Health-Related Quality of Life Among Spondyloarthritis and Chronic Low Back Pain Patients: Results from a Nationwide Population-Based Survey

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Competing interests

The authors declare that they have no conflict of interest, financial or non-financial, related to this research.

Author contributions

All authors contributed to the study conception and design. Materials preparation, data collection, and analysis were performed by Helena Santos, Ana Rita Henriques, and Ana Maria Rodrigues. The first draft of the manuscript was written by Helena Santos, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki, and approval was granted by the Ethics Committee of NOVA Medical School (nº123/2020/CEFCM).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

ABSTRACT

Purpose

Both spondyloarthritis and chronic low back pain (CLBP) significantly impact health-related quality of life (HRQoL). It is important to clarify whether these disorders have different impacts on the several domains of HRQoL as different mechanisms may necessitate different treatment interventions. Moreover, the factors associated with HRQoL can inform more targeted group interventions to promote HRQoL.

Methods

We used data from EpiReumaPt, a population-based survey conducted from September 2011 to December 2013. HRQoL was assessed with EuroQoL-5-Dimensions (EQ-5D). Spondyloarthritis was diagnosed by expert opinion (rheumatologist) and predefined criteria. CLBP was diagnosed if low back pain was present on the day of the interview and persisted for >90 days. Univariable and multivariable linear regression analyses compared HRQoL among subjects with spondyloarthritis, CLBP, and no rheumatic diseases. Multivariable linear regression analyses evaluated HRQoL factors in spondyloarthritis and CLBP subjects.

Results

We included 92 spondyloarthritis patients, 1376 CLBP patients, and 679 subjects without rheumatic diseases. HRQoL was similarly affected in spondyloarthritis and CLBP (ß=−0.03, 95% CI [−0.08; 0.03]) in all EQ5D dimensions. A much lower HRQoL was found in spondyloarthritis and CLBP patients compared with subjects without rheumatic diseases (ß=−0.14, 95% CI [−0.19; −0.10]; ß=−0.12, 95% CI [−0.14; −0.09], respectively). In spondyloarthritis subjects, multimorbidity and active disease were associated with worse HRQoL (ß=−0.18; 95% CI [−0.24; 0.03]; ß=−0.13; 95% CI [−0.29; −0.05], respectively), and regular physical exercise was associated with better HRQoL (ß=0.18; 95% CI [0.10; 0.30]). In CLBP subjects, multimorbidity (β=−0.11; 95% CI [−0.14; −0.08]), obesity (β=−0.04; 95% CI [−0.08; −0.01]), and low back pain intensity (β=−0.02; 95% CI [−0.03; −0.02]) were associated with worse HRQoL, and regular physical exercise (β=0.08; 95% CI [0.05; 0.11]) was significantly associated with better HRQoL.

Conclusion

Spondyloarthritis and CLBP subjects reported similar levels of impairment in the mental, physical, and social domains of HRQoL. Future health plans should address modifiable factors associated with HRQoL in these conditions to achieve better outcomes.

Keywords

Health-related quality of life; EQ5D; Chronic low back pain; Spondyloarthritis

INTRODUCTION

Health-related quality of life (HRQoL) is a subjective assessment of the impact of a disease and its treatment [1]. It is a broad, multidimensional concept that includes patient perspectives of life's positive and negative aspects in the physical, mental, and social domains [2]. HRQoL assessment is now a mandatory aspect of disease burden evaluation, so patient-oriented treatments can be developed to promote HRQoL.

Musculoskeletal disorders are the second most common cause of disability worldwide [3,4]. These disorders place a significant burden on patients [5–9], seeming to mainly impact the physical domain but also, to a lesser extent, the mental and social domains of HRQoL [5,7,9]. Moreover, musculoskeletal disorders are associated with poorer HRQoL than several other chronic medical conditions [10–14]. Within musculoskeletal disorders, lower back and neck pain are the leading global cause of disability in most countries [3,4]. Epidemiological studies have reported a median global prevalence of low back pain of 15.0%, although there is substantial heterogeneity in the results [15]. A study in Portugal found that self-reported low back pain was the most common rheumatic condition and that chronic low back pain (CLBP) had a national prevalence of 10.4% [16]. CLBP harms both physical and mental health [16–19], and its impact on HRQoL increases with both the duration of back pain [20] and pain severity. Irrespective of medication use [18], CLBP has been compared to the pain experienced by people diagnosed with life-threatening diseases [21].

Spondyloarthritis is a chronic inflammatory rheumatic disease affecting the axial (spine and sacroiliac joints) and peripheral skeleton; according to the cardinal manifestations of the disease, it can therefore be classified as axial [22] or peripheral spondyloarthritis [23]. Inflammatory low back pain is the most common manifestation of axial spondyloarthritis but is frequently seen in peripheral spondyloarthritis as well, and a recent study showed axial involvement in 55% of the included patients [24]. Axial and peripheral spondyloarthritis are potentially disabling conditions as the resulting inflammation and structural damage lead to pain and stiffness that can impair physical function and HRQoL [25–32].

Although both spondyloarthritis and CLBP affect the axial skeleton and share low back pain as the main symptom, they produce low back pain via different mechanisms (inflammatory vs. mechanical), leading to significant differences in treatment options. Non-steroidal anti-inflammatory drugs, disease-modifying anti-rheumatic drugs, and biologic treatments are recommended to reduce symptoms and improve HRQoL in spondyloarthritis [33,34], whereas a biopsychosocial framework of patient education, exercise, and self-management that avoids excessive pharmacological solutions is recommended for CLBP [35–37]. Given the differences in physiopathology, prognosis, and treatment options between spondyloarthritis and CLBP, one could expect that these disorders would have different impacts on HRQoL and different links between the physical, mental, and social domains of HRQoL. Salaffi et al. evaluated HRQoL in different rheumatic disorders [5] and found that patients with inflammatory rheumatic diseases (including spondyloarthritis) had poorer self-reported health in all domains of HRQoL than those without arthritis.

However, Kreis et al. found that spondyloarthritis and CLBP similarly affected the physical and mental components of HRQoL [38].

It is important to clarify whether spondyloarthritis and CLBP have different impacts on HRQoL and its domains as their shared symptom—low back pain—may benefit from different pharmacologic and non-pharmacologic interventions depending on the specific factors that impact HRQoL. Moreover, knowledge of the factors associated with HRQoL will allow HRQoL to be promoted in targeted group interventions.

