

### In a community-based setting spondyloarthritis patients report higher levels of physical disability than chronic low back pain patients - results from EpiReuma.pt

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Submitted: 12/03/2023

Accepted: 08/05/2023

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as an 'Accepted Article'

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#### Abstract

Objectives: Chronic low back pain (CLBP) is a common health problem and in most patients it is not possible to identify a specific cause (non-specific CLBP). Spondyloarthritis is a musculoskeletal disorder characterized by (often inflammatory) back pain and spinal stiffness. The impact of CLBP and spondyloarthritis on patients' physical function may be different. This study aims to compare physical disability in patients with spondyloarthritis and CLBP, in a population-based setting. Furthermore, we aim to identify modifiable risk factors for physical disability among these two populations.

Methods: Data from EpiReumaPt, a national health cohort with 10 661 individuals, conducted from September 2011 to December 2013, was used. Physical function was accessed by the Health Assessment Questionnaire Disability Index (HAQ-DI) and by the physical function dimension of the 36-Item Short Form Survey (SF-36). Univariable and multivariable linear regression analyses were used to assess the differences between groups. Factors associated with physical disability were explored for both diseases.

Results: We evaluated 92 patients with spondyloarthritis, 1376 patients with CLBP and 679 subjects without rheumatic and musculoskeletal diseases (RMDs). Spondyloarthritis and CLBP patients reported significantly higher levels of disability in HAQ-DI ( $\beta$ =0.33; p<0.001 and  $\beta$ =0.20; p<0.001, respectively) than subjects without RMDs. In comparison to CLBP patients, spondyloarthritis patients reported higher disability ( $\beta$ =0.14; p=0.03).

The physical domains of SF-36, bodily pain and general health, where more affected in spondyloarthritis patients than in CLBP patients ( $\beta$ =-6.61; p=0.02 and  $\beta$ =-5.94; p=0.001, respectively).



Spondyloarthritis and CLBP patients had a worse physical summary score (PCS) than mental summary score (MCS), and only PCS was significantly worse in comparison to subjects without RMDs. Factors associated with physical disability in CLBP were low back pain intensity, older age, obesity, multimorbidity, and retirement. Similarly, in spondyloarthritis physical disability was associated with retirement and multimorbidity. Factors associated with lower disability were alcohol consumption and male gender in CLBP, and regular physical exercise was associated with lower disability in both disorders.

Conclusions: In this nationwide cohort, spondyloarthritis and CLBP patients reported significant physical disability. Regular physical exercise was associated with lower disability in both diseases.

Keywords: Disability evaluation; Spondylarthritis; Quality of life.

Key messages:

- Spondyloarthritis and chronic low back pain patients have significant physical disability.
- Spondyloarthritis and chronic low back pain patients who engage in regular physical exercise may experience lower disability.
- Lifestyle interventions and improved management of comorbidities may enhance physical function in patients with spondyloarthritis and chronic low back pain.

#### Introduction

Rheumatic and musculoskeletal diseases (RMDs) are associated with significant disease burden, as they are an important cause of disability worldwide<sup>1</sup> and are associated with a negative impact on quality of life (QoL)<sup>2</sup>.

Within RMDs, spondyloarthritis and chronic low back pain (CLBP) are both diseases in which the impact on physical function and QoL is well recognized, affecting several domains of a patients' life, including physical, mental and social aspects of daily living<sup>3–5</sup>. Chronic low back pain (CLBP) is a common health problem, characterized by mechanical back pain, and in most patients is not possible to identify a specific cause (non-specific CLBP)<sup>6</sup>. Spondyloarthritis is a chronic musculoskeletal disease characterized by (often inflammatory) back pain and spinal stiffness, but peripheral joint/enthesis involvement, and extra-articular manifestations may occur during the disease course. Onset of this condition usually occurs in young adulthood, with a profound and long-lasting impact throughout an individuals' life<sup>7</sup>. Although being two chronic musculoskeletal diseases, with back pain as main symptom, physical disability and its determinants in these two diseases may be different. Due to its inflammatory nature with potential



structural damage and early age of onset, we hypothesize that spondyloarthritis patients experience higher physical disability than CLBP patients.

Our previous work compared QoL in patients with spondyloarthritis and CLBP, using EQ-5D, and we found no differences in the EQ-5D index score, EQ-5D visual analogic scale or in the five QoL domains, between these two disorders<sup>8</sup>. Salaffi et al<sup>9</sup> evaluated QoL in different rheumatic disorders and found that patients with inflammatory rheumatic diseases (including spondyloarthritis) had poorer self-reported health in all domains of QoL. Specifically, in this study patients with chronic non-specific low back pain showed better QoL than axial and peripheral spondyloarthritis patients, evaluated by EQ-5D and by SF-36 (physical and mental components).

Physical function, i.e. disability, is one of the most important outcomes in RMDs, and the negative impact of spondyloarthritis and CLBP on physical function is well-known<sup>10–12</sup>. Yet, the comparison of disability between different rheumatic diseases is scarce<sup>13</sup>, and it has never been done between these two disorders. Therefore, it is still not clear if the burden of disease regarding physical disability is different in CLBP and spondyloarthritis.

Measuring disease burden, namely physical disability, is of utmost importance for setting health research priorities, improving healthcare delivery, and planning for future needs. Also, data on the burden of disease are an essential source for economic models.

In this study, we aim to determine and compare physical disability in patients with spondyloarthritis and CLBP, in a population-based setting. Furthermore, we aim to identify modifiable risk factors of physical disability, such as lifestyle, among these two populations.

A comprehensive understanding of physical disability and its associated factors in these two disorders may help guiding treatment decisions for the individual patient, and the development of targeted and group specific approaches to promote function improvement and QoL.

