data from the different studies are analyzed together to see what they show overall. A meta-analysis is generally considered to be a highly reliable source of evidence as it is based on the results of several studies. The results of a meta-analysis are usually published in a scientific/medical journal.

MRI (magnetic resonance imaging) scan: A scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of the body. The patient lies on their back on a flat bed that passes into the MRI scanner.

Negative affective state: When a person's mood is dominated by negative thoughts and emotions.

nr-axSpA (non-radiographic axSpA): The non-radiographic stage of **axSpA**. The term 'non-radiographic' in this context means that **sacroiliitis** cannot be seen on an **X-ray** of an affected person. nr-axSpA generally relates to the earlier stages of **axSpA**, before it has progressed to **AS**, although some people remain at this stage and do not progress to **AS**.

NSAID (non-steroidal anti-inflammatory drug): A group of medicines typically prescribed for first-line (initial) treatment of **axSpA**. NSAIDs are used to relieve pain and reduce inflammation and are also sometimes used for other conditions such as headaches, muscle strains, and arthritis. Examples of NSAIDs include ibuprofen, naproxen, and diclofenac.

Orthopedist: A surgeon specializing in the musculoskeletal system (e.g. joints and bones). An orthopedist is often referred to as an orthopedic surgeon.

Osteopath: A healthcare professional who uses physical manipulation, stretching, and massage, for example to increase the mobility of joints or relieve muscle tension.

Osteoporosis: A condition that weakens bones, making them fragile and more likely to break than in people without osteoporosis.

P-value: A number (e.g. $p = 0.12$ or $p < 0.001$) generated by a statistical test that indicates whether or not the result is 'statistically significant'; p-values below 0.05 were considered statistically significant in the European IMAS survey. It is important to note that a statistically significant result may not be clinically significant or meaningful to the patient/doctor as it may sometimes just be a pattern observed in the numbers.

Passive coping style: When a person responds to a problem by using passive means such as avoidance or denial rather than actively dealing with the problem.

Pathophysiology: The changes from normal bodily structure, functions, and biochemistry associated with a medical condition. For example, the pathophysiology of axSpA may include pain and raised **inflammatory markers**.

Pearson correlation coefficient: A type of statistical test that is used to produce a **correlation coefficient** (i.e. a number given to illustrate the statistica; strength of an association between two things). There are many different statistical methods available to generate a correlation coefficient and the most appropriate type of test used is carefully determined by a statistician. Further details of the statistical tests used in the European IMAS survey can be found in Chap. 3.

Pearson χ^2 test: A type of statistical test that may be used to determine whether a result is statistically significant (see also **p-values**). There are many different statistical methods available and the most appropriate type of test used is carefully determined by a statistician. Further details of the statistical tests used in the European IMAS survey can be found in Chap. 3.

Pelvis: The area between your belly button and the top of your legs. The pelvis contains a ring structure of bone that connects the lower vertebrae to the legs. The pelvis surrounds and supports the reproductive organs, the lower urinary tract, and parts of the bowel.

Peripheral inflammation: When inflammation occurs in the peripheral joints (those other than the spine and **sacroiliac joints**), e.g. the knees or hips.

Peripheral manifestations: When axSpA affects joints or parts of the joint other than the spine and **sacroiliac joints**. Examples of possible peripheral manifestations include arthritis, **enthesitis**, and **dactylitis**.

Pharmacologic treatment: Treatment with medicines prescribed by your doctor or purchased at a pharmacy. This term refers to treatment using pharmaceutical drugs and does not include other types of therapy such as physiotherapy (see **physiotherapist**) or **complementary/alternative** medicine.

Physiotherapist: A healthcare professional who works with patients to help restore movement and function, for example due to illness, disability, or injury. Physiotherapists can give education/advice, recommend particular movements or exercises, or may use manual therapy (e.g. where the physiotherapist uses their hands to help relieve pain or stiffness; see also **manual therapist**).

Podiatrist: A healthcare professional trained to diagnose and treat conditions of the feet (e.g. ingrown toenails and bunions) and lower limbs. A podiatrist is often referred to as a chiropodist.

Prevalence: The prevalence of a condition (e.g. **axSpA**) refers to the number of people it affects. It is often stated as a global prevalence or a country-specific prevalence. Prevalence differs from incidence in that it refers to the total number of people with a condition (regardless of how long they have had it), whereas incidence generally refers to the number of people who have been diagnosed with a condition in a particular year.

Primary healthcare provider: A healthcare provider who is generally a first point of contact. It typically refers to general practitioners (family doctors) or nurse practitioners in a general practice but may also include community pharmacists, opticians and dentists.

Prognosis: A doctor's judgment of the expected course of a disease, for example the likelihood of it improving or getting worse.

Psoriasis: A skin condition that causes red, flaky, crusty patches of skin that are covered with silvery scales. Psoriasis is a potential **extra-articular manifestation** of **axSpA**.