In this population-based study, we assessed and compared the HRQoL of subjects with spondyloarthritis, those with CLBP, and those without rheumatic or musculoskeletal disorders (RMDs). We then investigated the factors associated with HRQoL in spondyloarthritis and CLBP subjects.

METHODS

Data source and study population

We collected data from the EpiReumaPt, a large, population-based, observational study conducted from September 2011 to December 2013, to estimate the prevalence of RMDs in Portugal and determine their impact on HRQoL, physical function, and mental health. To obtain a representative sample of the Portuguese population, participants were selected by multistage random sampling. The sampling was stratified in seven regions across the country according to the Nomenclature of Territorial Units for Statistics II (NUTS II): Norte, Centro, Lisboa e Vale do Tejo, Alentejo, Algarve, Região Autónoma dos Açores (the Azores), and Região Autónoma da Madeira (Madeira).

We used a three-stage approach to capture and characterize all cases of RMDs within the adult Portuguese population (Figure 1). First, interviewers (non-physicians, trained for this purpose) performed face-to-face interviews with a computer-assisted personal interview system at each participant's household. The detailed and comprehensive questionnaire included RMD symptom screening wherein participants were asked about self-reported RMDs and, subsequently, about specific rheumatic and musculoskeletal symptoms. An algorithm was applied to the survey data to screen for specific RMDs. Second, rheumatologists performed a clinical evaluation with a physical examination for all participants identified in the first interview as potentially having an RMD as well as for 20% of the asymptomatic individuals. Finally, three rheumatologists revised the gathered information and defined the final diagnoses. For this analysis, all participants from phase two were included. The study methodology has been described in detail elsewhere [39,40].

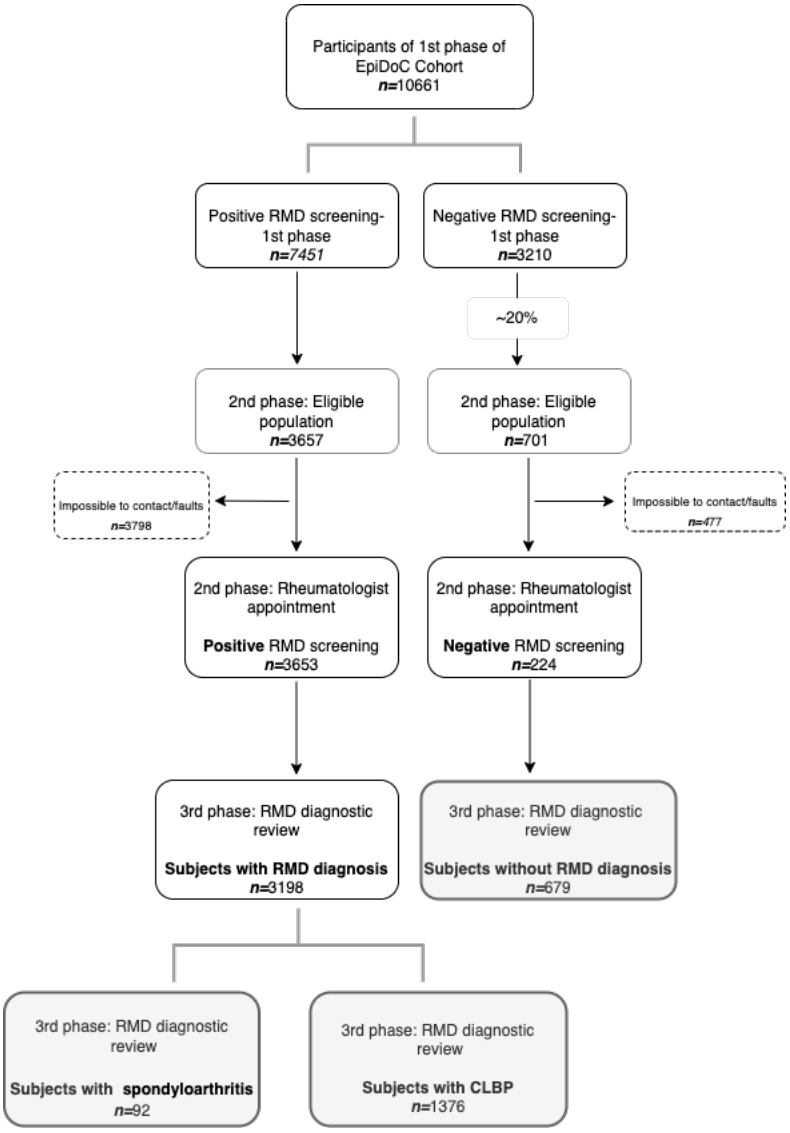

Fig 1 Flowchart of recruitment in the EpiReumaPt study

RMD, rheumatic and musculoskeletal disorders; CLBP, chronic low back pain

Case definition

Spondyloarthritis diagnosis was established after the second-phase clinical appointment based on expert opinion (in total, 95 rheumatologists were involved) and fulfillment of validated classification criteria [22,23]. Subtypes, such as ankylosing spondylitis, psoriatic arthritis, and other spondyloarthritis, were defined by expert opinion. CLBP was self-reported and defined as pain between the lower margin of the twelfth ribs and the lower gluteal folds (with or without pain referred to the lower limbs) that was present on the day of the interview and experienced most of the time for the previous 90 days. The population without RMDs was also identified by expert opinion after clinical history and physical examination.

Variables

Sociodemographic data were collected for all groups, including age, gender (male, female), ethnicity (Caucasian, other), marital status (married, other), and education level (0–4 years, 5–9 years, 10–12 years, >12 years). Lifestyle habits were also queried, including alcohol intake (daily, occasional, never), daily coffee intake (none, 1–3 cups, >3 cups), smoking habits (daily, occasionally, never), and regular physical exercise (defined as physical activity >1 hour/week; yes, no). Employment status (full-time active worker, part-time active worker, domestic worker, unemployed, retired, student, temporary work disability, other) was also registered.

Anthropometric data were collected (weight [kg], height [cm], body mass index [BMI; kg/m^2]), as were self-reported noncommunicable chronic diseases, including high cholesterol, high blood pressure, allergies, gastrointestinal disease, mental disorders, cardiac disease, diabetes, thyroid and parathyroid disease, renal disease, pulmonary disease, hyperuricemia, cancer, neurologic disease, and hypogonadism.

