Behçet's syndrome and health-related quality of life: influence of symptoms, lifestyle and employment status

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ABSTRACT

Objective. *Behçet's syndrome (BS) is a chronic multisystemic disorder. The complex pattern of BS symptoms can effect negatively on patients' quality of life. The aim of this study is to evaluate the influence of BS symptoms, oral health related lifestyles and employment status on Health Related Quality of Life (HRQoL).*

Methods. *A questionnaire was mailed to a cohort of 641 adult members of the Behçet's Syndrome Society (BSS) and patients attending a Behçet's syndrome centre in the UK. Respondents gave information on socio-demographic characteristics, disease duration, current symptoms, symptom control, health related lifestyle, diet, smoking and alcohol, employment status and quality of life (the EQ-5D index).*

Results. *315 out of 426 BS participants (males: females=136:179) were recruited. BS symptoms and EQ-5D score model (R=0.67 and R^2=0.45) and standardised coefficients for symptoms were; arthropathy (-0.336), headache (-0.227), neurological problems (-0.135), pathergy reaction (-0.119) and skin lesions (-0.107) in decreasing order. This finding was similar to a 2009 study of the same cohort. Regression analysis of tobacco consumption revealed that tobacco use was a risk factor for decreasing the EQ-5D score (beta value = - 0.72, p=0.001). Using an effective mouthwash has a positive impact on HRQoL (beta value= 0.149 and p=0.012). The mean EQ-5D in patients who continued in employment and who were not receiving benefits was better compared to other sub groups.*

Conclusion. *BS symptoms, Employment status, a healthy lifestyle combined with a good oral health have a significant impact on the HRQoL of BS patients.*

Introduction

Behçet's syndrome (BS) is a chronic inflammatory multi-systemic disorder and can significantly increase morbidity and mortality (1, 2). The diagnosis of BS is based primarily on a combination of clinical manifestations. BS may affect every age group, but onset before puberty or after the sixth decade is relatively rare (3). The complex pattern of symptoms in adults with BS can negatively impact on their psychological, physical and social wellbeing, and consequently limiting various daily activities. The current WHO definition of health, verbalised in 1948, describes health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (4). It has been recommended that the measure of health should be able to encompass not only differences in length of life but also differences in the quality of life (QoL), in terms of lack of disease symptoms and ability to function. WHO has developed several classification systems measuring gradations of health using different health variables including disability, functioning, perceived QoL and wellbeing (5).

The importance of QoL was recognised by the UK National Health Service (NHS) Review Working Paper on Medical Audit that saw QoL as an essential part of the audit procedure (6). Most of the previous studies looked at the relationship between disease activity and QoL (7-9), compared the QoL of patients with other groups (10) or explored the differential or cumulative impact of multiple symptoms on QoL (11). Additionally, Mumcu *et al.* in 2009 investigated the impact of oral health status on QoL and assessed the impact of oral health care (12).

Health Related Quality of Life (HRQoL) is a legitimate construct for evaluating treatment and its side ef-

fects. It is significantly associated with patients' survival regardless of the time of disease assessment (13). Many studies have used HRQoL as a tool to predict mortality (14, 15). The main advantage of generic HRQoL measures is that they allow comparison of various domains of QoL for the condition being studied, as well as across populations, group of patients and disease states. One of the most widely used generic HRQoL measures is the Euro QoL EQ-5D. The EQ-5D questionnaire is primarily designed for self-completion by respondents and is ideally suited for use in postal surveys, in clinics and face-to-face interviews. It can provide both a health profile and an index for individuals or groups that allow clinical and economic evaluation of health intervention (16, 17).

Since 2009 when baseline data was collected to assess the impact of BS on the QoL of BS patients, there have been significant health care interventions in this population cohort, particularly in those using the three commissioned Behçet's Centres. Notable among these interventions are changes to the type of medication and the guidelines of BS treatment. Others include oral health promotion and lifestyle interventions on; smoking and other types of tobacco use, alcohol, dietary habits and oral hygiene.

To our knowledge, no studies have reassessed the QoL in BS cohort after a number of years of significant healthcare interventions. The purpose of this study therefore is to assess and correlate the EQ-5D with BS symptoms, lifestyle factors (smoking/tobacco, alcohol, diet and oral care habits), career changes and applying for welfare support.