#### Methods

#### Data source ant study population

We collect data from the EpiReumaPt, a national and cross-sectional study, conducted in Portugal (mainland, Azores and Madeira) from September 2011 to December 2013. EpiReumaPt methodology, whose main goal was to estimate the prevalence of 12 RMDs in the Portuguese adult population, has been extensively described elsewhere<sup>14,15</sup>. A sample of 10,661 Portuguese adults representative of the Portuguese population was selected by a process of multistage random sampling and stratified by administrative territorial units (NUTS II). Study design involved a three-stage approach (figure 1): 1) firstly a face-to-face interview conducted by a team of trained interviewers through door-to-door visits; 2) secondly a clinical evaluation with physical examination performed by rheumatologists. This evaluation

was conducted in all participants previously identified in the first interview as potentially having a RMD and in 20% of asymptomatic individuals; 3) thirdly, a team of three experienced rheumatologists reviewed all clinical data and established the final diagnosis, according to predefined criteria for the different RMDs.

#### **Case definition**

Spondyloarthritis diagnosis was established after the clinical appointment of the second phase, by expert opinion (rheumatologist) combined with the fulfillment of validated classification criteria<sup>16,17</sup>. Subtypes like 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 in most of the time for the last 90 days. RMD absence in the participants was also established by expert opinion after clinical history and physical examination.

#### Variables

#### Outcomes

Physical function was assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI), Portuguese version. The HAQ-DI is a generic questionnaire and is one of the most widely used selfassessment instruments for measuring functional disability. It has been commonly used in a variety of rheumatic diseases<sup>18</sup>. This instrument contains questions on functional limitations addressing eight functional categories: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities. For each of these domains, patients answer 2-3 specific questions in performing specific activities, in the previous week. For each question there are 4 possible responses: without any difficulty (score=0); with some difficulty (score=1); with much difficulty (score=2); and unable to do (score=3). A HAQ-DI of 0 indicates no functional disability, while a HAQ-DI of 3 indicates severe functional disability<sup>19</sup>.

QoL data was collected, using 36-Item Short Form Survey (SF-36), Portuguese version<sup>20</sup>. SF-36 may be applied to any health condition, including rheumatic diseases<sup>21</sup>. It holds eight domains: physical functioning, physical role functioning, bodily pain, general health perception, vitality, social role functioning, emotional role functioning, and mental health. These domains can be categorized into two summary scores: Physical Component Score (PCS) which includes physical functioning, physical role functioning, bodily pain, and general health perception; and the Mental Component Score (MCS) which includes vitality, emotional role functioning, social role functioning, and mental health. The scores are transformed into a scale ranging from 0 (reflecting poor QoL) to 100 (reflecting excellent QoL). The generic and cross-cultural nature of SF-36 survey allows comparisons between different diseases and populations, and between studies.

#### **Covariables of interest**



For the three groups of participants, data regarding sociodemographic characteristics were collected: age (age groups considered: 18-35 years, 36-55 years, 56-75 years,  $\geq$ 76 years), gender (male, female), ethnicity (white, other), marital status (married, other), education level (0–4 years, 5–9 years, 10–12 years, >12 years). Lifestyle habits were inquired: alcohol intake (daily, occasional, never), daily coffee intake (none, 1 to 3 cups, more than 3 cups), smoking habits (smoker, non-smoker), and regular physical exercise (defined as physical activity >1 hour/week; yes, no). Employment status was also registered (full time active worker, part-time active worker, domestic worker, unemployed, retired, student, temporary work disability, other); for data analyses purpose, we combined employment status into four categories: active worker (full and part-time), unemployed, retired, other (domestic, student, temporary work disability).

Anthropometric data were collected (weight [kg], height [cm], and body mass index [BMI; kg/m<sup>2</sup>]): underweight – BMI<18.5; normal weight – 18.5 $\leq$ BMI<25; overweight - 25 $\leq$ BMI<30; obese – BMI  $\geq$  30). Data on self-reported non-communicable chronic diseases was collected (high cholesterol, high blood pressure, allergies, gastrointestinal disease, mental disorders, cardiac disease, diabetes, thyroid/parathyroid disease, renal disease, pulmonary disease, hyperuricemia, cancer, neurologic disease, and hypogonadism) and the number of noncommunicable diseases considered (0-2, 3 or more). Multimorbidity was defined as the presence of 3 or more noncommunicable diseases. For the spondyloarthritis group, we have also collected data on disease activity, assessed by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and function assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI).

#### Statistical methods

Descriptive data for each categorical variable was 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 with subjects without RMDs. CLBP patients were also compared to subjects without RMDs. First, comparisons were made using the chi-square test and Fisher's exact test for categorical variables and the t-test for continuous variables. To assess the differences between spondyloarthritis and CLBP patients, and between spondyloarthritis and subjects without RMDs, regarding physical disability (HAQ-DI), univariable and multivariable linear regression were used. In order to adjust the differences between the groups, and according to the results of univariable analyses, the following confounders were included: for comparison between spondyloarthritis and subjects without RMDs: gender, age-group, NUTS II, education level, marital status and noncommunicable chronic diseases; for comparison between CLBP and subjects without RMDs: gender, age-group, NUTS II, marital status, BMI, exercise, number of noncommunicable chronic diseases;



for comparison between spondyloarthritis and CLBP: gender, age-group, NUTS II, education level, employment status, BMI and number of noncommunicable chronic diseases.

To assess the differences between spondyloarthritis and CLBP patients, and between spondyloarthritis and subjects without RMDs, regarding QoL (SF-36), the same methodology was followed and independent variables tested were the same.

To access factors associated with disability, evaluated by HAQ-DI, 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. Individual variables tested were: gender, age group, education level, NUTS II, marital status, employment status, BMI, daily coffee intake, alcohol intake, smoking habits, regular physical exercise, number of noncommunicable diseases, and disease activity (for spondyloarthritis patients) or low back pain intensity (for CLBP patients). After selecting the variables to include in the multivariable model, through a backward conditional method, we sequentially excluded non-statistically significant variables and compared the models through ANOVA. Significance level was set at 0.05. All the analyses were performed using STATA IC V 16.1.

