

# Fatigue contributes to work productivity impairment in patients with axial spondyloarthritis: a cross-sectional UK study

S. Espahbodi<sup>1</sup>, P. Bassett<sup>2</sup>, C. Cavill<sup>1</sup>, M. Freeth<sup>1</sup>, J. Hole<sup>1</sup>, R. Sengupta<sup>1,3</sup>

<sup>1</sup>Royal National Hospital for Rheumatic Diseases (RNHRD), Bath, United Kingdom;

<sup>2</sup>StatsConsultancy Ltd., Buckinghamshire, United Kingdom; <sup>3</sup>University of Bath, United Kingdom.

---

## Abstract

### Objective

To determine factors associated with absenteeism, presenteeism, work productivity loss (WPL), and daily activity impairment in UK patients with AxSpA using standardised measures.

---

### Methods

490 patients with AxSpA completed (1) Work Productivity and Impairment questionnaire (WPAI), providing measures for absenteeism, presenteeism, WPL and daily activity impairment, and (2) BASDAI, BASFI, BASMI, Jenkins Sleep scale, Patient Global Assessment disease activity (PGA), back pain night and anytime, EQ-5D for mobility, self-care, daily activities, pain/discomfort, anxiety/depression, EQ-VAS Health State Today, FACIT fatigue, for health-related disease factors. Multivariate linear and logistic regression determined associations between WPAI measures and health-related factors.

---

### Results

301(61%) patients provided WPAI measurements, 76% were male, 87% HLA-B27+. Mean (SD) WPAI scores for absenteeism were 5.1%(19.2), presenteeism 22%(24.3), WPL 23.2%(25.7), activity impairment 34.8%(27.3). Absenteeism was associated with higher fatigue levels and more likely in patients with nrAxSpA. Presenteeism and WPL were both associated higher fatigue levels, BASDAI, and BASFI respectively. Daily activity impairment was associated with higher fatigue levels, BASFI, PGA, EQ-VAS, and smoking.

---

### Conclusion

Work productivity and impairment are associated with fatigue, disease activity, and functional ability in UK patients with AxSpA. The strong association of fatigue with all work measures as well as with daily activity impairment emphasises the need to better understand the impact of fatigue on patients' quality of life. Improving fatigue may help to optimise work status.

---

### Key words

axial spondyloarthritis, work productivity, fatigue, WPAI, BASDAI

Shima Espahbodi, PhD

Paul Bassett, MSc

Charlotte Cavill, MSc

Mandy Freeth

John Hole

Raj Sengupta, FRCP

Please address correspondence to:

Dr Shima Espahbodi,

Royal National Hospital for

Rheumatic Diseases,

Upper Borough Walks,

Bath BA1 1RL, United Kingdom.

E-mail: shimxi@yahoo.com

Received on September 16, 2016; accepted  
in revised form on December 6, 2016.

© Copyright CLINICAL AND

EXPERIMENTAL RHEUMATOLOGY 2017.

## Introduction

Axial spondyloarthritis (AxSpA), including ankylosing spondylitis (AS) is a chronic inflammatory disease that primarily affects the axial skeleton and sacroiliac joints, though involvement of the hips, shoulders, peripheral joints and tendons often occurs (1). Extra-articular manifestations (EAM) include uveitis, inflammatory bowel disease (IBD), psoriasis and cardiovascular impairment.

AxSpA typically presents early in life with a mean age of onset of 26 years (2) with symptoms of pain, fatigue, stiffness, and progressive disability, affecting men three times more often than women (3). The physical and emotional sequelae of AxSpA can restrict many aspects of a person's life including their ability to function at work. Gradual impairments in physical function, psychological well being (4), and contextual factors (5) can lead to presenteeism, absenteeism and eventual work disability (WD). Presenteeism is defined as decreased productivity at work, absenteeism is days/hours (sick leave) lost from work, and WD is the complete withdrawal from paid work or being forced to work fewer hours (partial WD) due to AxSpA respectively (6).

A number of studies have reported on employment status, healthcare costs, and WD in AxSpA as it commonly reduces a person's ability to work leading to long-term disability (7-20). Work disability has been found to be significantly prevalent in AxSpA and higher than expected in a matched general population (21-23). A further review reported that WD in AS patients ranged between 3 to 50% after 18 and 45 years disease duration respectively (9).

Presenteeism alone is an important outcome due to its human and economic consequences; however this may also provide insights into understanding the process that leads to WD. A few studies have assessed presenteeism and its associated factors (24-27), however, only one of these was based on a UK sample of AS patients (27). Results from the few studies assessing presenteeism have been variable, with the following factors found to be associated with presenteeism: BASFI, female sex, poor colleague contact (24), AS-related

quality of life, female sex, helplessness (26), BASDAI, depression, anxiety, self-efficacy, and age (27).

Variability in these studies' findings may in part be due to the large variation in endpoint definitions and use of different measurement instruments; both the Work Limitations Questionnaire (WLQ) (26) and the Work Productivity and Activity Impairment Questionnaire (WPAI) (24, 25) have been used. A standardised measurement of work productivity, validated in patients with AxSpA, would enable the consistent assessment of the impact of disease on work productivity across different countries, cultures, and AxSpA-sub groups.

