Determining factors related to poor quality of life in patients with axial spondyloarthritis: results from the British Society for Rheumatology Biologics Register (BSRBR-AS)

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ABSTRACT

Objective To determine modifiable factors associated with poor quality of life (QoL) in patients with axial spondyloarthritis.

Methods Analysis of data from the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS) and validation of a previous model, using data from 1810 patients with axSpA recruited 2012-17. Data collected included clinical and patient-reported measures. QoL was assessed using the Ankylosing Spondylitis Quality of Life measure (ASQoL). Linear regression models predicting ASQoL score were used firstly to validate a previous model from a national study, to extend this with additional information available in BSRBR-AS and finally to identify a *"de novo"* model from BSRBR-AS of which factors impact on poor QoL..

Results Four out of five factors included in a previous model of poor QoL in axSpA patients were confirmed: Bath measures of disease activity (BASDAI) and function (BASFI), fatigue and widespread pain, although the performance of the model was improved by the addition of measures of mood and sleep disturbance. In a "de novo" model in BSRBR-AS there were six factors (other than disease activity and function) which predicted ASQoL: depression (β=0.16), sleep disturbance (β=0.08), activity impairment (β=0.04), fibromyalgia (symptom severity scale (β=0.24) and widespread pain index (β=0.10)) and tobacco smoking (β=0.65).

Conclusion This study confirms that poor QoL in patients with axSpA, in addition to high disease activity and poor function, is independently influenced by sleep disturbance, mood and widespread pain These additional factors are not considered targets for treatment in current EULAR guidelines for managing the condition.

KEY WORDS: quality of life, axial spondyloarthritis; disease register; fatigue; mood; sleep

INTRODUCTION

When treating people with axial spondyloarthritis (axSpA) and other inflammatory conditions, rheumatologists are focussed on reducing disease activity and in so doing aim to reduce the impact which the disease has on their lives. The ultimate aim, however, is to improve patients' quality of life (QoL). Reducing disease activity is one way to do that, but there may be other factors not directly captured by disease activity measures, which impact on QoL. AxSpA has an impact on people's working lives, mental health and physical health symptoms, such as pain and fatigue, have been shown to have an important influence on QoL.[1,2] Further, we (and others) have shown that pharmacological therapy targeted at reducing disease activity in inflammatory arthritis may have modest effects on aspects such as mental health[3], fatigue[4] and work productivity.[5]

Previously, in an analysis of 959 patients from a national disease register (Scotland Registry for Ankylosing Spondylitis (SIRAS)), we have shown that five potentially modifiable factors predict poor QoL (using the Ankylosing Spondylitis Quality of Life Scale (ASQoL)[6]): high disease activity, poor physical function, fatigue, chronic widespread pain and poor spinal mobility.[7] Of these factors, disease activity had the lowest (20%) population attributable risk for poor QoL. In addition, there were a number of nonmodifiable factors or at least not easily modifiable in the clinic, which were also related to poor quality of life: female sex, fewer years of education, not in full-time employment, living in areas with higher deprivation, not able to drive and history of peripheral joint involvement. We concluded that "*these findings provide evidence that in addition to traditional clinical targets ….. , focus on nonspecific symptoms (CWP and fatigue), perhaps with nonpharmacological therapies, may yield important improvements in QoL*.". The positive predictive value for poor QoL varied from around 0% and 15% in those with 1 or two modifiable factors to around 60% and 80% in those with 4 or 5 such factors respectively.

The aims of the current study, using a Great Britain-wide registry of axial spondyloarthritis (British Society for Rheumatology Biologics Register in Ankylosing Spondylitis: BSRBR-AS), is a) to validate the previous model (above) of modifiable factors linked to poor QoL, b) given that the BSRBR-AS has collected a wider set of variables to determine whether these additional variables (related to mood and sleep disturbance) are independent in predicting poor QoL and c) using the BSRBR-AS to develop a model predicting poor QoL *"de novo"*, to determine how consistent are the factors which predict poor QoL across both populations