#### **Ethical Framework**

EpiReumaPt was performed according to the principles established by the Declaration of Helsinki<sup>22</sup> and revised in 2013 in Fortaleza. The study was reviewed and approved by the National Committee for Data Protection and by the NOVA Medical School Ethics Committee. Participants signed an informed consent prior to participation<sup>14</sup>.

#### Results

In the EpiReumaPT a total of 10,661 participants were interviewed. The analyses included 92 subjects with spondyloarthritis, 1376 with CLBP, and 679 without RMDs. In the spondyloarthritis group, 32 participants had ankylosing spondylitis, 20 had psoriatic arthritis and 40 had other forms of spondyloarthritis.

# Sociodemographic, anthropometric, lifestyle and health characteristics comparison in spondyloarthritis, CLBP, and subjects without RMDs

The mean age was  $48.4 \pm 13.7$  years for spondyloarthritis subjects,  $58.8 \pm 14.6$  years for CLBP and  $45.9 \pm 15.6$  years for subjects without RMDs. The 3 groups had a female predominance (64.1%, 70.3% and 53.9%, respectively). Sociodemographic and anthropometric data, lifestyle, and health characteristics of the three groups are summarized in Table I. CLBP subjects were older, less educated, and had a higher



proportion of retirement in comparison to spondyloarthritis patients. More patients with CLBP had overweight or were obese than spondyloarthritis patients, and had a lower coffee intake, but there were no differences regarding alcohol consumption, smoking habits or frequency of physical exercise between these two groups. CLPB subjects also had a higher number of self-reported noncommunicable diseases in comparison to spondyloarthritis subjects, namely high blood pressure, diabetes, and high cholesterol level. The spondyloarthritis group had a mean BASDAI score of 5.87 (3.48), with 5.73 (3.40) for ankylosing spondylitis, 4.63 (3.40) for psoriatic arthritis, and 6.31 (3.57) for other spondyloarthritis. Mean BASFI score was for spondyloarthritis group 4.76 (3.57) with 5.70 (4.46) for ankylosing spondylitis, 4.74 (3.58) for psoriatic arthritis, and 5.40 (4.47) for other spondyloarthritis.

#### Comparison of HRQoL summary scores in spondyloarthritis, CLBP and subjects without RMDs

The scores of the eight domains can be combined in two higher-order summary scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS), which were norm-based T-scores with a mean of 50 (and a standard deviation of 10). We have calculated PCS and MCS for the 3 groups and interestingly, for spondyloarthritis and CLBP patients, PCS scores ( $41.41\pm12.27$  and  $39.46\pm12.93$ , respectively) were lower than the MCS scores ( $49.05 \pm 12.34$  and  $50.45 \pm 11.88$ , respectively), therefore, physical dimensions were more affected than the mental dimensions in these two diseases (Table II). On the contrary, in subjects without RMDs, these scores had similar values (PCS  $51.97\pm10.72$ ; MCS  $51.55\pm10.43$ ), with physical and mental dimensions equally affected (Table II).

Spondyloarthritis and CLBP, after adjustment for confounders, had significantly worse PCS scores than subjects without RMDs ( $\beta$ =-8.51, p-value <0.001;  $\beta$ =-6.90, p-value <0.001) but there were no significant differences in PCS between spondyloarthritis and CLBP ( $\beta$ =-2.26, p-value=0.070). Regarding MCS, and after adjustment for confounders, there were no significant differences between spondyloarthritis or CLBP and subjects without RMDs, neither between spondyloarthritis and CLBP ( $\beta$ =-1.56, p-value=0.190;  $\beta$ =-0.370, p-value=0.532;  $\beta$ =-1.02, p-value=0.430, respectively). Thus, overall, physical health was worse than mental health in both diseases and only physical health was different in comparison to subjects without RMDs.

#### Comparison of physical disability in spondyloarthritis, CLBP and subjects without RMDs

There was a difference of 0.38 on HAQ-DI between spondyloarthritis and subjects without RMDs, with spondyloarthritis subjects reporting higher mean disability (higher score=higher disability), and this result was significant after adjustment for possible confounders ( $\beta$ =0.33, 95% CI [0.23; 0.44]; p-value <0.001). A similar result was found when we compared CLBP patients and subjects without RMDs, with a mean difference of 0.44 on HAQ-DI score, with significantly higher disability in CLBP patients ( $\beta$ =0.20, 95% CI [0.15; 0.25]; p-value <0.001). Comparison of physical disability between spondyloarthritis and CLBP



patients, showed a mean difference of 0.06 on HAQ-DI score, and after adjustment for possible confounders, showed a statistically significantly higher disability in spondyloarthritis patients ( $\beta$ =0.14, 95% CI [0.01; 0.26]; p-value=0.03) compared to CLBP patients (Table II).

Bodily pain and general-health (both physical dimensions of SF-36) were significantly worse in spondyloarthritis in comparison to CLBP patients, even after adjustment for possible confounders ( $\beta$ =-6.61, 95% CI -12.09; -1.12; p-value=0.02;  $\beta$ =-5.94, 95% CI -9.59; -2.30; p-value=0.001, respectively). Physical functioning item of SF-36 questionnaire was worse in CLBP patients than in spondyloarthritis patients ( $\beta$ =9.89, 95% CI 3.48; 16.30; p-value=0.003), but after adjustment for possible confounders, physical functioning was no longer significantly different ( $\beta$ =-0.51, 95% CI -5.98; 4.97; p-value=0.86) (Table II). PCS was significantly worse in patients with spondyloarthritis and with CLBP, in comparison to subjects without RMDs, and there were no differences in MCS and PCS between spondyloarthritis and CLBP, after adjustment for possible confounders ( $\beta$ =-2.26, 95% CI -4.69; 0.16; p-value=0.07) (Table II).