In UK patients with AxSpA, our understanding of the effects of the disease on adverse work outcomes are limited. The aim of our study was to identify, using standardised measures, health-related factors that contribute significantly to presenteeism, absenteeism, work productivity loss (WPL), and daily activity impairment amongst AxSpA patients in the UK.

## Materials and methods

### Study design

We performed a cross-sectional, observational, single centre study in UK patients with AxSpA attending the Royal National Hospital for Rheumatic Diseases (RNHRD), Bath, under the care of a single rheumatologist (RS).

### Patients

Four hundred and ninety patients (>18 years) who fulfilled the 2009 ASAS AxSpA classification criteria (28) were recruited to the study. Bristol local research ethics committee (LREC) approved the study, and all patients provided informed, written consent. Forty per cent of attending patients come from outside the local area, therefore this cohort represents a diverse geographical UK population of AxSpA. Criteria for inclusion to the study were: patients with a confirmed diagnosis of AxSpA (including nr-AxSpA and AS), between the ages of 18–85 years, who had completed at least 1 WPAI questionnaire. Exclusion criteria were: patients with other serious medical condi-

*Funding: the analysis and completion of this project was supported by a grant from Abbvie Ltd UK.*

*Competing interests: none declared.*

tions *e.g.* cancer, not willing to partake in the study, unable to give informed written consent. This cohort included those: (i) with long-standing, and newly diagnosed AxSpA, (ii) on anti-inflammatories, biologics, and no medication. During outpatient appointments patients were invited to complete the 'AxSpA Patient Questionnaire pack', which included the following 10 patient-reported outcome measures (PROMS).

#### *PROMS: work impairment*

WPAI-SpA is a 6-item participant rated questionnaire which has been modified and validated for AS patients (29). It asks: (Q1) if currently employed or not, (Q2) the number of hours missed due to AS-related health in the last week, (Q3) the number of hours missed due to other reasons in the last week, (Q4) the number of hours actually worked in the last week, (Q5) the effect of AS on productivity whilst at work (0–10 scale, 10=AS completely prevented working), and (Q6) the effect of AS on ability to do daily activities, other than paid job.

It produces 4 sub-scores to measure: work time missed (absenteeism), impairment while working (presenteeism or reduced on-the-job-effectiveness), overall work impairment (WPL or absenteeism plus presenteeism), and activity impairment (daily activity impairment other than that due to paid work). Sub-scores are converted to impairment percentages (0 to 100), with higher numbers indicating more impairment and less productivity.

Presenteeism was calculated as  $Q5/10$ ; absenteeism as  $Q2 / (Q2+Q3+Q4)$ ; WPL as  $Q2/(Q2+Q4) + [(1-(Q2/(Q2+Q4))) \times (Q5/10)]$ , and daily activity impairment as  $Q6/10$ . All values were then multiplied by 100 to obtain percentages.

#### *PROMS: health-related factors*

Disease activity and functional impairment were assessed by completion of the BASDAI (30) and BASFI (31) respectively. Both indices were scored between 0 and 10 with higher values indicating worse disease activity or function respectively. Jenkins Sleep Scale (32) evaluated sleep problems (recall period 1 month) with a brief 4-items: difficulty falling asleep, fre-

quent awakenings during the night, trouble remaining asleep, and feelings of fatigue and sleepiness despite having had a typical night's sleep. Subjective overall disease activity (recall period 7 days) was assessed with the Patient Global Assessment (PGA) on a Likert scale between 0 (none) to 10 (severe). Back pain (BP) (a) at night, and (b) at any time was measured on a 0 to 10 Likert scale (recall period 7 days). Health-related quality of life was measured with the EuroQOL (EQ-5D) (33) which consists of 2 parts: (i) 5-items addressing mobility, ability to self-care, ability to do usual activities, pain/discomfort, and anxiety/depression, and (ii) a vertical 20 cm line VAS (EQ-VAS) where the 'best' and 'worst' imaginable health states score 100 and 0 respectively. Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale V4, validated in AS patients (34), is a 13-item patient-reported measure of fatigue (7-day recall period). Items are scored on a 0–4 scale with anchors ranging from "Not at all" to "Very much so". To score the FACIT, all items are summed to create a single fatigue score with a range from 0 to 52. Items are reverse scored whereby higher scores represent better functioning or less fatigue (35, 36). Pain sites were assessed by use of shading on the Margolis Pain Diagram (37).

#### *Demographic and other measures*

Patients reported on sociodemographic questions including age, sex, smoking status, age at symptom onset, age at diagnosis, and whether or not there was a family history of SpA. Treating rheumatologist (RS) obtained measurements of the Bath Ankylosing Spondylitis Metrology Index (BASMI) (38), recorded clinical data on HLA-B27 status and radiographic changes according to the mNYC classification (39), and indicated whether patients had ever experienced EAM.

#### *Statistical analyses*

STATA v. 13.1 was used for all analyses. Data were summarised as mean (SD) or median (IQR) for skewed distributions. All four outcome measures derived from the WPAI; absenteeism,

presenteeism, WPL, and activity impairment were measured on a continuous scale. However absenteeism demonstrated extreme skew, with 89% of patients having missed 'no' time from work. As such, for analysis, absenteeism was categorised into 'no' time missed and 'some' time missed.