HRQoL data were collected using the EQ-5D, 3-level, Portuguese version (hereafter EQ-5D) [41]. The EQ-5D comprises a health descriptive component and a visual analog scale (VAS). The descriptive component evaluates five dimensions, each describing a different aspect of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems (labeled 1–3, respectively) [41,42]. For the analyses, we aggregated the "some problems" and "extreme problems" levels, thus considering only two levels in each domain. Scores from the three items can be used to derive a single utility score. The descriptive system was converted into a summary index score ranging from −1 (states worse than death, with 0 equivalent to death) to 1 (full health) [43]. The VAS is a 20-centimeter vertical scale of 0–100 points, where, similarly, scores of 0 and 100 correspond to the "worst imaginable health state" and the "best imaginable health state," respectively [42]. Subjects with CLBP recorded pain intensity on the interview day using a numeric rating scale of 0–10, and question 2 of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to evaluate back pain intensity in spondyloarthritis.

In the clinical appointment in the second phase of the EpiReumaPt study, spondyloarthritis subjects were evaluated with disease-specific assessments, including the Ankylosing Spondylitis Disease Activity Score (ASDAS), BASDAI, Bath Ankylosing Spondylitis Functional Index (BASFI), and patient's global assessment of the disease in the last week (PtGA), registered on a VAS (0–100 mm). Furthermore, a blood sample was drawn to measure C-reactive protein (CRP; mg/L). A physician's global assessment of the disease (PhGA) was also registered (VAS, 0–100 mm). In spondyloarthritis, remission/inactive disease was defined according to the predominant phenotype: ASDAS $\leq$ 1.3 defined inactive axial spondyloarthritis, and PhGA $\leq$ 20 mm was used for other forms of spondyloarthritis.

Statistical methods

Descriptive data for each categorical variable are presented as the absolute frequency and the corresponding proportion. Mean and standard deviation (SD) are shown for each continuous variable.

Subjects with spondyloarthritis were compared with subjects with CLBP and subjects without RMDs, and CLBP patients were also compared with subjects without RMDs. Comparisons were made using the Chi-square test and Fisher's exact test for categorical variables and the independent t-test for continuous variables. To assess HRQoL differences (measured by EQ-5D) between the three groups, univariable and multivariable linear regression analyses were used for continuous outcomes and univariable or multivariable logistic regression analyses were used for binary outcomes. According to the results of the univariable analyses, the following confounders were included: for comparison between spondyloarthritis and CLBP subjects—gender, age group, NUTS II region, education level, employment status, BMI, and number of noncommunicable chronic diseases; for comparison between spondyloarthritis subjects and those without RMDs—gender, age group, NUTS II region, education level, marital status, and noncommunicable chronic diseases; for comparison between CLBP subjects and those without RMDs—gender, age group, NUTS II region, education level, employment status, marital status, BMI, regular physical exercise, and number of noncommunicable chronic diseases.

To assess the determinants of HRQoL (evaluated by EQ-5D) in subjects with spondyloarthritis, univariable linear regression was first performed to select the variables to include in the final model, considering a significance level of 0.2 to avoid an early exclusion of potentially important variables. The individual variables tested were: gender, age group (18–35 years, 36–55 years, 56–75 years, ≥76 years), education level (0–4 years, 5–9 years, 10–12 years, >12 years), NUTS II region (Norte, Centro, Lisboa, Alentejo, Algarve, Azores, Madeira), marital status (married, other), employment status (active worker [full and part time], unemployed, retired, other [domestic, student, temporary work disability]), BMI (normal, overweight, obese), daily coffee intake (none, 1–3 cups, >3 cups), alcohol intake (daily, occasionally, never), smoking habits (smoker, non-smoker), regular physical exercise (yes, no), number of noncommunicable diseases (0–2, ≥3), and disease activity (active, inactive). After selecting the variables to include in the multivariable model, we sequentially excluded non-statistically significant variables through a backward conditional method and compared the models through ANOVA.

We followed the same methodology to assess determinants of HRQoL in subjects with CLBP. The independent variables tested were the same, except for disease activity, which was replaced by low back pain intensity (0–10).

The significance level was set at 0.05. All analyses were performed using Stata/IC (v.16.1).

Ethical framework

EpiReumaPt was performed according to the principles established by the Declaration of Helsinki. The study was reviewed and approved by the National Committee for Data Protection and the NOVA Medical School Ethics Committee. Participants signed informed consent documents before participation [39].

RESULTS

The analyses included 92 subjects with spondyloarthritis, 1376 with CLBP, and 679 without RMDs. Of the 92 subjects with spondyloarthritis, 32 had ankylosing spondylitis, 20 had psoriatic arthritis, and 40 had other forms of spondyloarthritis.

Spondyloarthritis subjects had a mean PtGA of 5.2±2.7, PhGA of 3.8±2.2, global spine pain (in the last 48 hours) of 4.6±2.8, BASDAI score of 5.9±3.1, ASDAS-CRP of 2.6±1.0 and BASFI score of 4.8±3.6. The mean low back pain intensity in subjects with CLBP was 5.5±2.2.

Sociodemographic, lifestyle, and health characteristics of subjects with spondyloarthritis, CLBP, or no RMDs

The mean age was 48.4±13.7 years for spondyloarthritis subjects, 58.8±14.6 years for CLBP subjects, and 45.9±15.6 years for subjects without RMDs. All three groups had a female predominance (64.1%, 70.3%, and 53.9%, respectively). Anthropometric data and sociodemographic, lifestyle, and health characteristics of the three groups are summarized in Tables 1 and 2.

Compared with spondyloarthritis subjects, CLBP subjects were older and had a lower level of education, a higher proportion of retired individuals (Table 1), more overweight or obese individuals, and a higher number of self-reported noncommunicable diseases, namely high blood pressure, diabetes, and high cholesterol (Table 2). They also had a lower coffee intake than subjects with spondyloarthritis. However, there were no differences in alcohol consumption, smoking habits, or regular physical exercise between these two groups (Table 2).

Sociodemographic and lifestyle characteristics were similar between spondyloarthritis subjects and those without RMDs, except for marital status, as the former had a higher proportion of married individuals; regarding noncommunicable chronic diseases (self-reported), spondyloarthritis patients had higher proportions of pulmonary, gastrointestinal, renal, and thyroid diseases (Tables 1 and 2).

HRQoL in subjects with spondyloarthritis, CLBP, or no RMDs

Spondyloarthritis subjects had much lower HRQoL than subjects without RMDs, reflected by the EQ-5D index score (0.69±0.25 and 0.86±0.21, respectively; β=−0.14, 95% CI [−0.19; −0.10]; p<0.001). The same was found when comparing CLBP subjects and those without RMDs (0.66±0.27 and 0.86±0.2, respectively; β=−0.12, 95% CI [−0.14; −0.09]; p<0.001) (Table 3).