#### Factors associated to physical disability among spondyloarthritis and CLBP patients

After univariable linear regression analysis (Table III), we performed a multivariable model to access determinants of physical disability, in patients with CLBP and spondyloarthritis.

Table IV shows that in CLBP patients, there was a positive association between having 76 or more years ( $\beta$  =0.398; 95% CI [0.221; 0.575]; p<0.001), being retired ( $\beta$  =0.260; 95% CI [0.159; 0.361]; p<0.001), being obese ( $\beta$  =0.179; 95% CI[0.097; 0.262]; p<0.001), having multimorbidity ( $\beta$  =0.196; 95% CI [0.126; 0.267]; p<0.001), and low back pain intensity ( $\beta$  =0.042; 95% CI [0.028; 0.056]; p<0.001), with physical disability. A negative association with physical disability was found for being a man in relation to woman ( $\beta$  =-0.219; 95% CI [-0.293; -0.145]; p<0.001), daily alcohol consumption ( $\beta$  =-0.108; 95% CI [-0.197; -0.020]; p=0.016), and practice of regular physical activity ( $\beta$  =-0.175; 95% CI [-0.244; -0.107]; p<0.001). Education level was no longer significant in the multivariable model.

In spondyloarthritis patients, there was a positive association between being retired ( $\beta$  =0.386;95% CI [0.087; 0.685]; p=0.012) and having multimorbidity ( $\beta$  =0.523; 95% CI [0.272; 0.774]; p<0.001), with physical disability. On the other hand, the practice of regular exercise ( $\beta$  =-0.389; 95% CI [-0.650; -0.128]; p=0.004) was negatively associated with physical disability. Education level and disease activity were no longer significant in the multivariable model.

It should be noted that a positive association means an association with a higher HAQ-DI score (worse physical function i.e. more disability) and a negative association means an association with a lower HAQ-DI score (better physical function i.e. less disability), due to the inverted nature of the HAQ-DI score, where higher values represent more disability.

#### Discussion

Our study shows that spondyloarthritis and CLBP patients report higher physical disability measured by two different instruments, HAQ-DI and SF-36, in comparison to a population without RMDs. Spondyloarthritis patients report higher physical disability and higher impact on some physical domains of SF-36 than CLBP patients. More characteristics associated with physical disability were identified in CLBP patients, such as older age and obesity, than in spondyloarthritis patients<sup>23,24</sup>; nevertheless spondyloarthritis patients still report higher levels of physical disability. While the exact reasons for the differences in physical disability between spondyloarthritis and CLBP patients are not fully understood, it may be related to the underlying inflammation and structural damage in spondyloarthritis<sup>25</sup>. However, further research is needed to fully elucidate the factors contributing to the differences in physical disability between these patient populations.

Physical function, was independently associated with QoL in CLBP<sup>12</sup> and in spondyloarthritis<sup>26–28</sup>, and building up from our previous findings using EQ-5D for QoL assessment<sup>8</sup>, in this study QoL was evaluated by a different instrument (SF-36), confirming that QoL is highly impaired in both disorders. Moreover, we also found no differences in QoL (PCS and MCS of SF-36) between spondyloarthritis and CLBP, comparable to our previous results<sup>8</sup>. Kreis et al<sup>29</sup>, using the Short-Form 12 survey (SF-12), compared 199 axial spondyloarthritis and 89 CLBP patients, and they also didn't find any differences in mental or physical summary scores of SF-12, between the two disorders. Bodily pain and general health (items of physical component of SF-36) were more impaired in spondyloarthritis. The differences in bodily pain scores may be explained by involvement of peripheral joints and entheses in spondyloarthritis. Additionally, differences in general health scores may be related to the early age of disease onset in spondyloarthritis, its inflammatory nature, and the possible occurrence of extra-articular manifestations. It is worth nothing that the "well-being paradox" may also explain why CLBP patients, despite being older and having more comorbidities, did not report a worse perception of general health compared to spondyloarthritis patients. Although aging can lead to cognitive and physical declines, research suggests that well-being may not necessarily decrease in older individuals when compared to younger individuals<sup>23</sup>.

Several factors have been associated with physical disability in CLBP. Our study showed that in CLBP patients a higher disability was associated with low back pain intensity, older age, obesity, multimorbidity, and retirement. A better outcome was associated with male gender, daily alcohol intake and regular physical exercise.

Pain intensity is a significant predictor of physical disability, as increased pain levels can limit individuals ability to perform daily activities<sup>30–33</sup>. In the WHO multinational Study on Global Aging and Adult Health (SAGE), pain intensity was independently associated with physical disability in older adults<sup>34</sup>. Older age has also been associated with a higher risk of physical disability in CLBP, as decreased mobility, strength, and flexibility can impact individuals' ability to perform activities of daily living<sup>33</sup>. Wettstein et al <sup>23</sup> specifically addressed the influence of age in CLBP physical disability, and they found that it increases with advancing age. Nevertheless others authors found no association of age with physical disability in



CLBP patients<sup>32</sup>. The population incidence of CLBP is directly associated with BMI<sup>35</sup>, and overweight/obesity are not only risk factors for CLBP<sup>36</sup> but also for physical disability<sup>24</sup>. In line with our study, Wertli et al<sup>37</sup>, analyzed the impact of obesity on physical disability and response to physical therapy treatment. They concluded that not only overweight and obesity were associated with higher levels of physical disability at baseline, but also that severe obese patients experience lower treatment responses. Besides obesity, multimorbidity (the coexistence of more than two long-term conditions) was also independently associated with higher physical disability. Multimorbidity has been previously shown to be associated with CLBP<sup>38</sup> and in a systematic review by Ryan et al<sup>39</sup> multimorbidity predicted future functional decline, with greater decline in patients with a higher numbers of morbid conditions. In the study by Øverås et al<sup>40</sup>, the presence of multimorbidity and musculoskeletal pain, in CLBP patients, was also associated with higher disability, but with no influence on the results of treatment interventions. Job demands, such as those that require heavy liftings or prolonged standing, have been associated with physical disability in CLBP, as individuals with these professions may be at increased risk of injury and may experience more severe pain<sup>41</sup>. While other studies have found no association between employment status and physical disability <sup>30,32</sup>, in our population retirement was associated physical disability, and although the underlying reasons for this remain unclear, it may reflect a consequence of the physical disability, that lead to an early retirement. Indeed, in a recent study by d'Errico et al<sup>42</sup>, chronic low back pain was associated with early-age retirement, independently of work factors.