WPAI outcomes were analysed using linear regression, except absenteeism for which logistic regression was applied. Each WPAI outcome was analysed in two stages; firstly the association between each factor and each WPAI outcome was examined separately in a series of univariable analyses. Subsequently a multivariable analysis examined the joint association between variables. Only those factors demonstrating an association ( $p < 0.2$ ) with the WPAI outcomes in the univariable analysis were included in this stage of the analysis. Backwards selection was used to retain only the statistically significant variables in the final model.

#### **Results**

The demographic characteristics in Table I show a male to female ratio of about 3:1, a delay in diagnosis of about 10 years and 94% met radiographic criteria (mNYC) for AxSpA – the remainder met the ASAS non-radiographic criteria. Disease activity was generally high (3.8), bordering the  $\geq 4$  cut-off used for treatment guidelines as eligibility criteria for anti-TNF treatment. Nearly one third (29%) were receiving biologics, the remainder not, and EAM (42% uveitis, 7% IBD, 17% psoriasis). Both sleep and fatigue problems were generally quite severe with means of 13 and 34 for Jenkins and FACIT respectively.

#### *WPAI measurements*

Table II shows summary measures for the WPAI. Mean scores for absenteeism and presenteeism were 5.1% (SD 19.2) and 22.0% (SD 24.3) respectively, leading to an overall WPL of 23.2% (SD 25.7). Absenteeism was reported as 0% by 268 patients and between 4 and 100% by 33 patients with a mean of 46.5%. Of these 33 patients who missed 'some' time, 9 missed 100% of their work time.

**Table I.** Patient demographics and clinical characteristics.

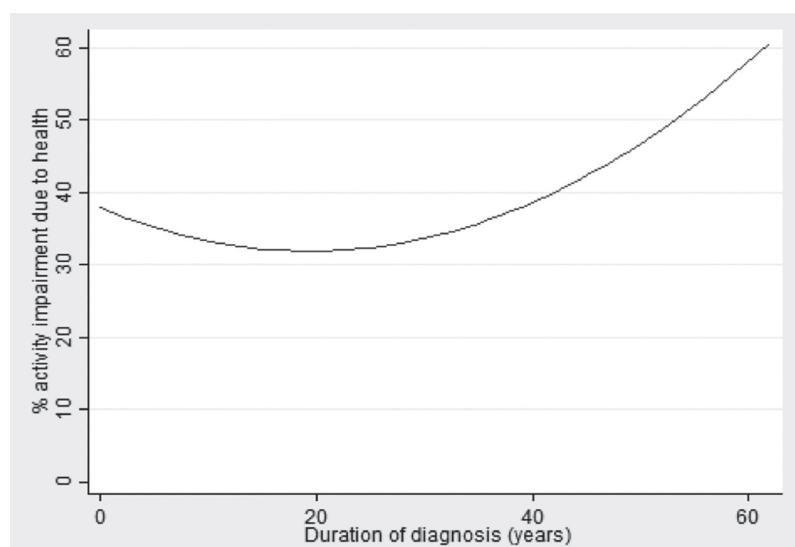
Variable	n	Mean (SD) or n (%)
Age at diagnosis	482	30.8 (11.7)
Age at onset of symptoms	476	21.5 (8.8)
Age at baseline	490	52.3 (12.8)
Female	490	120 (24%)
Duration of diagnosis (years)	482	21.7 (13.0)
Family history of SPA	305	113 (37%)
HLA B27 positive	392	342 (87%)
Radiographic change (mNYC)	490	461 (94%)
Smoking status: Non-smoker	488	272 (56%)
Ex-smoker		135 (28%)
Current smoker		81 (17%)
BASDAI score (0-10)	489	3.8 (2.2)
PGA disease activity (0-10)	391	3.9 (2.6)
BP night (0-10)	393	3.3 (2.6)
BP anytime (0-10)	393	3.6 (2.6)
BASFI score (0-10)	490	4.0 (2.7)
EQ-5D (0-1)	401	0.62 (0.28)
EQ-VAS (0-100)	390	63 (22)
FACIT score (0-52)	387	34 (12)
Jenkins score (0-20)	398	13.0 (5.7)
Margolis Pain score (0-45)	421	8.7 (6.9)
BASMI score (0-10)	486	3.8 (2.1)

Continuous data presented as mean (SD) and categorical data as n (%).

**Table II.** Patient WPAI scores and sub-scores.

Variable	n	Median (IQR) or n (%)	Mean (SD)
Q1 - Currently employed	490	301 (61%)	-
Q2 - Hours missed from work	301	0 (0, 0)	2.1 (8.8)
Q3 - Hours missed other reasons	301	0 (0, 0)	2.3 (7.3)
Q4 - Hours worked	490	37 (15, 45)	30.7 (19.4)
Q5 - Ability of working	482	1 (0, 4)	2.2 (2.4)
Q6 - Ability of regular activities	305	3 (1, 6)	3.5 (2.7)
% Absenteeism	301	0 (0, 0)	5.1 (19.2)
% Presenteeism	301	10 (0, 40)	22.0 (24.3)
% Work productivity loss	301	10 (0, 40)	23.2 (25.7)
% Daily activity impairment	490	30 (10, 60)	34.8 (27.3)

Data presented as median (IQR), n (%) and mean (SD).