Spondyloarthritis and CLBP subjects had similar HRQoL (0.69±0.25 and 0.66±0.27, respectively; β=−0.03, 95% CI [−0.08; 0.03]; p=0.33). Subjects with spondyloarthritis and CLBP reported problems in all EQ-5D dimensions in similar proportions but to a much greater extent than subjects without RMDs. Almost 60%

of spondyloarthritis subjects reported pain (moderate or extreme), and approximately one-third reported some or extreme problems with mobility and usual activities. Some or extreme problems with self-care were also more common in spondyloarthritis and CLBP subjects compared with subjects without RMDs.

Spondyloarthritis subjects showed a lower individual perception of health, measured by EQ-5D VAS (higher scores correspond to better health) than subjects without RMDs (65.28±18.1 and 75.69±17.64, respectively; β=−7.49, 95% CI [−11.2; −3.78]; p<0.001), and the same relationship was found for CLBP subjects and those without RMDs (60.92±19.86 and 75.69±17.64, respectively; β=−9.07, 95% CI [−10.96; −7.18]; p<0.001) (Table 3). After we adjusted for confounders, spondyloarthritis and CLBP subjects showed similar individual perceptions of health (65.28±18.1 and 60.92±19.86, respectively; β=0.20, 95% CI [−3.88; 4.27]; p=0.925).

Determinants of HRQoL in spondyloarthritis

After univariable linear regression analysis (Supplementary Table 1) we performed a multivariable model to assess determinants of HRQoL in subjects with spondyloarthritis (Table 4). Having three or more comorbidities was negatively associated with HRQoL (β=−0.18, 95% CI [−0.24; 0.03]; p<0.001). Specifically, patients with multimorbidity (≥3 noncommunicable diseases) had a mean EQ-5D score reduced by 0.18 points compared with patients with up to two noncommunicable diseases, holding all the other variables constant. Moreover, subjects with active disease also showed a worse HRQoL (β=−0.13, 95% CI [−0.29; −0.05]; p=0.036), with a mean EQ-5D score reduced by 0.13 points compared with patients with inactive disease, holding all the other variables constant. Regular physical exercise was significantly associated with better HRQoL (β=0.18, 95% CI [0.10; 0.30]; p<0.001), and patients who performed regular physical activity had a mean EQ-5D score increased by 0.18 points compared with patients who did not, holding all the other variables constant.

Determinants of HRQoL in CLBP

After univariable linear regression analysis (Supplementary Table 1) we performed a multivariable model to assess determinants of HRQoL in subjects with CLBP (Table 4). Several variables were significantly associated with HRQoL. Age ≥ 76 years (β=−0.09; 95% CI [−0.17; −0.01]; p=0.022), non-married marital status (β=−0.03; 95% CI [−0.06; −0.005]; p=0.024), retirement (β=−0.07; 95% CI [−0.12; −0.03]; p<0.001) or other employment status (β=−0.06; 95% CI [−0.11; −0.02]; p=0.007), obesity (β=−0.04; 95% CI [−0.08; −0.01]; p=0.022), multimorbidity (β=−0.11; 95% CI [−0.14; −0.08]; p<0.001), and low back pain intensity (β=−0.02; 95% CI [−0.03; −0.02]; p<0.001) were significantly associated with worse HRQoL in CLBP subjects. Patients who were 76 years old or more had a mean EQ-5D score reduced by 0.09 points compared with 18–35-year-old patients; non-married patients had a mean EQ-5D score reduced by 0.03 points compared with married patients; retired patients and patients with other work statuses (domestic

worker, student, temporary work disability) had mean EQ-5D scores reduced by 0.07 and 0.06 points, respectively, compared with full-time workers, holding all the other variables constant; obese patients had a mean EQ-5D score reduced by 0.04 points compared with normal-weight patients; patients with multimorbidity had a mean EQ-5D score reduced by 0.11 points compared with patients with up to two noncommunicable diseases; and for each centimeter increase in low back pain VAS, the mean EQ-5D score was reduced by 0.02 points, holding all the other variables constant. By contrast, patients from Alentejo (β=0.08; 95% CI [0.01; 0.14]; p=0.020), or Algarve (β=0.17; 95% CI [0.05; 0.28]; p=0.004) and those with daily alcohol intake (β=0.07; 95% CI [0.03; 0.10]; p<0.001) and regular physical exercise (β=0.08; 95% CI [0.05; 0.11]; p<0.001) had better HRQoL. Patients living in Alentejo or Algarve had EQ-5D scores increased by 0.08 and 0.17 points, respectively, compared with Lisbon residents. Daily alcohol intake was associated with an EQ-5D increase of 0.07 points compared with patients who did not drink alcohol, holding all the other variables constant. Moreover, regular physical exercise was significantly associated with better HRQoL, with a 0.08 increase in the mean EQ-5D score compared with patients who did not exercise regularly, holding all the other variables constant.

DISCUSSION

HRQoL in subjects with spondyloarthritis, CLBP, or no RMDs

Our study showed that spondyloarthritis and CLBP patients had a significantly decreased HRQoL compared with the population without RMDs. We used EQ-5D to assess HRQoL because it is one of the most commonly used generic instruments for this purpose in general population surveys and has been used in several RMD surveys [5,9,44]. Moreover, the validity and reliability of EQ-5D have been proven for spondyloarthritis [45–47] and CLBP [48–50].

Previous studies have also reported poorer HRQoL in spondyloarthritis patients compared with the general population [27,51,52]. In this study, spondyloarthritis patients showed worse HRQoL in all domains compared with adults without RMDs. However, after adjustment for confounders, anxiety/depression was no longer significantly different. Sixty-two percent of our patients reported moderate or extreme pain/discomfort, and 31.5% reported problems with mobility and usual activities, suggesting that there is inadequate disease control and significant disease burden despite the several different treatment approaches available to these patients [33,34]. Our findings regarding the impact on HRQoL are in line with a recent meta-analysis by Yang et al., who analyzed 38 studies on HRQoL in ankylosing spondylitis. These authors included studies that evaluated HRQoL by the Short-Form-36 questionnaire (SF-36) and concluded that the disease significantly impaired all SF-36 dimensions, although physical health was more likely to be affected than mental health [25].