Consistent with previous studies<sup>32,43</sup>, male gender was found to be associated with lower levels of physical disability compared to female gender. For example, Igwesi-Chidobe et al<sup>32</sup>, reported that female gender was primarily associated with performance-based disability rather than self-reported disability. However, a study by Doualla et al<sup>30</sup>, on a cohort of CLBP patients in Cameroon found no significant association between gender and disability. Our study confirms previous findings that daily alcohol intake is associated with lower disability in patients with CLBP<sup>30,44</sup> A one-year cohort study exploring factors related to disability found that not consuming alcohol was linked to greater disability<sup>44</sup>, contrary to some previous research<sup>43</sup>.

Our study demonstrated a significant association between regular physical exercise and lower disability, in contrast to previous studies where this relationship was not significant<sup>43</sup>. The difference in results may be attributed to the varying definitions of exercise used. For instance, Kahere et al.<sup>43</sup> considered frequent exercise as moderate to vigorous-intensity exercise lasting for at least 30 minutes, five times per week, while in our study, regular physical exercise was defined as engaging in physical activity for more than an hour per week.

This study identified several factors associated with physical disability in spondyloarthritis. Multimorbidity and retirement were found to be associated with higher disability, while regular physical exercise was associated with lower disability. These findings are consistent with previous research



showing that comorbidities adversely affect physical function<sup>45,46</sup> and that regular exercise can improve disease activity, pain, function and spinal mobility in spondyloarthritis patients<sup>47</sup>.

In spondyloarthritis, physical disability is determined independently by both the level of clinical disease activity and the degree of spinal mobility impairment<sup>3,26</sup>, even in early forms of disease<sup>27</sup>. However, in our study disease activity was no longer found to be associated with physical disability in the multivariable analysis. It is possible that disease activity was not well captured in our cohort, which included both axial and peripheral forms of disease.

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 bias selection. Second, we were able to compare physical function and QoL in an overall large sample of adults with spondyloarthritis, CLBP, and a population without RMDs, in a population-based setting. To our knowledge, this has never been done. Our study also has limitations. First, the small number of spondyloarthritis participants and the heterogeneity of this group (axial and peripheral forms of disease), resulted from the prevalence of 1.6% of spondyloarthritis in the Portuguese population<sup>48</sup>. Second, we used generic instruments, and not disease-specific instruments, to assess physical disability and QoL, which allowed us to compare different populations, but disease-specific instruments could probably capture more accurately the impact of the disease. 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.

In conclusion, spondyloarthritis and CLBP cause significant physical disability, and several factors have been associated with this outcome. This study highlights the impact of multimorbidity and regular physical exercise on physical disability and healthcare providers should consider these factors when developing treatment plans to optimize outcomes and minimize physical disability. Physical disability should be brought to focus, and interventions targeting risk factors and that maintain or improve patients' functional ability will likely have potential to decrease disease-related costs and improve QoL.



#### **Tables and Figures**

**Table I** – Comparison of sociodemographic, anthropometric, lifestyle, and health characteristics between spondyloarthritis, chronic low back pain and subjects without rheumatic and musculoskeletal diseases