**Fig. 1.** Relationship between duration of diagnosis (years) vs. daily activity impairment (%).

### Effect of AxSpA on WPAI measures

Of 490 patients, 301 were working at the time of this study that provided one or more measurements for the WPAI.

### Absenteeism

(% work time missed due to AS)

Univariate regression analysis demonstrated that smoking status ( $p=0.02$ ), non-radiographic (nr) AxSpA (0.001), BASDAI ( $p<0.001$ ), PGA disease activity ( $p=0.001$ ), BP night ( $p=0.002$ ), BP anytime ( $p=0.002$ ), BASFI ( $p<0.001$ ), EQ-VAS ( $p=0.001$ ), EQ-5D ( $p<0.001$ ), FACIT ( $p<0.001$ ), Margolis pain ( $p<0.001$ ) were associated with absenteeism. Only these covariates were then included in the multivariate backward regression analyses to retain the statistically significant variables shown in the final models below (Table III).

Current smokers and those with nrAxSpA were more likely to miss work time. The final model shows absenteeism (i) was almost 3 times higher in current smokers compared with non-smokers ( $p<0.1$ ), and (ii) 6 times higher in patients with nrAxSpA compared to those with radiographic changes (mNYC) *i.e.* AxSpA ( $p<0.05$ ). Absenteeism increased significantly with the severity of fatigue ( $p<0.01$ ).

### Presenteeism

(% impairment while working)

Univariate regression showed duration of diagnosis ( $p=0.08$ ), BASDAI ( $p<0.001$ ), PGA disease activity ( $p<0.001$ ), BP night ( $p<0.002$ ), BP anytime ( $p<0.002$ ), BASFI ( $p<0.001$ ), EQ VAS ( $p<0.001$ ), EQ-5D ( $p<0.001$ ), FACIT ( $p<0.001$ ), Jenkins ( $p<0.001$ ), Margolis pain ( $p<0.001$ ), and BASMI ( $p=0.04$ ) were associated with presenteeism.

Multivariate regression showed BASDAI, BASFI, FACIT, and duration of diagnosis (not quite significant) were all independently associated with presenteeism in the final model (Table III). Patients with higher disease activity and higher functional limitations had higher levels of presenteeism. A 1-unit increase in BASDAI score was associated with a 3-unit increase in presenteeism, whilst a 1-unit increase in BASFI was associated with a 1.6-unit increase in presenteeism. Patients with more se-



**Table III.** Factors associated with WPAI outcomes for work impairment.

WPAI outcome	n	Variable	§OR/ Coefficient (95% CI)	p-value
Absenteeism §	301	FACIT	-0.68 (0.56, 0.82)	<0.001
		Smoking ~ Non	1	0.07
		Ex	0.82 (0.24, 2.74)	
		Current	2.86 (1.07, 7.64)	
		Category ~ AS nrAxSpA	1 6.07, (1.83, 20.1)	<0.001
Presenteeism	301	FACIT	-3.1 (-4.7, -1.6)	<0.001
		BASDAI	3.0 (1.1, 5.0)	0.002
		BASFI	1.6 (0.0, 3.3)	0.04
		Duration diagnosis (yrs)	-2.0 (-4.2, 0.3)	0.08
WPL	301	FACIT	-3.9 (-5.5, -2.3)	<0.001
		BASDAI	3.0 (1.0, 4.9)	0.003
		BASFI	1.6 (0.1, 3.2)	0.05
Activity impairment	301	FACIT	-3.9 (-4.7, -3.1)	<0.001
		Smoking ~ Non	0 0.02	
		Ex	-4.4 (-7.6, -1.2)	
		Current	-0.8 (-4.8, 3.2)	
		BASFI	4.4 (3.6, 5.2)	<0.001
		EQ-VAS	-1.2 (-2.0, -0.4)	0.003
		PGA disease activity	1.7 (0.8, 2.5)	<0.001

Final multivariate models after backward regression.

§Absenteeism: Odds ratio (OR) reported after logistic regression. 95% Confidence interval (CI). FACIT: Functional Assessment of Chronic Illness Therapy; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; EQ-VAS: EuroQol Visual Analogue Scale for health state; PGA: Patient Global Assessment for disease activity.

vere fatigue had higher levels of presenteeism where a 5-unit increase in the severity of fatigue was associated with a 3-unit increase in presenteeism. A longer duration of diagnosis was associated with lower levels of presenteeism where a 10-year increase in duration was associated with a 2-unit reduction in presenteeism.

#### Work productivity loss (% overall work impairment)

Univariate regression showed HLA-B27 ( $p=0.04$ ), BASDAI ( $p<0.001$ ), PGA disease activity ( $p<0.001$ ), BP night ( $p<0.002$ ), BP anytime ( $p<0.002$ ), BASFI ( $p<0.001$ ), EQ VAS ( $p<0.001$ ), EQ-5D ( $p<0.001$ ), FACIT ( $p<0.001$ ), Jenkins ( $p<0.001$ ), Margolis pain ( $p<0.001$ ), and BASMI ( $p=0.04$ ) were associated with WPL.

