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

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/978-3-030-97606-4_6.

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

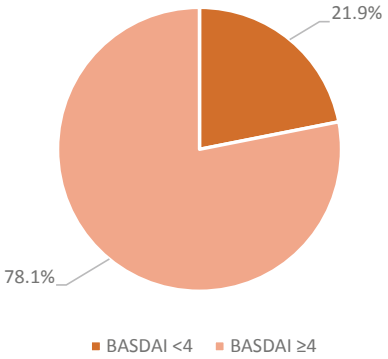

Fig. 6.1 Level of disease activity of participants (BASDAI <4 or ≥4) (N = 2,584). *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index

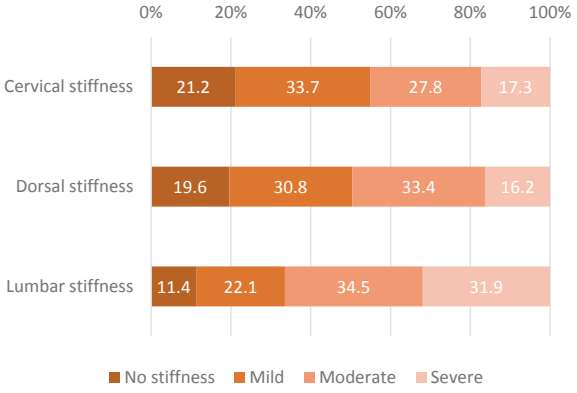

Fig. 6.2 Degree of spinal stiffness (cervical, dorsal, and lumbar) in participants

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.

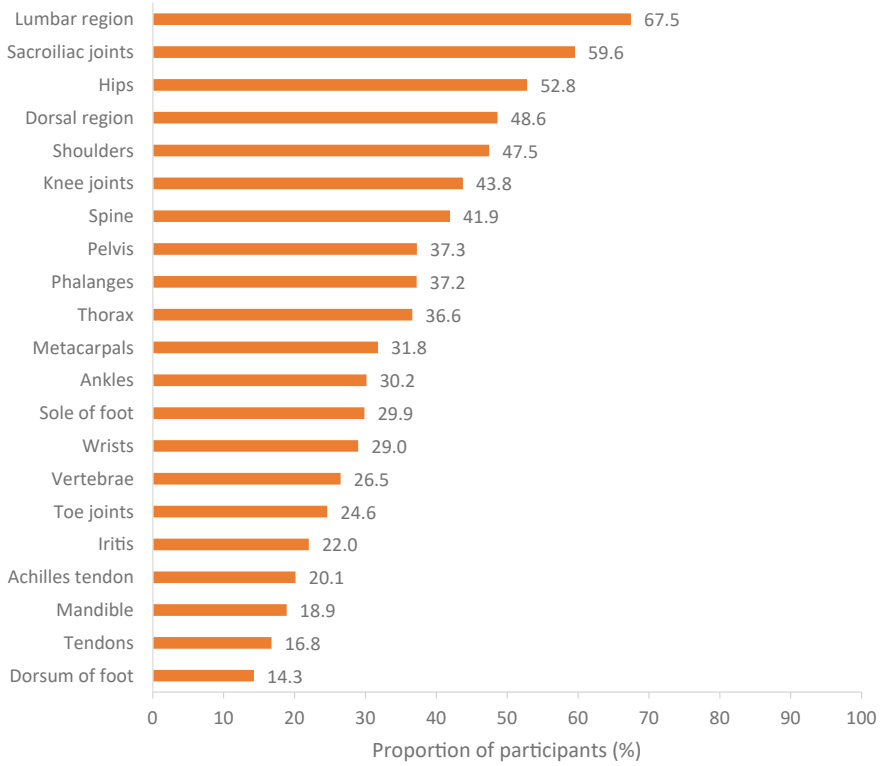

Fig. 6.3 Body areas where survey participants reported experiencing inflammation (N = 2,727)

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).

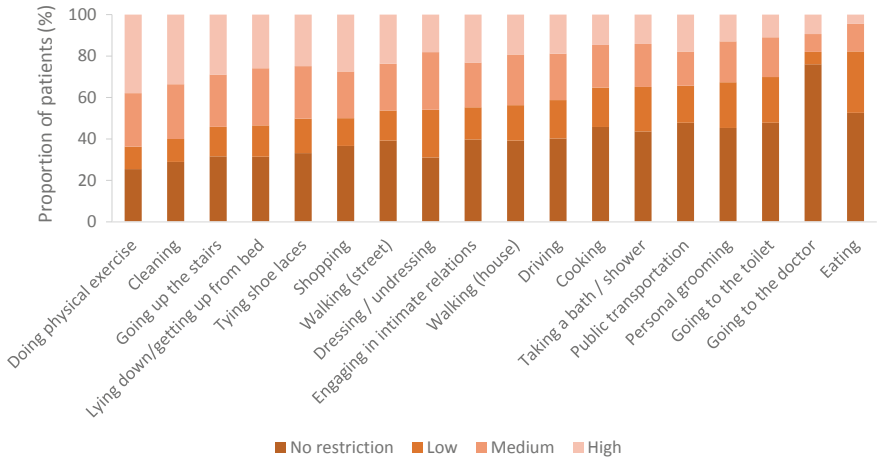

Fig. 6.4 Restricted daily activities reported by survey participants (N = 2,771)

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).