Our results showed that HRQoL was globally impaired in CLBP compared with an adult population without RMDs. Previous cross-sectional and prospective studies also showed lower HRQoL in CLBP, with a

255 significant negative impact on both the physical and mental domains [16–20]. In our study, more than
256 half of the patients reported moderate to extreme pain/discomfort and 38% reported mobility limitations;
257 however, even less-affected domains (e.g., self-care) showed a significant difference from the population
258 without RMDs. These findings suggest that particular attention should be given to pain control in CLBP
259 patients to improve HRQoL. The need for a biopsychosocial approach to CLBP, with patient education,
260 exercise, and self-management [35–37], has been universally accepted; however, this approach may
261 undervalue pain control—a major driver of HRQoL—resulting in a higher disease burden. Eusébio et al.
262 [53] concluded that intake of analgesics and other pain relief drugs was very low among 1487 patients
263 with active CLBP, even for those who reported severe pain, confirming the insufficient pain control in
264 these patients.

265 Direct comparison of HRQoL in spondyloarthritis with that in other rheumatic conditions is scarce and has
266 focused mainly on rheumatoid arthritis, where substantial differences do not seem to exist [27,51,54–
267 56]. In our study, spondyloarthritis and CLBP showed similar impacts on HRQoL. We found no differences
268 in the physical, emotional, and social HRQoL domains between spondyloarthritis and CLBP despite
269 different physiopathology, prognosis, and treatment options. Because low back pain is the leading cause
270 of years lived with disability in most countries [3], these results are perhaps not unexpected. However,
271 HRQoL has rarely been compared among spondyloarthritis patients, and this is the first study to make a
272 direct comparison between spondyloarthritis and CLBP at a population level. Kreis et al. [38] used the
273 Short-Form 12 survey to compare HRQoL in 199 axial spondyloarthritis and 89 CLBP patients, finding
274 similar HRQoL for both diseases. This aligns with our results, as the EQ-5D index scores we obtained for
275 spondyloarthritis and CLBP were not significantly different between conditions. Still, the scores were
276 significantly lower than those of the adult Portuguese population without RMDs, confirming poorer
277 HRQoL in both diseases [43].

278 Individual perception of health, assessed by EQ-5D VAS, is a much broader concept including both
279 rheumatic problems and the general state of health. In our study, individuals with spondyloarthritis
280 showed a worse perception of health than the population without RMDs, likely related to their rheumatic
281 condition as we found no significant differences in the other variables. CLBP patients also showed worse
282 perceptions of health than the population without RMDs; however, in this group, factors other than the
283 rheumatic condition—e.g., older age, a higher proportion of retired subjects, a higher prevalence of
284 overweight/obesity, and more self-reported chronic noncommunicable diseases like high blood pressure,
285 diabetes, and high cholesterol—could have substantially influenced health perception. Spondyloarthritis
286 and CLBP patients did not show significant differences in individual perceptions of health. Hence, these
287 two chronic disorders are associated with a significantly low individual perception of health independent
288 of the different physiopathology, prognoses, and treatment options.

289

290 *Determinants of HRQoL in spondyloarthritis*

This study also identified determinants of HRQoL. We found that higher disease activity was an independent factor associated with HRQoL among spondyloarthritis patients. Previous studies have also found disease activity to be an independent determinant of HRQoL in early and advanced forms of axial spondyloarthritis [28,57,58]. This finding is clinically relevant as it suggests that strict control of disease activity is crucial to achieving better HRQoL in spondyloarthritis patients. Furthermore, we found that multimorbidity was associated with worse HRQoL in spondyloarthritis patients. Fitzgerald et al. [59] found a similar association between multimorbidity and worse HRQoL, evaluated by a disease-specific instrument (Ankylosing Spondylitis Quality of Life questionnaire), in the Ireland national registry, although they defined multimorbidity as the presence of two or more chronic noncommunicable diseases. There has been a growing interest in the prevalence and impact of comorbidities in spondyloarthritis in recent years. Several studies have found a higher prevalence of comorbidities, specifically cardiovascular and metabolic disorders [59,60], in spondyloarthritis patients than in the general population, which was reinforced in a recent meta-analysis that identified a higher prevalence of hypertension, dyslipidemia, and obesity in axial spondyloarthritis patients [61]. Our results emphasize the importance of addressing multimorbidity to minimize its impact on HRQoL.

Regular physical exercise was strongly associated with better HRQoL in spondyloarthritis. Even considering that regular exercise was self-reported and prone to recall and reporting bias, this result likely reflects the positive effect of exercise on overall well-being (not only in specific aspects of HRQoL, such as function) and emphasizes the benefit of exercise in different health dimensions. Although patients with lower disease activity may have better HRQoL and be able to exercise more regularly due to experiencing less pain, these two factors were independently associated with HRQoL in our study. Nevertheless, the cross-sectional design of our study does not allow us to infer a causal effect of the benefit of regular exercise on HRQoL, and a follow-up study of this cohort would be valuable. Exercise as a recreational activity is less well studied in spondyloarthritis than physical therapy or therapeutic exercise, and previous work has mainly addressed the effect of exercise on physical function, specifically associating exercise with improved function [62,63].

Determinants of HRQoL in CLBP

Our results show that being female was negatively associated with HRQoL, in line with previous studies showing that HRQoL was lower in female subjects than in male subjects with CLBP [64,65]. However, other authors did not find any association between HRQoL and gender in this population [66–69]. Age has been linked to HRQoL in other cohorts with contradictory results. As in our study, some research [64,66,70] has found that older age was associated with a worse HRQoL, but other authors have come to different conclusions [65,71]. For example, Wettstein et al. evaluated 228 patients with CLBP and found that HRQoL was the same or higher in older patients compared with younger patients and that increasing age was mainly associated with disability [71]. Most other studies [17,66,69,71–73] have shown that low back pain

intensity negatively influenced HRQoL, and this finding is corroborated by our results; by contrast, Aminde et al. did not find any association between low back pain intensity and HRQoL [67]. We found an association between not being married and worse HRQoL, confirming data from the literature [20,65]. Uchmanowicz et al. [65] similarly found that single, divorced, or widowed people had worse HRQoL than people who were married or in a relationship, with the social domain being the most affected. The same authors also showed improvements in the social domain of HRQoL for professionally active individuals compared with unemployed people. In our study, retirement and other employment statuses (including domestic workers, students, and those with a temporary work disability) were also associated with a worse HRQoL.