METHODS

The BSRBR-AS is a prospective cohort study of people with axSpA. Patients were naïve to biologic therapy on recruitment but some were about to start such therapy (the biologic cohort) while others continued on other therapy (non-biologic cohort). The study protocol has been published previously.[8] Briefly, recruitment took place across 83 secondary care centres between December 2012 and December 2017, initially for those patients, aged at least 16 years, meeting the Assessment of SpondyloArthritis international Society (ASAS) imaging criteria for axSpA[9] or the modified New York (mNY) definition of Ankylosing Spondylitis.[10] From November 2014 those meeting the ASAS clinical criteria were also eligible. Clinical data were collected from medical notes and patients completed questionnaires which were handed out in the clinic and could be completed there, or at home and posted back to the recruitment centre. For the current study, the data used was from the time of recruitment (for non-biological cohort) and just prior to commencing biological therapy (biological cohort) which was also mainly at the time of recruitment. QoL was assessed by ASQoL,[6] an 18-item questionnaire which gives a score between 0 (best QoL) and 18 (worst QoL).

Clinical information included extra-spinal manifestations (uveitis, psoriasis, inflammatory bowel disease (IBD), enthesitis, dactylitis), inflammatory markers (C-Reactive Protein (CRP), peripheral joint involvement, symptom duration, body mass index (BMI), and information on 14 comorbidities (related to cardiovascular, respiratory, gastrointestinal, renal, neurological conditions and cancer) Patient reported measures included age, gender, level of education, employment status and lifestyle factors (tobacco smoking and alcohol intake) as well as Bath Ankylosing Spondylitis indices for disease activity (BASDAI),[11] function (BASFI),[12] and metrology (BASMI).[13] These Bath indices all produce scores ranging from 0 – 10 (least to most severe). Participant postcodes were used to determine a deprivation quintile, with reference to either the population of Scotland or England & Wales.[14-16] This ranged from 1 (most deprived) to 5 (least deprived). Mental health was assessed by the Hospital Anxiety and Depression Scale (HADS) scored from 0 (best) to 21 (worst).[17] Overall work impairment (including absenteeism, presenteeism) and other activity (non-work) impairment by the Work Productivity and Activity Impairment Specific Health Problem (WPAI:SHP), all scored from 0-100%.[18,19] The widespread pain index (WPI) (0 – 19) and symptom severity scale (SSS) were assessed through the 2011 fibromyalgia “research” criteria.[20] This was only collected amongst persons recruited from August 2015. Fatigue was collected through the Chalder fatigue scale (CFS, 0 – 33),[21] and sleep disturbance by the Jenkins Sleep Evaluation Questionnaire (0 – 20),[22] with higher scores on each indicating worse state.

Ethical approval was obtained from the National Research Ethics Service Committee North East—County Durham and Tees Valley (reference 11/NE/0374) and informed consent was obtained from all participants. Patients attended meetings to identify priority areas for analysis.

Analysis

In validating the model linking modifiable factors to quality of life previously reported by Dean *et al*,[7] the five modifiable factors reported (fatigue, BASFI, Chronic widespread pain (CWP), BASDAI and BASMI) were included in a multivariable linear regression model. The model was adjusted for non-modifiable factors associated with QoL on univariable analysis at $p \leq 0.2$. The current study did not have information available to determine the presence of CWP according to the American College of Rheumatology (ACR) 1990 criteria for fibromyalgia,[23] and instead used the WPI subscale of the 2011 "research" criteria for fibromyalgia.[20] Building upon this 5 factor model, the second analysis offered three additional modifiable factors (anxiety, depression and sleep disturbance), which were available in BSRBR-AS, but had not been available within SIRAS. The stepwise selection therefore had eight candidate variables. Variables were entered into the model at $p \leq 0.1$ and excluded at $p \geq 0.15$. Adjustment for nonmodifiable factors was applied as previously. The third analysis was a multivariable linear regression model, "*de novo"*, with forward stepwise selection, using modifiable factors from BSRBR-AS with $p \leq 0.2$ from the univariable analysis. The model examined which factors, in addition to disease activity and function, influenced poor quality of life, but omitted the work productivity factors (absenteeism, presenteeism and work impairment), which were only available for employed participants. Adjustment for nonmodifiable factors was applied as previously. For each model, once the variables to be included were determined, the model was re-run using all the participants with data for the included variables (rather than only participants with data available for each of the candidate variables).

All statistical analysis was undertaken using STATA (StataCorp LP version 15) and on the August 2017 version of the BSRBR-AS dataset.