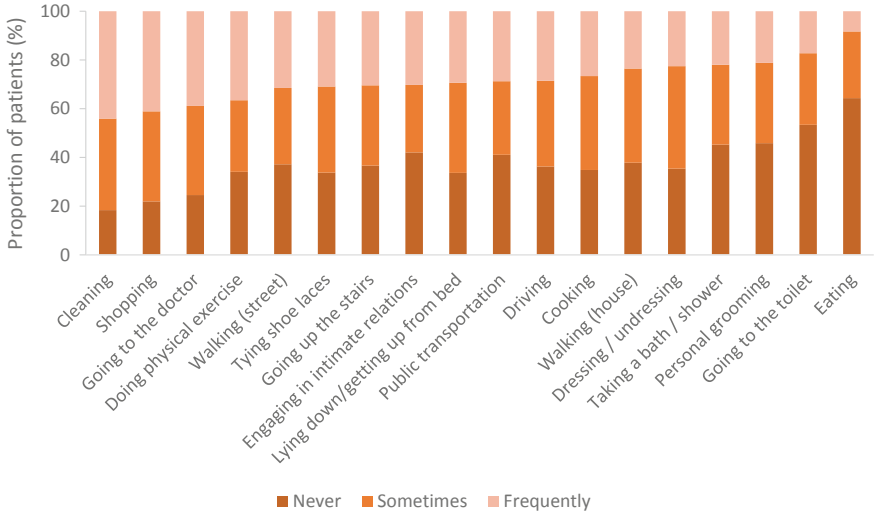

Fig. 6.5 Daily activities for which survey participants declared needing help (N = 664–1,969)

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).

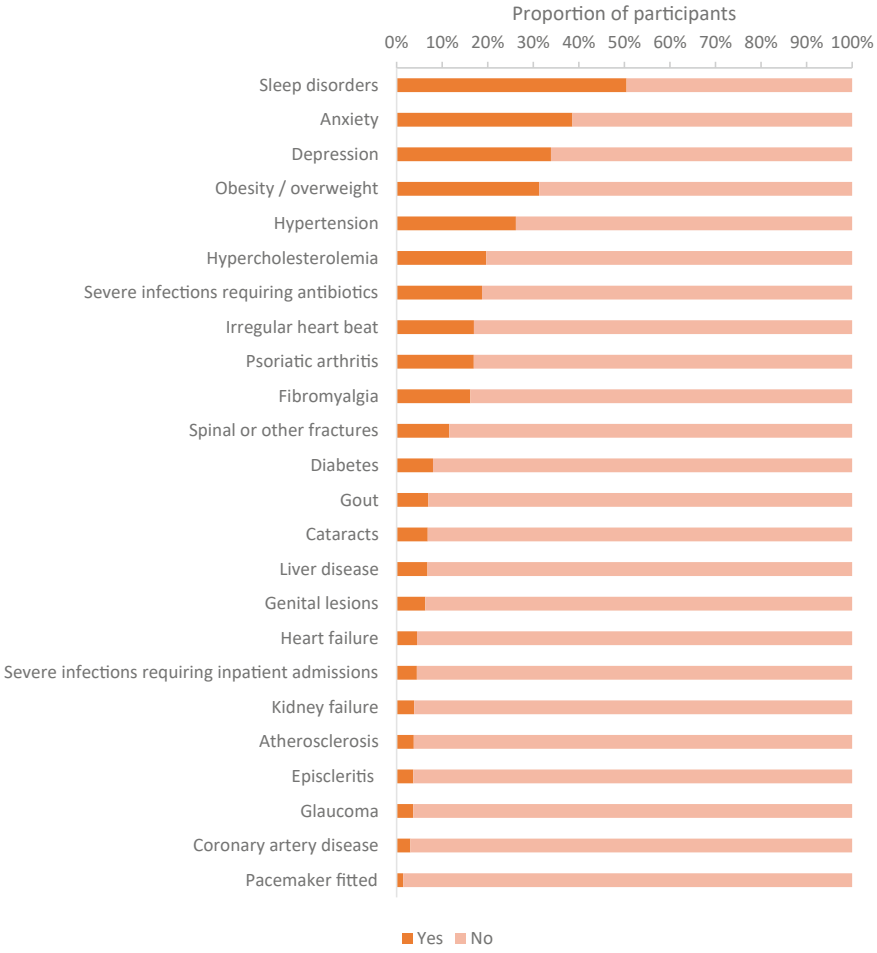

Fig. 6.6 Comorbidities reported by participants (N = 2,096)

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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