As in the spondyloarthritis subjects, we found an association between worse HRQoL and multimorbidity in people with CLBP. Comorbidities are being increasingly recognized as an important aspect of patients' conditions as they influence several disease outcomes, including HRQoL [59,61,74,75] We found an association between obesity and worse HRQoL in CLBP patients. It is well known that the population incidence of CLBP is directly associated with BMI [76] and that overweight and obesity are risk factors for CLBP [77]; moreover, obesity impairs HRQoL [78], and higher degrees of obesity are associated with greater impairment [79]. Our results were therefore somewhat excepted, but they have not been previously reported. The positive association of two NUTS II regions (Alentejo and Algarve) with HRQoL is intriguing because no regional differences in HRQoL were found in the EpiDoc cohort [6]. Other authors have reported a better HRQoL in people living in cities compared with those living in villages or small towns, contradicting our results [65]. Also intriguing is the positive association between daily alcohol intake and HRQoL as alcohol consumption is usually associated with worse HRQoL [80]. This might suggest that a small daily consumption is associated with a more positive psychological profile, but this is purely speculative. Finally, as in the spondyloarthritis subjects, regular physical exercise was positively associated with better HRQoL in CLBP. Several studies have addressed the effects of exercise in CLBP patients, but their results are considerably heterogeneous and mainly focus on pain, for which exercise seems beneficial [81]. In line with our findings, Schaller et al. [82] reported that patients achieving the World Health Organization recommendation for leisure time physical activities (≥600 metabolic equivalent of task minutes/week) had a better HRQoL than those reporting no such activities. As previously mentioned, patients with lower pain intensity may be able to exercise more regularly, so only a future longitudinal study that follows up with these patients will be able to confirm our findings on the benefits of exercise for HRQoL.

Strengths and limitations

Our study has several strengths. First, it is a population-based study with a representative sample of the Portuguese adult population, minimizing the risk of biased selection. Second, we compared HRQoL in a

large sample of adults with spondyloarthritis, CLBP, or no RMDs. To our knowledge, this has never been done before.

Our study also has limitations. First, the number of spondyloarthritis participants was small and the disease type was heterogeneous (i.e., including both the axial and peripheral forms) as a result of the low prevalence of spondyloarthritis (1.6%) in the Portuguese population [83]. Also, the study methodology and population recruitment led to a smaller group of adults without RMDs than the CLBP group. Nevertheless, this allowed us to include a control group and make direct comparisons of HRQoL between the participants without RMDs and those with spondyloarthritis/CLBP without extrapolating the necessary data from other studies. Second, we used PhGA as a surrogate marker of disease activity instead of a disease-specific validated score, like BASDAI or ASDAS. Although this is not ideal, previous research has demonstrated that this measure is a simple and reliable instrument to evaluate disease activity in an outpatient setting, using a cut-off of ≤20 mm to define inactive disease [84]. Third, the cross-sectional design limits the prognostic value of our analyses and does not allow us to draw conclusions about causal relationships. Only a future longitudinal study that follows up with these patients will allow us to draw more robust conclusions.

Conclusions

In summary, we have shown that spondyloarthritis and CLBP patients experience significantly impaired HRQoL compared with a population without RMDs. However, we found no differences between spondyloarthritis and CLBP in the physical, mental, and social aspects of HRQoL. Our data also suggest that disease activity, exercise, and the presence of chronic noncommunicable diseases are important determinants of HRQoL in spondyloarthritis patients. Considering that one of the primary goals of treating spondyloarthritis is to maximize long-term HRQoL, we should pay careful attention to controlling disease activity, identifying and treating chronic noncommunicable diseases, and promoting regular physical exercise from disease onset. Our study further highlights several important interventions that can target modifiable factors associated with HRQoL in CLBP patients: identifying and treating chronic noncommunicable diseases, promoting weight reduction and regular physical exercise, and assessing and controlling low back pain with pharmacological and non-pharmacological interventions.

These results are valuable for rheumatologists, as they enable a better understanding of the burden associated with CLBP and spondyloarthritis, as well as for policymakers and national healthcare systems, as they can inform adjustments to future health plans.

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Table 1 Sociodemographic characteristics of participants with spondyloarthritis, those with chronic low back pain, and those without rheumatic or musculoskeletal disorders

	Spondyloarthritis n=92	**CLBP n=1376**	**noRMD n=679**	**p-value (SpA/noRMD)**	**p-value (CLBP/noRMD)**	**p-value (SpA/CLBP)**
Female	59 (64.13%)	965 (70.13%)	366 (53.90%)	0.074[a]	**<<0.001**[a]	0.241[a]
Age (mean ± SD)	48.4 ± 13.7	58.8 ± 14.6	45.9 ± 15.6	0.145[b]	**<<0.001**[b]	**<<0.001**[b]
Age group				0.546[c]	**<<0.001**[c]	**<<0.001**[c]
18–35 years	19 (20.65%)	88 (6.4%)	187 (27.54%)			
36–55 years	47 (51.09%)	446 (32.41%)	311 (45.80%)			
56–75 years	23 (25.00%)	654 (47.53%)	159 (23.42%)			
≥76 years	3 (3.26%)	188 (13.66%)	22 (3.24%)			
Education level				0.709[c]	**<<0.001**[c]	**<<0.001**[c]
0–4 years	32 (34.78%)	811 (59.24%)	207 (30.53%)			
5–9 years	22 (23.91%)	275 (11.69%)	138 (20.35%)			
10–12 years	20 (21.74%)	160 (20.09%)	179 (26.40%)			
>12 years	18 (19.57%)	123 (8.98%)	154 (22.71%)			
NUTS II region				0.075[c]	**<<0.001**[c]	0.085[c]
Norte	21 (22.83%)	425 (30.89%)	196 (28.87%)			
Centro	27 (29.35%)	349 (25.36%)	122 (17.97%)			
Lisboa	12 (13.04%)	232 (16.86%)	122 (17.97%)			
Alentejo	7 (7.60%)	92 (6.69%)	39 (5.74%)			
Algarve	6 (6.52%)	25 (1.82%)	27 (3.98%)			
Azores	11 (11.96%)	140 (10.17%)	74 (10.90%)			
Madeira	8 (8.70%)	113 (8.21%)	99 (14.58%)			
Marital status				**0.043**[a]	**0.001**[a]	0.500[a]
Married	63 (68.48%)	890 (64.68%)	388 (57.31%)			
Other	29 (31.52%)	486 (35.32%)	289 (42.69%)			
Employment status				0.406[c]	**<<0.001**[c]	**<<0.001**[c]
Full-time worker	48 (52.75%)	400 (29.52%)	352 (52.93%)			
Unemployed	14 (15.38%)	132 (9.74%)	93 (13.98%)			
Retired	23 (25.27%)	649 (47.90%)	142 (21.35%)			
Other	6 (6.59%)	174 (12.84%)	78 (11.73%)			

[a]Fisher's exact test; [b]t-test; [c]Chi-square test

SD, Standard deviation; SpA, Spondyloarthritis; CLBP, Chronic low back pain; noRMD, Without rheumatic or musculoskeletal disorders; NUTS II, Nomenclature of Territorial Units for Statistics II.