In the final model BASDAI, BASFI, and FACIT were all independently associated with WPL (Table III). Patients with higher levels of disease activity and functional impairment demonstrated more WPL. A 1-unit increase in BASDAI score was associated with a 3-unit increase in WPL, whilst a 1-unit increase in BASFI was associated with

a 1.6-unit increase in WPL. As seen with both absenteeism and presenteeism, patients with more severe fatigue had higher WPL.

#### Activity impairment (% daily activity impairment)

490 patients had scores for this measure as it applied to all, whilst the other 3 WPAI measures applied only to those in work.

In univariate analysis, duration of diagnosis was significantly associated with activity impairment however the relationship was non-linear (Fig. 1). This suggests little relationship between duration and activity impairment for those with less than 30 years duration of diagnosis. However, activity impairment increased with increasing duration for patients with more than 30 years duration of diagnosis.

Univariate regression also showed that smoking ( $p=0.05$ ), HLA-B27 ( $p=0.002$ ), BASDAI ( $p<0.001$ ), PGA disease activity ( $p<0.001$ ), BP night ( $p<0.002$ ), BP anytime ( $p<0.002$ ), BASFI ( $p<0.001$ ), EQ VAS ( $p<0.001$ ), EQ-5D ( $p<0.001$ ), FACIT ( $p<0.001$ ), Jenkins ( $p<0.001$ ), Margolis pain ( $p<0.001$ ), and BASMI

( $p<0.001$ )) were associated with daily activity impairment.

Final model showed smoking status, PGA disease activity, BASFI, EQ VAS, and FACIT were all associated with activity impairment (Table III). Ex-smokers had the lowest scores, on average 4 units lower than non-smokers, and little difference in outcome between non-smokers and current smokers.

As seen with absenteeism, presenteeism, and WPL, patients with more severe fatigue had higher levels of activity impairment. Patients with higher PGA disease activity and BASFI scores had a higher level of activity impairment, whilst higher EQ VAS was associated with lower levels of activity impairment.

#### Discussion

To the best of our knowledge, this study is the first to report on (i) fatigue as a significant contributor to absenteeism, presenteeism, WPL, and daily activity impairment, and (ii) WPAI outcomes and their predictors in UK AxSpA patients. In addition to disease-related measures BASDAI and BASFI, other factors including smoking, duration of diag-

nosis, condition sub-type (nrAxSpA), and fatigue are associated with work productivity impairment in AxSpA patients. Furthermore, daily activity impairment is also associated with fatigue and with EQ-VAS, BASFI, PGA disease activity, and smoking status. Activity impairment can impact productivity at work and should be considered when assessing a person for work instability (40).

There is growing interest in absenteeism and presenteeism as they can be indicators of future work disability and are also important outcomes in themselves (27, 40–44). Patients in our study experienced mild-moderate loss in work productivity related to WPAI measures; absenteeism due to AxSpA was 5.1% and presenteeism was 22%, resulting in an overall WPL of 23.2% and activity impairment of 34.8%. Our results are comparable to Sieper *et al.* (45) who reported overall WPL of 29.8% to our 23.2%, but somewhat lower compared with those of two others whom also used the WPAI. Boonen *et al.* (24) reported absenteeism as 30.2%, presenteeism 49.1%, and overall WPL as 53.1% in 80 patients. ATLAS trial baseline data (25) on 205 AS patients starting anti-TNF treatment reported scores of 41.7% for presenteeism, 43.9% for overall WPL, and 49.2% for overall activity impairment, however absenteeism was 9% comparable to our 5.1%. Whilst the reasons for these differences will be multifactorial, studies do not report the level of intervention provided to support people at work and a direct comparison across studies is therefore difficult. Our hospital does have therapists who provide support to keeping patients at work; additionally we may be using biologic therapies earlier in the disease course than other cohorts, and these reasons may contribute to our lower results. In addition, others used different measurement tools to the WPAI thus direct comparisons with their findings is not possible.

Interestingly the strong association between absenteeism and nrAxSpA (Table III) may well be responsible for the early peak seen in Figure 1. This strengthens the case for the implementation of strategies to help reduce the

delay in diagnosis and interventions to support these patients to stay in work in what may be a 'window of opportunity' in minimising work disability.

Limitations in physical function (BASFI) and disease activity levels (BASDAI) both had a significant impact on presenteeism and overall WPL. However, absenteeism was not independently affected by either of these variables but was by patients with nrAxSpA, fatigue and smoking ( $p=0.07$ ). Our data suggests that disease activity levels and functional limitations have a greater influence on patients' productivity while at work, than on their decision to take sick leave which is only independently influenced by fatigue levels and nrAxSpA. Several others have also shown that health-related factors are associated with absenteeism, presenteeism, and overall WPL in patients with AxSpA. Comparable to ours, Boonen *et al.* (24) also found that BASFI was associated with presenteeism and overall WPL but not with absenteeism, and ASDAS-CRP, age and smoking were associated with absenteeism. The ATLAS trial (25), reported BASFI and BASDAI were associated with presenteeism.