RESULTS

A total of 1810 participants were eligible for the current analyses. Approximately two-thirds were male (67%), their median age was 49 years (Inter-quartile range (IQR) 38, 61), with a median time since symptom onset of 17 years (IQR 8, 31) (table 1). Of those who had been tested 80% were HLA-B27 positive. Most participants (67%) met the mNY criteria for AS, an additional 29% fulfilled ASAS imaging criteria but not mNY and 4.1% fulfilled only ASAS clinical criteria for axSpA. The median BASDAI and ASQoL scores were 4.8 (IQR: 2.5 – 6.8) and 9 (IQR: 3 – 13), respectively.

Factors associated with poor QoL

Amongst clinical factors, all extra-spinal manifestations, with the exception of uveitis, were associated with poorer QoL (table 2). Higher BMI and a greater number of comorbidities were also associated with poorer QoL. Longer symptom duration, however, was associated with better QoL (β per year = -0.05, 95% CI (-0.07, -0.04)). Most patient-reported factors demonstrated a relationship. Worse disease activity, function and metrology were significantly associated with poorer QoL (BASDAI (β per unit increase = 1.82, BASFI β = 1.56, BASMI β = 0.97). Females reported slightly poorer QoL (β = 1.58, 95% CI 1.02, 2.13), and there were important associations with low socio-economic status (e.g. those who had attended only secondary school/those living in the highest levels of deprivation had on average around 4 points higher ASQoL score than those with a further degree/living in an area with lowest levels of deprivation respectively). Current smoking was associated with significantly worse QoL (β = 4.45 95% CI (3.74, 5.16)). Higher level of fatigue (β per one unit increase in score = 0.63, 95% CI 0.60, 0.67), fibromyalgia (SSS) (β = 1.34 per unit increase, 95% CI 1.24, 1.44), fibromyalgia (WPI) (β = 0.69, 95% CI 0.61, 0.77), sleep disturbance (β = 0.56, 95% CI 0.52, 0.59), anxiety (β = 0.72, 95% CI 0.67, 0.76) and depression (β =0.97, 95% CI 0.92, 1.01) were all related to poorer QoL. Non-work activity impairment due to AS (β = 0.16 per % impairment, 95% CI 0.15, 0.16) was also associated with poor QoL. Amongst those working, a higher percentage of time absent (β = 0.11 per % time absent, 95% CI 0.09, 0.13)), or working with reduced productivity (presenteeism) (β = 0.14 per % time work impaired, 95% CI 0.13, 0.15)) were related to poor QoL.

Validation of model predicting poor quality of life

There were 555 participants in the current study who provided the necessary information to be part of the validation of the QoL model reported in the SIRAS study (the lower number was due mainly to the fact that WPI was only collected part-way through the study and there were missing data for

BASMI). Four of the previously reported five factors (BASDAI (β = 0.69, 95% CI 0.51, 0.87), BASFI (β = 0.85, 95% CI 0.69, 1.01), fatigue (β = 0.14, 95% CI 0.08, 0.19) and widespread pain (WPI) (β = 0.07, 95% CI 0.00, 0.14)) were related to poor QoL, but there was no independent relationship with BASMI (β = 0.01, 95% CI -0.16, 0.18) (table 3). A stepwise model was then run with these five factors and additional psychosocial factors available in the current study. All three extra added factors (sleep disturbance (β = 0.10, 95% CI 0.07, 0.12), anxiety (β = 0.12, 95% CI 0.09, 0.16) and depression (β = 0.19, 95% CI 0.14, 0.24)) were included in the new best-fitting model, together with disease activity (BASDAI) (β = 0.55, 95% CI 0.45, 0.64) and function (BASFI) (β = 0.85, 95% CI 0.77, 0.93) (table 4).

Developing a new model predicting poor QoL

Finally, a "*de novo"* stepwise model within BSRBR-AS utilised data from 642 participants. The patient reported factors included in the final model were disease activity (BASDAI (β = 0.31, 95% CI 0.14, 0.47), function (BASFI (β = 0.59, 95% CI 0.45, 0.73)), depression (β = 0.16, 95% CI 0.09, 0.24) and sleep disturbance (β = 0.08 95% CI 0.04, 0.13) in agreement with results of previous models (table 5). In addition, activity impairment (β = 0.04, 95% CI 0.02, 0.05), fibromyalgia (SSS) (β = 0.24, 95% CI 0.13, 0.35) and fibromyalgia (WPI) (β = 0.10, 95% CI, 0.03, 0.17) entered the model as did current tobacco smoking (β = 0.66, 95% CI 0.10, 1.21).