Table 2 Anthropometric data and lifestyle and health characteristics among participants with spondyloarthritis, those with chronic low back pain, and those without rheumatic or musculoskeletal disorders

	Spondyloarthritis n=92	CLBP n=1376	noRMD n=679	p-value (SpA/noRMD)	p-value (CLBP/noRMD)	p-value (SpA/CLBP)
BMI (kg/m^2)				0.585[a]	**<<0.001**[a]	**0.003**[a]
Normal	41 (46.07%)	372 (29.11%)	315 (47.51%)			
Overweight	32 (35.96%)	527 (41.24%)	255 (38.46%)			
Obese	16 (17.98%)	379 (29.66%)	93 (14.03%)			
Daily coffee intake (cups)				0.141[a]	**<<0.001**[a]	**<<0.001**[a]
None	23 (25%)	512 (37.21%)	179 (26.36%)			
1–3	53 (57.61%)	785 (57.05%)	429 (63.18%)			
>3	16 (17.39%)	79 (5.74%)	71 (10.46%)			
Alcohol intake				0.194[a]	**<<0.001**[a]	0.959[a]
Daily	20 (21.74%)	285 (20.73%)	132 (19.44%)			
Occasionally	30 (32.61%)	426 (30.98%)	288 (42.41%)			
Never	42 (45.65%)	664 (48.29%)	259 (38.14%)			
Smoking habits				0.468[a]	**<<0.001**[a]	0.339[a]
Daily	14 (15.22%)	160 (11.63%)	140 (20.62%)			
Occasionally	2 (2.17%)	20 (1.45%)	16 (2.36%)			
Non-smoker	76 (82.61%)	1196 (86.92%)	523 (77.03%)			
Regular physical exercise				0.165[b]	**<<0.001**[b]	0.812[b]
Yes	27 (29.35%)	388 (28.20%)	253 (37.32%)			
No	65 (70.65%)	988 (71.80%)	425 (62.68%)			
Chronic noncommunicable diseases, n (self-reported)				**<<0.001**[b]	**<<0.001**[b]	**0.048**[b]
0–2	51 (55.43%)	617 (44.84%)	517 (76.37%)			
≥3	41(44.57%)	759 (55.16%)	160 (23.63%)			
Chronic noncommunicable diseases (self-reported)						
High blood pressure	20 (21.74%)	610 (44.65%)	158 (23.51%)	0.793[b]	**<<0.001**[b]	**<<0.001**[b]
Diabetes	4 (4.35%)	211 (15.45%)	63 (9.36%)	0.165[b]	**<<0.001**[b]	**0.002**[b]
High cholesterol	31 (34.07%)	615 (45.52%)	181 (27.05%)	0.171[b]	**<<0.001**[b]	**0.038**[b]
Pulmonary disease	11 (11.96%)	116 (8.49%)	41 (6.07%)	**0.045**[b]	0.063[b]	0.251[b]
Cardiac disease	11 (12.09%)	267 (19.62%)	56 (8.33%)	0.237[b]	**<<0.001**[b]	0.097[b]
Gastrointestinal	23 (25.56%)	407 (29.86%)	78 (11.61%)	**0.001**[b]	**<<0.001**[b]	0.474[b]
Neurological	1 (1.09%)	64 (4.69%)	22 (3.27%)	0.344[b]	0.159[b]	0.121[b]
Allergy	23 (25.00%)	364 (26.67%)	145 (21.61%)	0.502[b]	**0.014**[b]	0.808[b]
Mental	14 (15.38%)	332 (19.62%)	71 (10.52%)	0.159[b]	**<<0.001**[b]	0.056[b]
Cancer	3 (3.26%)	67 (4.91%)	36 (5.33%)	0.611[b]	0.669[b]	0.619[b]
Thyroid	14 (15.22%)	193 (14.26%)	51 (7.55%)	**0.025**[b]	**<<0.001**[b]	0.759[b]
Hypogonadism	1 (1.11%)	13 (0.97%)	7 (1.04%)	0.953[b]	0.878[b]	0.599[b]
Hyperuricemia	5 (5.43%)	137 (10.18%)	24 (3.60%)	0.382[b]	**<<0.001**[b]	0.203[b]
Renal	11 (12.09%)	167 (12.31%)	38 (5.66%)	**0.036**[b]	**<<0.001**[b]	0.951[b]

[a] Chi-square test; [b] Fisher's exact test

SpA, Spondyloarthritis; CLBP, Chronic low back pain; noRMD, Without rheumatic or musculoskeletal disorders; BMI

Table 3 Comparison of health-related quality of life by diagnosis (spondyloarthritis, chronic low back pain, or no rheumatic/musculoskeletal disorders)