Materials and methods

The data of 641 potential participants was provided by the Behçet's Syndrome Society (BSS) and the Behçet's Patients Centres (BPC). 426 who returned the questionnaires had a confirmed diagnosis of BS. 111 BS patients were excluded in our analysis. The exclusion criteria were; those aged under 18, pregnant mothers, lactating mothers, incomplete questionnaire (missing answers) and non-respondents. This resulted in the participants' number decreasing to 315 [males: females = 136:179; mean age = 41.1±23.3: 52±13.2]. A survey pack containing a cover letter, information sheet, survey questionnaire and pre-paid envelope was sent to each participant. One reminder was sent to increase the response rate. This study applied a cross-sectional postal survey study design, the same methodology used in a 2009 study on this same cohort of BS patients (11). Ethical approval was obtained from the Queen Mary Research Ethics Committee; City Research Ethical Committee (COREC) approved study "Immune-regulation at the mucosal barrier" (P/03/122) at Barts Health NHS Trust in full compliance with the Helsinki Declaration (18).

The survey questionnaire gathered information on participants' socio-demographic (sex, age, ethnicity, marital status and education) and disease-related characteristics (age of diagnosis, current symptoms and symptom control). The symptoms recorded were those experienced by BS patients on the day the survey was completed. This included a list of the 10 most common BS manifestations; mouth ulcers, genital ulcers, skin lesions, fatigue, arthropathy, gastrointestinal symptoms, ocular problems, pathergy reaction, headache and other neurological manifestations (minus headache). Information on tobacco use (cigarettes, cigar, pipes, cannabis and snuff), alcohol consumption and portions of fruits and vegetables eaten in a week were also obtained.

Oral hygiene measures included oral hygiene advocacy, use of dental floss, interdens/toothpicks/wood sticks, dental disclosing tablets, dental chewing gum, mouthwash, inter-space brush, electric toothbrush, lauryl sulphate free or smokers' toothpaste and other measures including oral irrigators for orthodontic appliances or fixed bridges, denture cleaners, tongue scrapers and cleaners.

Questions were also asked on career changes as a result of BS: No-never needed to change career, Yes-reduced my working hours, Yes-changed to a less stressful job, Yes-have had to give up work. In addition, claiming benefits as a direct result of BS were: No- not claiming benefits, No-unsuccessful in claiming Disability Living Allowance (DLA) [DLA, is a tax-free benefit for disabled people who need financial assistance with mobility and /or care], No-unsuccessful in claiming Employment and Support Allowance (ESA) [ESA, is a financial benefit for people who are unable to work due to illness or disability], No-unsuccessful in claiming Attendance Allowance (AA) [AA, is a financial benefit for severely disabled people aged 65 or over who need help with personal care], No-not now but have received benefits in the past, Yes-receive DLA, Yes-receive ESA, Yes-receive AA.

The EQ-5D consists of five questions covering the following health domains: mobility, self-care, usual activity, pain and anxiety/depression. The UK calculation score programme was used to obtain the EQ-5D score of each BS patient. Participants were asked to rate their problems using a 1–3 scale. These were 1 (no problems), 2 (moderate problems) and 3 (extreme problems). This results in a five-digit score for each participant, which reflects a single measure for their state of health. The concept of health in EQ-5D encompasses both positive aspects (well-being) and negative aspects (illness). The Health Utility scores in the UK EQ-5D value set range from [-0.59] for the worst possible health status to [1.0] for perfect health (19).

Statistical analysis

The data was analysed using SPSS Statistics software (v. 20 for Windows; IBM Corporation, New York, USA). Descriptive analysis (mean and standard deviation), *t*-test, ANOVA, MANOVA and the Chi-square test were applied to detect the differences between study variables. Multiple linear regression analysis was performed in this study, as the outcome measure resembled the normal distribution. R^2 and Beta values were used for the interpretation of the regression analysis outcomes [R^2 is a statistical measure of how close the data are to the fitted regression line and Beta value (standardised regression coefficients) is a measure of how strongly each predictor variable influences the dependent variable]. The higher the beta value the greater the impact of the predictor variables on the dependent

variable. It is also known as the coefficient of determination or the coefficient of multiple determinations for multiple regressions. One-way ANOVA tests were also carried out respectively to explore the association of the variables with EQ-5D index, and to determine if there are any significant differences between the means of three or more independent (unrelated) groups by using Fisher's Least Significant Difference (LSD) test. A *p*-value <0.05 is accepted to be a significant result.