	Spondyloarthritis n=92	CLBP n=1376	noRMD n=679	p-value (SpA/noRMD)	p-value (CLBP/noRMD)	p-value (SpA /CLBP
-emale gender	59 (64.13%)	965 (70.13%)	366 (53.90%)	0.074ª	<0.001°	0.241ª
Age years (mean ± sd)	48.4 ± 13.7	58.8 ± 14.6	45.9± 15.6	0.145°	<0.001°	<0.001°
Age group				0.546 <sup>b</sup>	<0.001 <sup>b</sup>	<0.001 <sup>b</sup>
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	5 (5.20%)	100 (15.00%)	22 (3.2470)	0.709 <sup>b</sup>	<0.001 <sup>b</sup>	<0.001 <sup>b</sup>
	-	011 (50 240/)		0.709	NU.001	<0.001
0-4 years	32 (34.78%)	811 (59.24%)	207 (30.53%)		VVJ	
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	-			0.075 <sup>b</sup>	<0.001 <sup>b</sup>	0.085 <sup>b</sup>
Norte	21 (22.83%)	425 (30.89%)	196 (28.87%)			
Centro	27 (29.35%)	349 (25.36%)	122 (17.97%)	$\sim$		
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 (10.9%)	<b>N Y</b>		
Madeira	8 (8.70%)	113 (8.21%)	99 (14.58%)	/ <b>P</b>		
Marital status	· · ·	. ,		0.043ª	0.001°	0.500ª
Married	63 (68.48%)	890 (64.68%)	388 (57.31%)			
Other	29 (31.52%)	486 (35.32%)	289 (42.69%)			
Employment status	25 (51.5270)	100 (00.0270)	205 (12:05/0)	0.406 <sup>b</sup>	<0.001 <sup>b</sup>	<0.001 <sup>b</sup>
Full time worker	48 (52.75%)	400 (29.52%)	352 (52.93%)	0.400	0.001	0.001
		132 (9.74%)				
Unemployed	14 (15.38%)		93 (13.98%)			
Retired	23 (25.27%)	649 (47.9%)	142 (21.35%)			
Other	6 (6.59%)	174 (12.84%)	78 (11.73%)	a sash		e eesh
BMI (kg/m²)	-			0.585 <sup>b</sup>	<<0.001 <sup>b</sup>	0.003 <sup>b</sup>
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%)			
Coffee intake				0.141 <sup>b</sup>	<0.001 <sup>b</sup>	<0.001 <sup>b</sup>
None	23 (25%)	512 (37.21%)	179 (26.36%)			
1 to 3	53 (57.61%)	785 (57.05%)	429 (63.18%)			
More than 3	16 (17.39%)	79 (5.74%)	71 (10.46%)			
Alcohol intake		. ,	, ,	0.194 <sup>b</sup>	<0.001 <sup>b</sup>	0.959 <sup>b</sup>
Daily	20 (21.74%)	285 (20.73%)	132 (19.44%)			
Occasional	30 (32.61%)	426 (30.98%)	288 (42.41%)			
Never	42 (45.65%)	664 (48.29%)	259 (38.14%)			
Smoking habits	42 (45.0570)	004 (40.2070)	233 (30.1470)	0.468 <sup>b</sup>	<0.001 <sup>b</sup>	0.339 <sup>♭</sup>
	14 (15 220/)	160 (11 620/)	140 (20 62%)	0.400	10.001	0.555
Daily	14 (15.22%)	160 (11.63%)	140 (20.62%)			
Occasional	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°	<0.001°	0.812ª
Yes	27 (29.35%)	388 (28.20%)	253 (37.32%)			
No	65 (70.65%)	988 (71.80%)	425 (62.68%)			
Chronic Noncommunicable				<0.001ª	<0.001ª	0.048ª
Diseases, n (self-reported)	_					
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 (22 51%)	0.793ª	<0.001°	<0.001ª
• .	. ,	610 (44.65%)	158 (23.51%)			
Diabetes	4 (4.35%)	211 (15.45%)	63 (9.36%)	0.165ª	<0.001°	0.002ª
High cholesterol level	31 (34.07%)	615 (45.52%)	181 (27.05%)	0.171ª	<0.001ª	0.038ª
Pulmonary disease	11 (11.96%)	116 (8.49%)	41 (6.07%)	0.045°	0.063ª	0.251ª
Cardiac Disease	11 (12.09%)	267 (19.62%)	56 (8.33%)	0.237ª	<0.001°	0.097ª
Gastrointestinal disease	23 (25.56%)	407 (29.86%)	78 (11.61%)	0.001 <sup>a</sup>	<0.001ª	0.474ª
Neurological disease	1 (1.09%)	64 (4.69%)	22 (3.27%)	0.344ª	0.159ª	0.121ª



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23 (25.00%)	364 (26.67%)				
	504 (20.07%)	145 (21.61%)	0.502ª	<b>0.014</b> <sup>a</sup>	0.808ª
14 (15.38%)	332 (19.62%)	71 (10.52%)	0.159ª	<0.001°	0.056ª
3 (3.26%)	67 (4.91%)	36 (5.33%)	0.611ª	0.669ª	0.619ª
14 (15.22%)	193 (14.26%)	51 (7.55%)	0.025ª	<0.001ª	0.759ª
1 (1.11%)	13 (0.97%)	7 (1.04%)	0.953ª	0.878ª	0.599ª
5 (5.43%)	137 (10.18%)	24 (3.60%)	0.382ª	<0.001ª	0.203ª
11 (12.09%)	167 (12.31%)	38 (5.66%)	0.036ª	<0.001ª	0.951ª
	3 (3.26%) 14 (15.22%) 1 (1.11%) 5 (5.43%)	3 (3.26%)       67 (4.91%)         14 (15.22%)       193 (14.26%)         1 (1.11%)       13 (0.97%)         5 (5.43%)       137 (10.18%)	3 (3.26%)       67 (4.91%)       36 (5.33%)         14 (15.22%)       193 (14.26%)       51 (7.55%)         1 (1.11%)       13 (0.97%)       7 (1.04%)         5 (5.43%)       137 (10.18%)       24 (3.60%)	3 (3.26%)       67 (4.91%)       36 (5.33%)       0.611°         14 (15.22%)       193 (14.26%)       51 (7.55%) <b>0.025°</b> 1 (1.11%)       13 (0.97%)       7 (1.04%)       0.953°         5 (5.43%)       137 (10.18%)       24 (3.60%)       0.382°	3 (3.26%)       67 (4.91%)       36 (5.33%)       0.611 <sup>a</sup> 0.669 <sup>a</sup> 14 (15.22%)       193 (14.26%)       51 (7.55%) <b>0.025<sup>a</sup></b> <0.001 <sup>a</sup> 1 (1.11%)       13 (0.97%)       7 (1.04%)       0.953 <sup>a</sup> 0.878 <sup>a</sup> 5 (5.43%)       137 (10.18%)       24 (3.60%)       0.382 <sup>a</sup> <0.001 <sup>a</sup>

<sup>a</sup> Fisher's exact test; <sup>b</sup> Chi-square test; <sup>c</sup> t-test; SpA- spondyloarthritis; CLBP- chronic low back pain; noRMD – rheumatic and musculoskeletal diseases; BMI-Body mass index; BMI\_cat - Body mass index category.