In addition to ours, only one other study assessed work outcomes in UK patients using standardised measures (27). However, Healey *et al.* (27) used the WLQ, which scores patients' limitations at work over the past four weeks. Higher BASDAI and depression were associated with absenteeism, and presenteeism was also associated with BASDAI, depression, anxiety, and poor self-efficacy. Our novel finding is that fatigue is independently and significantly associated with absenteeism, presenteeism, WPL, and daily activity impairment respectively. Only two others reported on fatigue but using only a 10-cm VAS to assess fatigue. In 81 SpA patients Rohkar and Pope (44) found that fatigue (VAS) as well as BASFI, BASDAI, and BAS-G were highly correlated with losses in work productivity using the WLQ. Work disability (loss of paid employment) was associated with fatigue (VAS) in 33 AS patients and was also the main challenge for those still working who reported that the effects of fatigue spilled over into other areas

of their lives (27). This is comparable to our findings that fatigue has a significant independent effect on the ability of patients to do their regular daily activities (*e.g.* housework, hobbies, socialising) other than working at their paid jobs ( $p<0.001$ ).

Our results suggest that fatigue has a stronger influence on patients' decision to take time off work more so than either disease activity (BASDAI) and/or functional impairments (BASFI). This is commonly seen in clinical practice when patients often express that they can cope with the pain of AxSpA (with pain killers for example) but it is the fatigue that they really struggle with and are unable to manage. It may be hypothesised that despite pain and challenges with physical limitations, many patients may push themselves to go into work, but struggle to do so if fatigue levels become sufficiently severe.

Fatigue is one of patients' most troubling symptoms along with pain and stiffness (46) with prevalence rates of over 70% (47). However its causes are not yet well defined; some suggest sociodemographic and psychological factors are responsible (48, 49), whilst others believe its main determinant is disease activity (50, 51).

We have also demonstrated that in this AxSpA cohort, higher fatigue levels correlated with higher disease activity (BASDAI), with higher levels of physical impairment (BASFI), and also with higher PGA of disease activity. Furthermore, lower fatigue levels were significantly correlated with better self-reported health states (higher EQ-VAS), suggesting patients felt their overall health was better when fatigue was low. However, there was no correlation found with the duration of diagnosis ( $p=0.94$ ), with smoking status, or with condition sub-type. Fatigue levels for this cohort were quite severe despite about one third being on biologics.

Some limitations of our study include the fact that it was cross sectional in design and as such did not allow for determining significant factors that are the predictors of adverse work outcomes in AxSpA patients; a longitudinal study would be needed. Although this is the only study to investigate

WPAI outcomes in UK patients, our observations are nonetheless from a single country and this may limit the generalisability of the study. Other countries have different social security systems, different cultural attitudes towards work and illness, and different work related factors all of which may influence work outcomes.

This study has not examined the impact of all medication use on work outcomes. About one third of our cohort were receiving biologic therapy; multiple regression analyses on this sub-set did not show any statistical difference. Fabreguet *et al.* (52) similarly found no association between work instability and biologics use however a recent review (53) reported the efficacy of Adalimumab in multiple measures including work productivity. Greater numbers and a prospective analysis would be needed to examine this factor.

In conclusion this study of UK patients with AxSpA has demonstrated that fatigue contributes significantly to absenteeism, presenteeism, work productivity loss, and impairment whilst doing daily activities other than paid work respectively. Presenteeism and WPL were also significantly influenced by both BASDAI and BASFI respectively. Work impairment and disability in AxSpA is an important outcome, both from a patient and clinician perspective. Treating disease early in the disease course, helping patients to stop smoking and improving fatigue may be useful strategies to optimise work status in AxSpA patients.

## Acknowledgments

We would like to thank Mrs Janine McCaulder-Ojeda for her support and advice with the manuscript.