Pulmonologist: A doctor who specializes in respiratory conditions, such as lung diseases.

Radionuclide scintigraphy: This is a scan (also called a radionuclide scan) that involves having a radioactive chemical put into your body that is then detected by a scanner. The dose of radioactivity is very low (about the same as an **X-ray**) and almost all of it leaves the body within a few days. Radionuclide scintigraphy can be used to look at inflammation in people with **axSpA**.

Real-world setting: A term used in medical research to refer to a general setting where patients are living with a particular condition in the 'real world'. Studies in the real-world setting generally examine how patients are affected by diseases or treatments over time in their normal day-to-day lives – these studies differ from a clinical trial setting where patients who meet specific criteria receive a particular drug over a relatively short period of time under strictly controlled conditions. Most clinical trials take place before a drug is licensed and the data would then be used in an application for approval of the drug. Real-world studies then often follow to examine how well a drug is working, tolerated, or accepted in the 'real world'.

Registry: In a medical context, this often refers to a source/database of information regarding a disease or treatment. For example, a registry may be set up to collect information about how patients with **axSpA** are treated. Scientists and clinicians can then review this information and consider whether any changes to clinical practice should be recommended. Patients' details can only be held in a registry with their consent and personal information (e.g. your name or address) is kept strictly confidential.

Rheumatologist: A doctor who specializes in rheumatic conditions, such as **axSpA** and rheumatoid arthritis.

Sacroiliac joints: The joints between the lower spine and the left and right hand sides of the pelvis.

Sacroiliitis: Inflammation of one or both of the **sacroiliac joints**.

Scatter diagram: A type of graph that shows the statistical relationship between two factors (see also **correlation coefficient**). For example, the scatter diagrams in Chap. 5 of the European IMAS survey report use circles to represent individual participants—this allows you to see if there is a clear relationship between the two factors, indicated by most of the circles (people) fitting an obvious trend (either a pattern going upwards or downwards). If the circles are widely scattered with no obvious trend, this suggests that the two factors may not be statistically linked.

Spondyloarthritis (SpA, also called spondylitis): A general term that refers to a group of related inflammatory diseases that involve both the joints and the entheses (where the **ligaments** and **tendons** attach to the bone; see also **enthesitis**). **axSpA** is a type of SpA.

Standard deviation (SD): A measure of the amount of spread among a set of values (e.g. the ages of patients included in a study). A small SD indicates that most of the individual values are close to the mean; a large SD indicates that the individual values are spread out over a large range.

Systematic review: As there are often many different studies performed in medicine, it is useful to carry out regular systematic reviews to see how many articles have been published on a particular topic and to evaluate and summarize what they are saying. A systematic search is performed where specific terms (e.g. **axSpA** AND pain AND treatment) are used to search databases to ensure all the published articles are found. The reviewer then goes through the retrieved articles to select only those that are directly relevant to the particular topic they are studying.

These articles are then reviewed by scientists and/or clinicians who then prepare a concise summary of the findings from the studies and discuss any potential implications for patients and their treatment. A systematic review is usually published in a scientific/medical journal so that other people can read it. Sometimes, where appropriate, a **meta-analysis** of the data may also be performed.

Tendon: A tissue that attaches a muscle to a bone.

Thorax: The chest area of the body (between the neck and the abdomen). The thorax includes the ribs, heart, lungs, and diaphragm. The term '**dorsal**' spine or 'thoracic spine' is used to refer to the corresponding area of the spine.

TNF (inhibitor): TNF (tumor necrosis factor) is a cytokine that causes inflammation. TNF inhibitors are a group of **biological therapies** that work by neutralizing the activity of TNF. You may also hear TNF inhibitors described as 'anti-TNFs'. TNF was initially discovered as a protein produced by immune cells that could suppress tumor cells but it was later also found to be involved in inflammatory processes—the word 'tumor' in TNF therefore relates to the name of the protein and does not mean that the drug is a cancer drug.

Tolerability: How well tolerated a drug is. The word tolerability is often used interchangeably with safety, but it is a broader term that includes factors that might mean that some people cannot tolerate a drug (see also **adverse events**).

Ulcerative colitis: A type of **IBD** that affects the colon (large intestine/bowel) and rectum (the end of the bowel where stools are stored). Ulcerative colitis is a potential **extra-articular manifestation** of **axSpA**.

Ultrasound scan: A scan that uses high-frequency sound waves to allow an image to be seen from inside the body. An ultrasound is the type of scan used on pregnant women to monitor an unborn baby, but it can be also used to look at inflammation in people with **axSpA**.

Uveitis: Inflammation of the middle layer of the eye (the uvea). Uveitis is a potential **extra-articular manifestation** of **axSpA**.

X-ray: a type of radiation. Informally we refer to X-rays as a scan that uses radiation to examine most areas of the body but they are mainly used to assess the bones and joints.