Bold indicates statistically significant results (significance level set at 0.05)

Acepted

**Table II -** Comparison of physical disability, evaluated by HAQ-DI and by SF-36, among subjects with spondyloarthritis, chronic low back pain and subjects without rheumatic and musculoskeletal diseases

	Spondylo Chronic Lov		onic Low General	Adjusted Analyses						
		Back Pain n=1376	population n=679	ß [95% CI] SpA/noRMDª	p-value SpA/noRMD <sup>a</sup>	ß [95% Cl] CLBP/noRMD⁵	p-value CLBP/noRMD <sup>♭</sup>	ß [95% Cl] SpA/CLBP፡	p-value SpA/CLBP <sup>c</sup>	
HAQ DI (mean ± sd)	0.56 ± 0.69	0.62 ± 0.66	0.18 ± 0.45	0.33 [0.23; 0.44]	<<0.001	0.20 [0.15; 0.25]	<<0.001	0.14 [0.01; 0.26]	0.03	
SF-36 score (mean ± sd)										
Physical functioning	70.97 ± 29.80	61.08 ± 30.37	84.53 ± 25.10	-9.73 [-14.98; -4.48]	<0.001	-8.98 [-11.52; -6.44]	<0.001	-0.51 [-5.98; 4.97]	0.86	
Role Physical	60.05 ± 46.00	58.02 ± 44.30	84.06 ± 32.60	-19.34 [-26.68; -11.99]	<0.001	-15.08 [-19.09; -11.06]	<0.001	-5.55 [-14.66; 3.56]	0.232	
Bodily Pain	52.13 ± 24.41	53.52 ± 27.05	79.13± 18.25	-22.72 [-28.1; -17.35]	<0.001	-17.95 [-20.53; -15.38]	<0.001	-6.61 [-12.09; -1.12]	0.02	
General Health	45.87 ± 18.91	46.84 ± 18.76	62.49 ± 18.25	-12.93 [-16.59; -9.27]	<0.001	-8.16 [-9.88; -6.44]	<0.001	-5.94 [-9.59; -2.30]	0.001	
Vitality	51.49±23.05	49.70±23.80	66.00±21.98	-10.2 [-15.83; -5.56]	<0.001	6.21 [-10.01; -2.41]	<0.001	-2.64 [-7.39; 2.19]	0.29	
Social functioning	77.58 ± 26.31	79.66 ± 25.7	88.48 ± 19.96	-8.28 [-12.73; -3.84]	<0.001	-9.22 [-11.44; -7.01]	<0.001	-3.95 [-9.29; 1.38]	0.15	
Role Emotional	70.65 ± 42.17	72.04 ± 41.33	86.25 ± 30.58	-12.6 [-19.3; -5.21]	<0.001	-6.70 [-8.96; -4.43]	0.001	-4.5 [-13.07; 4.08]	0.3	
Mental Health	60.20 ± 24.30	59.31 ± 24.60	72.66 ± 21.80	-8.76 [-13.34; -4.19]	<0.001	-4.32 [-6.67; -1.96]	<0.001	-2.74 [-7.71; 2.23]	0.28	
Physical health (PCS)	41.41±12.27	39.46±12.93	51.97±10.72	-8.51 [-10.73; -6.3]	<0.001	-6.90 [-8.02; -5.78]	<0.001	-2.26 [-4.69; 0.16]	0.07	
Mental health (MCS)	49.05 ± 12.34	50.45 ± 11.88	51.55 ± 10.43	-1.56 [-3.87; 0.76]	0.19	-0.37 [-1.53; 0.79]	0.532	-1.02 [-3.543; 1.5]	0.43	

SpA- Spondyloarthritis; CLBP- Chronic Low back pain; GP – General population; <sup>a</sup>OR adjusted for gender, age-group, NUTS II, marital status and number of noncommunicable Diseases; <sup>b</sup>OR adjusted for gender, age-group, NUTS II, marital status and number of noncommunicable Diseases; <sup>c</sup>OR adjusted for gender, age-group, administrative territorial units (NUTS II), education level, employment status, body mass index categories and number of noncommunicable Diseases.

Bold indicates statistically significant results (significance level set at 0.05)



## Table III - Factors associated with disability (HAQ-DI), stratified by diagnostic category (Univariable analysis)

	Chronic low back pain n = 1376				Spondyloarthritis n = 92				
	β	Std error	95% CI	p-value	β	Std	95% CI	p-	
	-				,	error		value	
Gender	_								
Female	1				1				
Male	-0.352	0.038	[-0.426; -0.278]	<0.001	-0.076	0.150	[-0.373; 0.222]	0.613	
Age									
18-35 years	1	0.074		0.464	1				
36-55 years	0.100	0.071	[-0.040; 0.240]	0.161 <b>&lt;0.001</b>	0.302	0.180	[-0.057; 0.660]	0.10	
56-75 years	0.373	0.069	[0.237; 0.509]		0.550	0.206	[0.141; 0.960]	0.00	
≥76 years	0.856	0.079	[0.703; 1.013]	<0.001	0.882	0.412	[0.063; 1.700]	0.03	
Education Level 0-4 years	1				1		$\mathbf{V}$		
5-9 years	-0.335	0.044	[-0.422; -0.248]	<0.001	-0.171	0.200	[-0.543; 0.201]	0.36	
10-12 years	-0.355	0.044	[-0.470; -0.254]	<0.001	-0.350	0.192	[-0.732; 0.033]	0.30	
> 12 years	-0.424	0.055	[-0.544; -0.303]	< 0.001	-0.330	0.132	[-0.811; -0.018]	0.04	
NUTS II	-0.424	0.001	[-0.344, -0.303]	<0.001	-0.415	0.107	[-0.011, -0.010]	0.04	
Lisboa	1				1				
Porto	-0.005	0.054	[-0.111; 0.101]	0.924	0.253	0.254	[-0.251; 0.757]	0.32	
Centro	0.027	0.056	[-0.082; 0.137]	0.624	0.308	0.243	[-0.175; 0.791]	0.20	
Alentejo	0.102	0.081	[-0.058; 0.261]	0.212	0.170	0.333	[-0.493; 0.832]	0.61	
Algarve	0.154	0.139	[-0.119; 0.427]	0.268	0.250	0.350	[-0.446; 0.946]	0.47	
Azores	0.0001	0.071	[-0.139; 0.139]	0.998	0.358	0.292	[-0.223; 0.934]	0.22	
Madeira	0.044	0.076	[-0.105; 0.193]	0.560	0.359	0.320	[-0.276; 0.995]	0.26	
Marital status							,		
Married	1				1				
Other	0.127	0.037	[0.054; 0.200]	<0.001	0.033	0.155	[-0.275; 0.340]	0.83	
Employment status				<b>P</b>			• • •		
Active worker	1		$\sim$		1				
Unemployed	0.087	0.062	[-0.035; 0.209]	0.161	-0.076	0.196	[-0.466; 0.314]	0.700	
Retired	0.513	0.039	[0.435; 0.590]	<0.001	0.561	0.164	[0.235; 0.887]	0.00	
Other	0.279	0.056	[0.170; 0.389]	<0.001	0.379	0.262	[-0.140; 0.899]	0.15	
BMI									
Normal	1				1				
Overweight	0.095	0.043	[0.012; 0.178]	0.026	0.282	0.163	[-0.042; 0.605]	0.08	
Obese	0.316	0.046	[0.226; 0.406]	<0.001	0.285	0.203	[-0.118; 0.689]	0.16	
Coffee intake	. (	/ . <b>`</b>							
1 to 3	1		P		1				
None	0.182	0.037	[0.109; 0.255]	<0.001	-0.136	0.170	[-0.474; 0.202]	0.42	
More than 3	-0.100	0.077	[-0.250; 0.053]	0.202	-0.346	0.194	[-0.732; 0.041]	0.07	
Alcohol intake									
Never	1				1				
Daily	-0.294	0.046	[-0.384; -0.204]	<0.001	-0.204	0.186	[-0.574; 0.167]	0.27	
Occasional	-0.250	0.040	[-0.328; -0.171]	<0.001	-0.198	0.164	[-0.524; 0.128]	0.23	
Smoking	-								
Non-smoker	1				1				
Smoker	-0.232	0.052	[-0.335; -0.130]	<0.001	-0.248	0.188	[-0.621; 0.126]	0.19	
Regular physical exercise									
No	1				1				
Yes	-0.282	0.039	[-0.358; -0.206]	<0.001	-0.405	0.152	[-0.707; -0.103]	0.00	
Number of comorbidities	-								
0-2	1	0.000			1				
≥3	0.449	0.034	[0.383; 0.515]	<0.001	0.594	0.130	[0.335; 0.853]	<0.00	
BASDAI	_								
Inactive	-	-	-	-	1		to		
Active	-	-	-	-	0.487	0.182	[0.126; 0.848]	0.00	