## References

- DAYLAN M, GUNER A, TUNCER S, BILGIC A, ARASIL T: Disability in ankylosing spondylitis. *Disab Rehabil* 1999; 22: 74-9.
- KLIPPEL JH: Primer on the Rheumatic Diseases. 12<sup>th</sup> ed. Atlanta, Georgia: The Arthritis Foundation; 2001.
- VAN DER LINDEN SM, VALKENBURG HA, DE JONGH BM, CATS A: The risk of developing ankylosing spondylitis in HLA-B27 positive individuals. A comparison of relatives of spondylitis patients with the general population. *Arthritis Rheum* 1984; 27: 241-9.
- BRIONEZ TF, ASSASSI S, REVEILLE JD *et al.*: Psychological correlates of self-reported functional limitation in patients with ankylosing spondylitis. *Arthritis Res Ther* 2009; 11: R182.
- STOLWIJK C, CASTILLO-ORTIZ JD, GIGNAC M, LUIJE J, BOONEN A: OMERACT WORKER PRODUCTIVITY GROUP: Importance of Contextual Factors When Measuring Work Outcome in Ankylosing Spondylitis: A Systematic Review by the OMERACT Worker Productivity Group. *Arthritis Care Res (Hoboken)* 2015; 67: 1316-27.
- GOBELET C, LUTHI F, AL-KHODAIRY AT, CHAMBERLAIN MA: Work in inflammatory and degenerative joint diseases. *Disabil Rehabil* 2007; 29: 1331-9. Review
- GUILLEMIN F, BRIANÇON S, POUREL J, GAUCHER A: Long-term disability and prolonged sick leaves as outcome measurements in ankylosing spondylitis. Possible predictive factors. *Arthritis Rheum* 1990; 33: 1001-6.
- WARD MM, KUZIS S: Risk factors for work disability in patients with ankylosing spondylitis. *J Rheumatol* 2001; 28: 315-21.
- BOONEN A, DE VET H, VAN DER HEIJDE D, VAN DER LINDEN S: Work status and its determinants among patients with ankylosing spondylitis. A systematic literature review. *J Rheumatol* 2001; 28: 1056-62.
- BARLOW JH, WRIGHT CC, WILLIAMS B, KEAT A: Work disability among people with ankylosing spondylitis. *Arthritis Rheum* 2001; 45: 424-9.
- BOONEN A, VAN DER HEIJDE D, LANDEWÉ R *et al.*: Work status and productivity costs due to ankylosing spondylitis: comparison of three European countries. *Ann Rheum Dis* 2002; 61: 429-37.
- BOONEN A, SEVERENS JL: Ankylosing spondylitis: what is the cost to society, and can it be reduced? *Best Pract Res Clin Rheumatol* 2002; 16: 691-705.
- BOONEN A: A review of work-participation, cost-of-illness and cost-effectiveness studies in ankylosing spondylitis. *Nat Clin Pract Rheumatol* 2006; 2: 546-53.
- ARIZA-ARIZAR, HERNÁNDEZ-CRUZ B, COLLANTES E *et al.*: Work disability in patients with ankylosing spondylitis. *J Rheumatol* 2009; 36: 2512-6.
- BAKLAND G, GRAN JT, BECKER-MEROK A, NORDVÅG BY, NOSSENT JC: Work disability in patients with ankylosing spondylitis in Norway. *J Rheumatol* 2011; 38: 479-84.
- RAMOS-REMUS C, HERNANDEZ-RIOS G, DURAN-BARRAGAN S *et al.*: Fifteen-year trends of long-term disability and sick leaves in ankylosing spondylitis. *Clin Rheumatol* 2011; 30: 361-7.
- RAFIA R, ARAR, PACKHAM J, HAYWOOD KL, HEALEY E: Healthcare costs and productivity losses directly attributable to ankylosing spondylitis. *Clin Exp Rheumatol* 2012; 30: 246-53.
- STRÖMBECK B, JACOBSSON LT, BREMANDER A *et al.*: Patients with ankylosing spondylitis have increased sick leave—a registry-based case-control study over 7 yrs. *Rheumatology (Oxford)* 2009; 48: 289-92.
- BOONEN A, CHORUS A, MIEDEMA H, VAN DER HEIJDE D, VAN DER TEMPEL H, VAN DER LINDEN S: Employment, work disability, and work days lost in patients with ankylosing spondylitis: a cross sectional study of Dutch patients. *Ann Rheum Dis* 2001; 60: 353-8.
- MAU W, LISTING J, HUSCHER D, ZEIDLER H, ZINK A: Employment across chronic inflammatory rheumatic diseases and comparison with the general population. *J Rheumatol* 2005; 32: 721-8.
- BOONEN A, CHORUS A, MIEDEMA H *et al.*: Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. *Ann Rheum Dis* 2001; 60: 1033-9.
- MARENGO MF, SCHNEEBERGER EE, CITERA G, COCCO JA: Work status among patients with ankylosing spondylitis in Argentina. *J Clin Rheumatol* 2008; 14: 273-7.
- WARD MM, REVEILLE JD, LEARCH TJ, DAVIS JC JR, WEISMAN MH: Impact of ankylosing spondylitis on work and family life: comparisons with the US population. *Arthritis Rheum* 2008; 59: 497-503.
- BOONEN A, BOONE C, ALBERT A, MIELANTS H: Understanding limitations in at-work productivity in patients with active ankylosing spondylitis: the role of work-related contextual factors. *J Rheumatol* 2015; 42: 93-100.
- MAKSYMOWYCH WP, GOOCH KL, WONG RL, KUPPER H, VAN DER HEIJDE D: Impact of age, sex, physical function, health-related quality of life, and treatment with adalimumab on work status and work productivity of patients with ankylosing spondylitis. *J Rheumatol* 2010; 37: 385-92.
- GORDEEV VS, MAKSYMOWYCH WP, SCHACHNA L, BOONEN A: Understanding presenteeism in patients with ankylosing spondylitis: contributing factors and association with sick leave. *Arthritis Care Res (Hoboken)* 2014; 66: 916-24.
- HEALEY EL, HAYWOOD KL, JORDAN KP, GARRATT A, PACKHAM JC: Impact of ankylosing spondylitis on work in patients across the UK. *Scand J Rheumatol* 2011; 40: 34-40.
- SIEPER J, RUDWALEIT M, BARALIAKOS X *et al.*: The assessment of SpondyloArthritis International Society (ASAS) handbook: a guide to assess spondyloarthritis. *Ann Rheum Dis Suppl* 2009; 68 (Suppl. 2): ii1-ii44.
- REILLY MC, GOOCH KL, WONG RL, KUPPER H, VAN DER HEIJDE D: Validity, reliability and responsiveness of the Work Productivity and Activity Impairment Questionnaire in ankylosing spondylitis. *Rheumatology (Oxford)* 2010; 49: 812-9.
- GARRETT S, JENKINSON T, KENNEDY LG, WHITELOCK H, GAISFORD P, CALIN A: A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol* 1994; 21: 2286-91.
- CALIN A, GARRETT S, WHITELOCK H *et al.*: A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. *J Rheumatol* 1994; 21: 2281-5.
- JENKINS CD, STANTON BA, NIEMCRYSK SJ, ROSE RM: A scale for the estimation of sleep problems in clinical research. *J Clin Epidemiol* 1988; 41: 313-21.
- GROUP TE: EuroQol— a new facility for the