DISCUSSION

The results of this study provide consistent evidence of which modifiable factors are associated with poor QoL in patients with axSpA. A model previously proposed in a Scotland-wide study was partly validated, confirming that worse disease activity, poor function and high levels of fatigue and widespread nature of pain symptoms were strongly related to poor QoL. The results were then extended by showing that in addition, mood (anxiety, depression), sleep disturbance and both widespread pain and somatic symptom components related to fibromyalgia were importantly related to poor QoL.

The participants in BSRBR-AS are broadly representative of the patients with axSpA in clinics across Great Britain, with the exception that none of them were currently prescribed biologics (although around one third of the participants were about to commence biologics). We have used BASDAI as the measure of disease activity as it is the measure most commonly used in the UK and is part of national guidelines by the National Institute of Health and Clinical Excellence and the BSR. A second reason is that the necessity to have a measure of inflammation (such as for the Ankylosing Spondylitis Disease

Activity Score (ASDAS)) [24] would have resulted in a much higher level of missing data, where this had not been measured in the required time-frame.

Some models have many fewer subjects included than others. This was partly a result of variables related to fibromyalgia (WPI and SSS) which were only collected for part of the duration of the study and in relation to BASMI which was only measured on some participants. Once the variables included in a specific model were determined, the analysis was,however, re-run including all participants with the required data available. In validating the model predicting poor QoL, the information collected was not in exactly the same format between studies (for pain, WPI was collected instead of CWP). However the information collected in BSRBR-AS was more detailed and was analysed in a statistically more efficient manner (i.e. using continuous variables where available). Overall the results, however, were consistent across both studies. There can be a certain amount of circularity, since factors which are potentially associated with poor QoL can themselves be used in assessing QoL. Within ASQoL, for example, there are items on function, mental health, sleep and pain. These are all aspects (assessed by specific questionnaires) which the current study has found were associated with overall QoL. Such circularity is unavoidable but in the current study the regressions model the association per unit change in score, so there is limited influence of one aspect of QoL on the overall score and secondly in our analysis as part of the SIRAS study, items were removed (in turn) from ASQoL on pain and tiredness, and associations with chronic widespread pain and fatigue (respectively) were still observed.[7] Finally, one may debate whether function is modifiable independent of disease activity. In this dataset, there is a clear correlation between them (correlation = 0.76). We have considered both as EULAR recommendations include each as targets for management and the results suggest they make an independent contribution to QoL. The correlations between SSS and BASDAI (correlation = 0.68) and between BASFI and non-work physical impairment as measured by WPAI (correlation = 0.78) also suggest important relationships. However, as part of the model assessment we calculated the variance inflation factor as a method of assessing potential multicollinearity and this confirmed that there were no concerns.

The current study confirms the important role of disease activity and function in terms of QoL but adds to the literature by emphasising the important independent role of additional features associated with axSpA: mental health, fatigue and sleep problems, and widespread pain. Fatigue has been recognised to have an important influence on health-related QoL in rheumatoid arthritis (RA)[25] and indeed it was a priority for RA patients who participated in a focus group study in Sweden, in terms of being a key component to measure in evaluating treatment success.[26] Zhao *et al*[27] in a meta-analysis of sixteen studies estimated the prevalence of at least moderate depression in patients

with axSpA as 15%, based on a Hospital Anxiety and Depression score of ≥11. Garrido-Cumbrera et al [28] in a sample of 680 patients as part of the Atlas of Axial Spondyloarthritis in Spain, reported that high disease activity was a risk factor for poor mental health, but the current study emphasises that poor mental health independently predicts worse QoL. A meta-analysis of the co-occurrence of fibromyalgia in axSpA estimated a prevalence of 13%,[29] compared with a prevalence in the general population of around 2-5%[30], and we have previously shown within BSRBR-AS that patients who have co-morbid fibromyalgia have the same absolute improvement in QoL when treated with anti-TNFα therapy, but their QoL prior to and on treatment remains worse. Further, a high score on the SSS (rather than the WPI) is predicative of lack of improvement.[31] The fact that these additional features are common has been recognised, but not that they contribute independently to poor QoL and there has been a lack of studies on how they can be effectively treated (including alongside inflammatory arthritis). Nevertheless we acknowledge that there are some who propose that it is sufficient to focus on inflammation and that in so doing other aspects which impinge on quality of life will also improve [32].