NUTS II – nomenclature of territorial units for statistics; BMI – Body mass index;  $\beta$  - parameter estimates; Std – Standard; CI – Confidence Interval

Bold indicates statistically significant results (significance level set at 0.05)



**Table IV** - Factors associated with disability (HAQ-DI), stratified by diagnostic category (multivariable model).

		Chronic low back pair	<u></u> ו		Spondyloarthritis		
		n= 1376		n= 92			
	β	95% CI	p-value	β	95% CI	p-value	
Gender							
Female	1			-	-	-	
Male	-0.219	[-0.293; -0.145]	<0.001	-	-	-	
Age							
18-35 years	1			-	-	-	
36-55 years	0.021	[-0.110; 0.151]	0.756	-	-	-	
56-75 years	0.052	[-0.093; 0.198]	0.480	-	-	-	
$\geq$ 76 years	0.398	[0.221; 0.575]	<0.001	-	-	-	
Employment status							
Active worker	1			1		1	
Unemployed	0.086	[-0.028; 0.200]	0.138	-0.184	[-0.534; 0.165]	0.298	
Retired	0.260	[0.159; 0.361]	<0.001	0.386	[0.087; 0.685]	0.012	
Other	0.101	[-0.006; 0.207]	0.062	0.159	[-0.313; 0.631]	0.509	
Weight							
Normal	1						
Overweight	0.024	[-0.051; 0.099]	0.532	- X `		-	
Obesity	0.179	[0.097; 0.262]	<0.001			-	
Alcohol intake							
Never	1			-	-	-	
Daily	-0.108	[-0.197; -0.020]	0.016		-	-	
Occasional	-0.041	[-0.114; 0.033]	0.557		-	-	
Regular physical exercise							
No	1			1			
Yes	-0.175	[-0.244; -0.107]	<0.001	-0.389	[-0.650; -0.128]	0.004	
Number of comorbidities							
0-2	1		<u> </u>	1			
≥3	0.196	[0.126; 0.267]	<0.001	0.523	[0.272; 0.774]	<0.001	
Low back pain intensity	0.042	[0.028; 0.056]	<0.001				
		R <sup>2</sup> =0.280			R <sup>2</sup> =0.300		

NUTS II – nomenclature of territorial units for statistics; BMI- body mass index;  $\beta$  - parameter estimates; CI –Confidence interval.

Bold indicates statistically significant results (significance level set at 0.05)



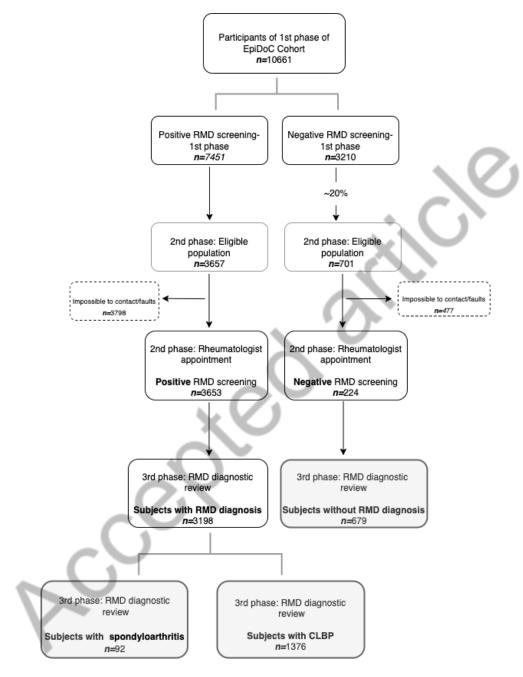


Figure 1 – Flowchart of recruitment in the EpiReumaPt study

RMD - rheumatic and musculoskeletal diseases; CLBP, chronic low back pain



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Acepted