Results

426 participants who returned the questionnaires had a confirmed diagnosis of BS. The total number of participants dropped to 315 (74%) [males: females = 136:179; mean age = 41.1±23.3: 52±13.2].

Women respondents in this study were 56.8% compared to 43.2% men. Almost all the respondents were White-British 93.6%. The EQ-5D scores of 19-30 years old participants were 0.761±0.206 but less with other age ranges. The mean EQ-5D of single BS patients was 0.664±0.118, while that for the married group was 0.597±0.012. Patients in different education levels had nearly similar score of EQ-5D. 55% and 58.4% of our cohort consumed between 1–15 portions of vegetables and fruits per week with EQ-5D score of 0.646±0.234 and 0.591±0.170 respectively. About 45% of the participants had never smoked and 124 patients out of 295 smoked in the past. 57.5% and 33.3% had moderate and extreme pain respectively. Almost half of our cohort suffered from anxiety and depression. 40% of patients reported that they have problems with washing and dressing themselves (self-care) and 77.2% had problems performing common daily activities. More than half of the cohort has had to stop working and 61% of the whole cohort claimed different forms of benefit because of morbidity associated with BS symptoms (Table I).

Analysis using the MANOVA test revealed that the BS patients symptoms were significantly associated with the gender and ethnicity (p=0.022, and p=0.001 respectively). The results indicated that the number of symptoms was

Table I. Socio-demographic characteristics of the BS cohort (n=315).

Variables	n	EQ-5D index Mean ± SD	*p*-value
Gender	**315**		
Men	136	0.629 ± 0.229	0.83
women	179	0.6227 ± 0.225	
Age in years	**297**		
19-30	19	0.761 ± 0.206	
31-40	42	0.622 ± 0.163	0.187
41-50	75	0.606 ± 0.24	
51-60	81	0.625 ± 0.19	
61-70	58	0.568 ± 0.202	
71 and over	22	0.642 ± 0.209	
Marital	**293**		
Single	55	0.664 ± 0.118	
Married	115	0.597 ± 0.012	0.083
Separated	33	0.626 ± 0.220	
Divorced	42	0.591 ± 0.133	
Ethnicity	**297**		
White British	278	0.624 ± 0.220	
White non-British	6	0.712 ± 0.05	**0.012***
Asian	8	0.620 ± 0.112	
Others	5	0.275 ± 0.241	
Education level	**293**		
No education/degree	43	0.581 ± 0.209	
Secondary school (O-level/GCSE)	80	0.620 ± 0.224	**0.005***
A level	31	0.527 ± 0.247	
Technical qualifications	43	0.598 ± 0.219	
First degree (university)	64	0.711 ± 0.209	
Higher degree (post graduate)	32	0.633 ± 0.222	
Fruit portions/week	**289**		
0 (no fruit)	19	0.556 ± 0.239	
1-15 portions/week	169	0.646 ± 0.234	0.44
16-29 portions/week	70	0.624 ± 0.240	
>30 portions/week	31	0.620 ± 0.207	
Vegetable portions/week	**287**		
0 (no vegetables)	18	0.544 ± 0.216	
1-15 portions/week	159	0.591 ± 0.170	0.07
16-29 portions/week	66	0.625 ± 0.243	
>30 portions/week	44	0.633 ± 0.221	
Tobacco	**295**		
Never	133	0.655 ± 0.223	
Yes (currently)	31	0.562 ± 0.227	**0.027***
Yes (in the past)	124	0.616 ± 0.200	
Yes (with cannabis)	10	0.492 ± 0.272	
Career changes	**292**		
No	72	0.668 ± 0.196	
Yes (reduced my working hours)	59	0.647 ± 0.223	**0.048***
Yes (changed to a less stressful job)	22	0.584 ± 0.268	
Yes (have had to give up work)	139	0.585 ± 0.220	
Benefit claim	**295**		
No	115	0.690 ± 0.205	
Yes (receive DLA)	81	0.560 ± 0.235	
Yes (receive ESA)	56	0.623 ± 0.212	**0.013***
Yes (receive attendance allowance)	12	0.571 ± 0.240	
No (unsuccessful in claiming DLA)	11	0.625 ± 0.201	
No (unsuccessful in claiming ESA)	4	0.592 ± 0.362	
Not now but have received benefits in the past	16	0.579 ± 0.190	

*p-value was significant at the level <0.05.
Values are presented as mean ± SD. *t*-test and ANOVA test were performed to obtain the significance between variables.