The most recent EULAR/ASAS guidelines for the management of axial spondyloarthritis state, in Recommendation 2, that "the primary goal of treating the patient with axSpA is to maximise long-term health-related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalisation of function and social participation".[33] The results of the current study confirm that disease activity and function as a focus, is appropriate. However, it is not sufficient. In the guidelines there is no mention of sleep problems, widespread pain or mental health and specifically how these aspects should be managed. The results from this study suggest that their role is important – and independent of disease activity and functional limitation. Results from others studies, as noted above, suggest that patients will continue to experience fatigue, poor mental health and fibromyalgia-like symptoms if management is focused on inflammation alone.[3,4] Effecting improvement in such additional disease features is challenging – studies are underway to test behavioural approaches to management and/or physical activity for fatigue and fibromyalgia symptoms in patients with a range of inflammatory arthritides.[34,35] Currently evidence suggests, for example, that community-based exercise programmes exert a positive (albeit modest) effect on anxiety[36,37] and depression[38] amongst patients with arthritis and other rheumatic conditions. A recent trial demonstrated that group-based cognitive behavioural therapy delivered within rheumatology teams reduced the impact of fatigue in RA patients[39]. Such therapy aims to reduce the *impact* of, for example, fatigue and widespread pain rather then improving symptoms *per se*, and not all patients are willing to engage with them. Further, the expertise and resources to deliver

the interventions to target these additional factors are not easily available to many rheumatology teams.

In summary, the current study has shown, through analysis of factors related to poor QoL and validation of a previously published model, that improving the QoL of patients with axSpA means that in addition to improving disease and activity and function in patients, there must be attention to the co-morbid features of fatigue, poor sleep and mental health, and other common symptoms.

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Table 1 Characteristics of the BSRBR-AS patients

Variable		**N**	**% or Median (IQR)***
Quality of life (ASQoL)	Continuous	1810	9(3, 13)
Clinical factors			
Symptom duration, years	Continuous	1809	17.3(7.6, 30.8)
Uveitis	Not present	1364	76.0
	Present	431	24.0
Psoriasis	Not present	1598	89.0
	Present	197	11.0
Inflammatory bowel disease (IBD)	Not present	1617	90.1
	Present	178	9.9
Enthesitis	Not present	1612	89.8
	Present	183	10.2
Peripheral joint disease	Not present	1477	82.3
	Present	318	17.7
Dactylitis	Not present	1726	96.2
	Present	69	3.8
Inflammation (CRP), mg/dL	Continuous	1404	0.5(0.2, 2.0)
Body mass index (BMI), kg/m^2	Continuous	1810	26.9(23.9, 30.8)
Number of comorbidities	Continuous	1788	0(0, 1)
Patient reported factors			
Disease activity (BASDAI)	Continuous	1785	4.8(2.5, 6.8)
Physical function (BASFI)	Continuous	1801	4.5(2.0, 7.0)
Spinal mobility (BASMI)	Continuous	1340	3.8(2.4, 5.4)
Age, years	Continuous	1810	49.1(37.6, 60.8)
Gender	Male	1208	66.8
	Female	602	33.2
Education	Secondary school	583	32.5
	Apprenticeship	173	9.7
	Further education college	539	30.0
	University degree	354	19.7
	Further degree	146	8.1
Employment	Working full-time	870	48.2
	Working part-time	258	14.3
	Retired	318	17.6
	Retired early (ill-health)	103	5.7
	Unemployed (ill-health), not seeking work	164	9.1
	Other†	93	5.1
Deprivation, quintiles of general population	1. most deprived	278	15.4
	2	313	17.3
	3	382	21.1
	4	430	23.8
	5. least deprived	407	22.5
Smoking status	Never	787	44.1
	Ex	664	37.2
	Current	334	18.7
Alcohol consumption	Never	122	6.8