- measurement of health-related quality of life. *Health Policy* 1990; 16: 199-208.
34. REVICKI DA, RENTZ AM, LUO MP, WONG RL: Psychometric characteristics of the short form 36 health survey and functional assessment of chronic illness Therapy-Fatigue subscale for patients with ankylosing spondylitis. *Health Qual Life Outcomes* 2011; 22: 9-36.
35. CELLA D, LAI JS, CHANG CH, PETERMAN A, SLAVIN M: Fatigue in cancer patients compared with fatigue in the general United States population. *Cancer* 2002; 94: 528-38.
36. YELLEN SB, CELLA DF, WEBSTER K, BLENDOWSKI C, KAPLAN E: Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage* 1997; 13: 63-74.
37. MARGOLIS RB, TAIT RC, KRAUSE SJ: A rating system for use with patient pain drawings. *Pain* 1986; 24: 57-65.
38. JENKINSON TR, MALLORIE PA, WHITELOCK HC, KENNEDY LG, GARRETT SL, CALIN A: Defining spinal mobility in ankylosing spondylitis (AS): the Bath AS Metrology Index. *J Rheumatol* 1994; 21: 1694-8.
39. VAN DER LINDEN S, VALKENBURG HA, CATS A: Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum* 1984; 27: 361-68.
40. HAGLUND E, PETERSSON IF, BREMANDER A, BERGMAN S: Predictors of presenteeism and activity impairment outside work in patients with spondyloarthritis. *J Occup Rehabil* 2015; 25: 288-95.
41. TRAN-DUY A, NGUYEN TT, THIJS H *et al.*: Longitudinal analyses of presenteeism and its role as a predictor of sick leave in patients with ankylosing spondylitis. *Arthritis Care Res (Hoboken)* 2015; 67: 1578-85.
42. VAN DER WEIJDEN MA, BOONEN A, VAN DER HORST-BRUIJNSMA IE: Problems in work participation and resource use should not be underestimated in patients with early spondyloarthritis. *J Rheumatol* 2014; 41: 2413-20.
43. BOONEN A, BRINKHUIZEN T, LANDEWÉ R, VAN DER HEIJDE D, SEVERENS JL: Impact of ankylosing spondylitis on sick leave, presenteeism and unpaid productivity, and estimation of the societal cost. *Ann Rheum Dis* 2010; 69: 1123-8.
44. ROHEKAR S, POPE J: Assessment of work disability in seronegative spondyloarthritis. *Clin Exp Rheumatol* 2010; 28: 35-40.
45. SIEPER J, HOLBROOK T, BLACK CM, WOOD R, HU X, KACHROO S: Burden of illness associated with non-radiographic axial spondyloarthritis: a multiperspective European cross-sectional observational study. *Clin Exp Rheumatol* 2016 Aug 31.
46. CALIN A, EDMUNDS L, KENNEDY LG: Fatigue in ankylosing spondylitis – why is it ignored? *J Rheumatol* 1993; 6: 991-15.
47. SCHNEEBERGER EE, MARENGO MF, DALPRA F, MALDONADO COCCO JA, CITERA G: Fatigue assessment and its impact in the quality of life of patients with ankylosing spondylitis. *Clin Rheumatol* 2015; 3: 497-501.
48. DUMUS D, SARISOY G, ALAYLI G *et al.*: Psychiatric symptoms in ankylosing spondylitis: their relationship with disease activity, functional capacity, pain and fatigue. *Compr Psychiatry* 2015; 62: 170-7.
49. LOPEZ-MEDINA C, SCHIOTIS RE, FONTUGALDE P *et al.*: Assessment of fatigue in spondyloarthritis and its association with disease activity. *J Rheumatol* 2016; 4: 751-7.
50. BEDAIWI M, SARI I, THAVANESWARAN A, AYEARST R, HAROON R, INMAN RD: Fatigue in ankylosing spondylitis and non-radiographic axial spondyloarthritis: Analysis from a longitudinal observation cohort. *J Rheumatol* 2015; 12: 2354-60.
51. GOSSECL, DOUGADOS M, D'AGOSTINO MA, FAUTREL B: Fatigue in early axial spondyloarthritis. Results from the French DESIR cohort. *Joint Bone Spine* 2016; 4: 427-31.
52. FABREGUET I, KOUMAKIS E, BURKI V *et al.*: Assessment of work instability in spondyloarthritis: a cross-sectional study using the ankylosing spondylitis work instability scale. *Rheumatology (Oxford)* 2012; 51: 333-7.
53. GIOVANNINI L, ORLANDI M, LODATO C *et al.*: One year in review 2015: spondyloarthritis. *Clin Exp Rheumatol* 2015; 6: 769-78.