	SpA n=92	CLBP n=1376	noRMD n=679	Crude OR SpA/noRMD [95% CI]	Crude p-value SpA/noRMD	Adjusted OR SpA/noRMD[a] [95% CI]	Adjusted p-value SpA/noRMD[a]	Crude OR CLBP/noRMD [95% CI]	Crude p-value CLBP/noRMD	Adjusted OR CLBP/noRMD[b] [95% CI]	Adjusted p-value CLBP/noRMD[b]	Crude OR SpA/CLBP [95% CI]	Crude p-value SpA/CLBP	Adjusted OR SpA/CLBP[c] [95% CI]	Adjusted p-value SpA/CLBP[c]
EQ5D															
Mobility				4.34 [2.59; 7.18]	**<0.001**	4.54 [2.50; 8.21]	**<0.001**	5.86 [4.47; 7.79]	**<0.001**	3.11 [2.28; 4.31]	**<0.001**	0.74 [0.47; 1.16]	0.196	1.37 [0.81; 2.28]	0.229
No problems, n (%)	63 (68.5)	849 (61.7)	613 (90.4)												
Some problems/ extreme problems, n (%)	29 (31.5)	527 (38.3)	65 (9.6)												
Self-care				4.23 [1.83; 9.23]	**<0.001**	4.86 [1.85; 1.26]	**0.001**	6.54 [4.16; 10.90]	**<0.001**	3.21 [1.90; 5.78]	**<0.001**	0.65 [0.31; 1.21]	0.204	1.37 [0.63; 2.76]	0.397
No problems, n (%)	82 (89.1)	1156 (84.1)	659 (97.2)												
Some problems/ Extreme problems, n (%)	10 (10.8)	218 (15.9)	19 (2.8)												
Usual activities				4.42 [2.64; 7.34]	**<0.001**	4.65 [2.56; 8.44]	**<0.001**	4.62 [3.51; 6.17]	**<0.001**	2.50 [1.83; 3.47]	**<0.001**	0.96 [0.60; 1.49]	0.849	1.59 [0.94; 2.64]	0.075
No problems, n (%)	63 (68.5)	927 (67.5)	615 (90.6)												
Some problems/ extreme problems, n (%)	29 (31.5)	446 (32.5)	64 (9.4)												
Pain/discomfort				5.15 [3.28; 8.20]	**<0.001**	4.73 [2.94; 7.70]	**<0.001**	4.80 [3.91; 5.92]	**<0.001**	3.46 [2.75; 4.37]	**<0.001**	1.07 [0.70; 1.67]	0.748	1.35 [0.85; 2.19]	0.213
No pain or discomfort, n (%)	35 (38.0)	546 (39.7)	516 (76.0)												
Moderate/extreme pain or discomfort, n (%)	57 (62.0)	828 (60.3)	163 (24.0)												
Anxiety/depression				1.961 [1.18; 3.17]	**0.007**	1.50 [0.87; 2.49]	0.135	2.02 [1.61; 2.54]	**<0.001**	1.58 [1.21; 2.07]	**<0.001**	0.97 [0.60; 1.53]	0.908	1.14 [0.68; 1.88]	0.604
Not anxious or depressed, n (%)	65 (70.7)	958 (70.1)	557 (82.5)												
Moderately/extremely anxious or depressed, n (%)	27 (29.4)	409 (29.9)	118 (17.5)												
				Crude ß SpA/ noRMD [95% CI]	**Crude p-value SpA/noRMD**	**Adjusted ß SpA/noRMD[a] [95% CI]**	**Adjusted p-value SpA/noRMD[a]**	**Crude ß CLBP/noRMD [95% CI]**	**Crude p-value CLBP/noRMD**	**Adjusted ß CLBP/noRMD[b] [95% CI]**	**Adjusted p-value CLBP/noRMD[b]**	**Crude ß SpA vs. CLBP**	**Crude p-value SpA/CLBP [95% CI]**	**Adjusted ß SpA/CLBP[c]**	**Adjusted p-value SpA/CLBP[c]**
EQ-5D score (mean ± SD)	0.69 ± 0.25	0.66 ± 0.27	0.86 ± 0.21	−0.17 [−0.21; −0.12]	**<0.001**	−0.14 [−0.19; −0.10]	**<0.001**	−0.20 [−0.22; −0.174]	**<0.001**	−0.12 [−0.14; −0.09]	**<0.001**	0.03 [−0.03; 0.09]	0.300	−0.03 [−0.08; 0.03]	0.33
EQ-5D VAS (mean ± SD)	65.28 ± 18.1	60.92 ± 19.86	75.69 ± 17.64	−10.41 [−14.34; 6.49]	**<0.001**	−7.49 [−11.20; −3.78]	**<0.001**	−14.77 [−16.57; −12.97]	**<0.001**	−9.07 [−10.96; −7.18]	**<0.001**	4.36 [0.11; 8.60]	**0.040**	0.03 [−4.06; 4.12]	0.989

EQ-5D, EuroQoL 5 dimensions; EQ-5D-VAS, EQ5D Visual Analogue Scale; SpA, Spondyloarthrits; CLBP, Chronic low back pain; noRMD, Without rheumatic or musculoskeletal diseases; SD, Standard deviation; CI, Confidence interval; OR, Odds ratio; [a]OR adjusted for: gender, age group, NUTS II region, marital status, number of noncommunicable diseases; [b]OR adjusted for: gender, age group, NUTS II region, education level, employment status, marital status, body mass index category, regular physical exercise, number of noncommunicable diseases; [c]OR adjusted for: gender, age group, NUTS II region, education level, employment status, body mass index category, number of noncommunicable diseases.

Table 4 Factors associated with health-related quality of life (EQ5D), stratified by diagnostic category (multivariable model)

	Chronic low back pain n = 1376			Spondyloarthritis n = 92		
	β	95% CI	p-value	β	95% CI	p-value
Age						
18–35 years	1					
≥76 years	−0.09	[−0.17; −0.01]	**0.022**	-	-	-
NUTS II region				-	-	-
Lisbon	1					
North	0.03	[−0.01; 0.07]	0.158			
Center	0.03	[−0.01; 0.07]	0.132			
Alentejo	0.08	[0.01; 0.14]	**0.020**			
Algarve	0.17	[0.05; 0.28]	**0.004**			
Azores	0.01	[−0.04; 0.06]	0.667			
Madeira	0.03	[−0.03; 0.08]	0.350			
Marital status						
Married	1					
Non-married	−0.03	[−0.06; −0.005]	**0.024**	-	-	-
Employment status				-	-	-
Full-time work	1					
Retired	−0.07	[−0.12; −0.03]	**<0.001**			
Other	−0.06	[−0.11; −0.02]	**0.007**			
Weight						
Normal	1					
Obese (BMI ≥ 30 kg/m^2)	−0.04	[−0.08; −0.01]	**0.022**	-	-	-
Alcohol intake						
Never	1					
Daily	0.07	[0.03; 0.10]	**<0.001**	-	-	-
Regular physical exercise						
No	1					
Yes	0.08	[0.05; 0.11]	**<0.001**	0.18	[0.10; 0.30]	**<0.001**
Number of comorbidities						
0–2	1					
≥3	−0.11	[−0.14; −0.08]	**<0.001**	−0.18	[−0.24; −0.03]	**<0.001**
Disease activity (BASDAI)						
Inactive	1					
Active	-	-	**-**	−0.13	[−0.29; −0.05]	**0.036**
Low back intensity (0–10)	−0.02	[−0.03; −0.02]	**<0.001**	-	-	-
		R^2=0.214			R^2=0.329	

EQ5D, European Quality of Life Questionnaire Five Dimensions; NUTS II, Nomenclature of Territorial Units for Statistics II; BMI, Body mass index; β, Parameter estimates; CI, Confidence interval; BASDAI, Bath Ankylosing Spondylitis