	Ex	311	17.5
	Current	1350	75.7
Chalder fatigue	Continuous	1806	14(11, 19)
Symptom Severity Scale (SSS)	Continuous	675	6(3, 8)
Widespread pain index (WPI)	Continuous	863	4(2, 7)
Sleep disturbance (Jenkins)	Continuous	1796	10(5, 16)
Anxiety (HADS)	Continuous	1788	7(4, 11)
Depression (HADS)	Continuous	1787	5(2, 9)
Absenteeism (WPAI) (%)	Continuous	1011	0(0, 0)
Presenteeism (WPAI) (%)	Continuous	1015	20(10, 50)
Work impairment (WPAI) (%)	Continuous	987	30(10, 50)
Activity (non-work) impairment (%)	Continuous	1774	40(20, 70)

*% given for discrete variables, median (IQR) for continuous variables.

†Because of small numbers in certain categories, we collapsed employment status (Unpaid work, Unemployed, but seeking work, Student) into Other.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C – reactive protein; HADS, Hospital Anxiety and Depression Scale; Jenkins, Jenkins scale for sleep disturbance; WPAI, Work Productivity and Activity Impairment.

Table 2 Predictors of ASQoL from univariable linear regression analysis

Variable		**Regression coefficient, β, (95% CI)***
Clinical factors		
Symptom duration (years)	Continuous	-0.05(-0.07, -0.04)
Uveitis	Not present	-
	Present	-1.32(-1.94, -0.70)
Psoriasis	Not present	-
	Present	1.46(0.62, 2.31)
Inflammatory bowel disease (IBD)	Not present	-
	Present	1.25(0.36, 2.13)
Enthesitis	Not present	-
	Present	1.72(0.85, 2.60)
Peripheral joint disease	Not present	-
	Present	1.82(1.13, 2.51)
Dactylitis	Not present	-
	Present	0.99(-0.39, 2.37)
Inflammation (CRP), mg/dL	Continuous	0.02(0.00, 0.04)
Body mass index (BMI), kg/m^2	Continuous	0.16(0.10, 0.21)
Number of comorbidities	Continuous	0.75(0.43, 1.07)
Patient reported factors		
Disease activity (BASDAI)	Continuous	1.82(1.75, 1.88)
Physical function (BASFI)	Continuous	1.56(1.51, 1.62)
Spinal mobility (BASMI)	Continuous	0.97(0.82, 1.11)
Age (years)	Continuous	-0.05(-0.064, -0.03)
Gender	Male	-
	Female	1.58(1.02, 2.13)
Education	Secondary school	-
	Apprenticeship	-1.25(-2.20, -0.30)
	Further education college	-0.97(-1.62, -0.31)
	University degree	-2.78(-3.52, -2.04)
	Further degree	-3.95(-4.96, -2.93)
Employment	Working full-time	-
	Working part-time	1.90(1.89, 2.61)
	Retired	0.18(-0.48, 0.83)
	Retired early (ill-health)	5.07(4.02, 6.11)
	Unemployed (ill-health), not seeking work	8.54(7.69, 9.40)
	Other†	2.71(1.61, 3.80)
Deprivation, quintiles of general population	1. most deprived	-
	2	-2.20(-3.09, -1.3)
	3	-3.00(-3.86, -2.14)
	4	-3.64(-4.48, -2.8)
	5. least deprived	-4.37(-5.22, -3.52)
Smoking status	Never	-
	Ex	1.37(0.80, 1.94)
	Current	4.45(3.74, 5.16)
Alcohol consumption	Never	-

	Ex	-0.07(-1.23, 1.09)
	Current	-3.6(-4.63, -2.58)
Chalder fatigue	Continuous	0.63(0.60, 0.67)
Symptom Severity Scale (SSS)	Continuous	1.34(1.24, 1.44)
Widespread pain index (WPI)	Continuous	0.69(0.61, 0.77)
Sleep disturbance (Jenkins)	Continuous	0.56(0.52, 0.59)
Anxiety (HADS)	Continuous	0.72(0.67, 0.76)
Depression (HADS)	Continuous	0.97(0.92, 1.01)
Absenteeism (WPAI) (%)	Continuous	0.11(0.09, 0.13)
Presenteeism (WPAI) (%)	Continuous	0.14(0.13, 0.15)
Work impairment (WPAI) (%)	Continuous	0.14(0.13, 0.15)
Activity (non-work) impairment (%)	Continuous	0.16(0.15, 0.16)

*A positive regression coefficient means a poorer quality of life compared with a reference category or per unit increase in the risk factor, for continuous variables.

†Because of small numbers in certain categories, we collapsed employment status (Unpaid work, Unemployed, but seeking work, Student) into Other.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; CRP, C – reactive protein; HADS, Hospital Anxiety and Depression Scale; Jenkins, Jenkins scale for sleep disturbance; WPAI, Work Productivity and Activity Impairment.

Table 3 Validation of a model predicting poor quality of life

Variable	**Model derived from SIRAS study***		**BSRBR-AS model****
		Relative Risk (95% CI)	**Regression coefficient, β, (95% CI)†**
Disease activity (BASDAI)	BASDAI < 4	1.00	0.69(0.51, 0.87)
	BASDAI ≥ 4	1.52(1.09, 2.12)	
Physical function (BASFI)	BASFI < 4	1.00	0.85(0.69, 1.01)
	BASFI ≥ 4	3.46(1.76, 6.82)	
Spinal mobility (BASMI)	BASMI < 4	1.00	0.01(-0.16, 0.18)
	BASMI ≥ 4	1.52(0.93, 2.50)	
Fatigue	None/mild	1.00	0.14(0.08, 0.19)
	Moderate/severe	1.60(1.13, 2.28)	
Widespread pain index (WPI)‡	No	1.00	0.07(0.00, 0.14)
	Yes	1.92(1.33, 2.75)	

N=555

*Scotland Registry of Ankylosing Spondylitis.

**Model adjusted for gender, age, education, symptom duration, employment, deprivation, alcohol consumption, and history of peripheral joint involvement.

†All variables in the model are continuous (in contrast to dichotomous in SIRAS).

‡Chronic Widespread Pain was available in SIRAS and WPI was available in BSRBR-AS.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; SIRAS, Scotland Registry for Ankylosing Spondylitis; BSRBR-AS, British Society for Rheumatology Biologics Register in Ankylosing Spondylitis.

Table 4 Validation of a model predicting poor QoL – the additional role of depression, anxiety and sleep disturbance

Variable	Regression coefficient, β, (95% CI)[*†]
Disease activity (BASDAI)	0.55(0.45, 0.64)
Physical function (BASFI)	0.85(0.77, 0.93)
Sleep disturbance (Jenkins)	0.10(0.07, 0.12)
Anxiety (HADS)	0.12(0.09, 0.16)
Depression (HADS)	0.19(0.14, 0.24)

N=1692

[*]Model adjusted for gender, age, education, symptom duration, employment, deprivation, alcohol consumption, history of peripheral joint involvement and number of comorbidities.

[†]Regression coefficients represents change in QoL per unit increase in predictor.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; HADS, Hospital Anxiety and Depression Scale; Jenkins: Jenkins scale for sleep disturbance.

Table 5 Variables associated with poor quality of life: the BSRBR-AS study

Variable[*]		**Regression coefficient, β, (95% CI)**[†]
Disease activity (BASDAI)	per unit increase	0.31(0.14, 0.47)
Physical function (BASFI)	per unit increase	0.59(0.45, 0.73)
Symptom Severity Scale (SSS)	per unit increase	0.24(0.13, 0.35)
Widespread pain index (WPI)	per unit increase	0.10(0.03, 0.17)
Sleep disturbance (Jenkins)	per unit increase	0.08(0.04, 0.13)
Depression (HADS)	per unit increase	0.16(0.09, 0.24)
Activity (non-work) impairment (%)	per % increase	0.04(0.02, 0.05)
Smoking – current smoker	Yes/No	0.66(0.10, 1.21)

N=642

[*]Work variables were not offered to the model as these were only relevant to persons in employment. Inflammation not offered to the model because of level of missing data.

[†]Model adjusted for gender, age, education, symptom duration, current employment, deprivation, , history of peripheral joint involvement, uveitis, psoriasis, inflammation bowel disease, enthesitis, dactylitis and number of comorbidities.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; HADS, Hospital Anxiety and Depression Scale; Jenkins, Jenkins scale for sleep disturbance.