Table II. The differences of socio-demographic and symptoms characteristics of BS patients (n=315) based on the mean of BS symptoms, patients' age and gender.

	MANOVA Test		Chi-Square Test
Variables	Mean of BS symptoms *p*-value	Patients' age *p*-value	Gender *p*-value
Gender	**0.022***	0.157	-
Ethnicity	**0.001***	**0.002***	**0.024***
Education level	0.345	0.404	**0.010***
Marital status	0.692	0.281	0.724
Mouth ulcers	**0.001***	0.448	**0.001***
Genital ulcers	**0.001***	0.621	**0.001***
Skin lesions	**0.001***	0.983	0.152
Fatigue	**0.001***	0.500	**0.024***
Arthropathy	**0.001***	**0.037***	**0.005***
GIT problems	**0.042***	0.862	**0.016***
Eye problems	**0.001***	0.735	0.164
Pathergy reaction	**0.021***	0.134	0.862
Headaches	**0.001***	0.770	0.271
Other CNS problems	**0.001***	0.556	0.204
Career change	0.474	0.631	**0.048***
Benefit claim	0.839	0.869	**0.014***

*p-value was significant at the level <0.05.

Table III. The impact of BS symptoms on the EQ-5D index (n=315).

Predictors	n (yes)	Unstandardised Coefficients		Standardised Coefficients	*p*-value
		B	Std. Error	Beta	
Mouth ulcers	248	0.014	0.015	0.046	0.347
Genital ulcers	145	-0.017	0.012	-0.069	0.165
Skin lesions	150	-0.026	0.012	**-0.107**	**0.028***
Fatigue	269	-0.029	0.018	-0.084	0.107
Arthropathy	244	-0.098	0.015	**-0.336**	**0.001***
Gastrointestinal symptoms	187	-0.023	0.012	-0.092	0.066
Occular problems	129	-0.002	0.011	-0.007	0.882
Pathergy reaction	62	-0.036	0.014	**-0.119**	**0.011***
Headache	193	-0.056	0.012	**-0.227**	**0.001***
Other neurological problems	111	-0.034	0.012	**-0.135**	**0.006***

a. Dependent variable: EQ-5D.
Predictors: mouth ulcers, genital ulcers, skin lesions, fatigue, arthropathy, gastrointestinal symptoms, occular problems, pathergy reaction, headache, other neurological problems.
*p-value was significant at the level <0.05.
Beta value represents the influence of each predictor on the dependent variable. BS symptoms which had impact on patients' HRQoL were: arthropathy, headache, neurological features, pathergy reaction and skin lesions in decreasing order.

different between males and females. Similarly, the number of symptoms was varied between the different ethnic groups. In addition, the mean of BS symptoms had significant association with the individual BS symptoms (p-values were <0.005). However, there was significant differences between patients' age with ethnicity and with arthropathy (p=0.002 and p=0.037, respectively).

When Chi-Square test was performed to reveal the association between the categorical variables and patients' gender, we found that patients' educational level (p=0.01), patients ethnicities (p=0.024), claiming benefits (p=0.014) and career change (p=0.048) all vary significantly with gender. The BS symptoms namely oral ulcer, genital ulcer, arthropathy, fatigue and gastric intestinal tract (GIT) problems (which included any combination of abdominal pain, and diarrhoea/constipation with or without blood and mucous) were significantly higher in females than males in this cohort (p values were <0.05) (Table II).

The study model of the BS symptoms and EQ-5D score was (R=0.67, R^2=0.45, p=0.001). The regression analysis revealed that the symptoms which had impact on patients' HRQoL were: arthropathy, headache, neurological features (minus headache), and pathergy reaction and skin lesions in decreasing order (p-values were <0.05 and the standardised coefficients beta value were; -0.336, -0.227, -0.135, -0.119 and -0.107 respectively). In addition, 85.4% of patients suffered from fatigue (Table III).

A multiple regression analysis was performed to evaluate the impact of using a number of oral hygiene items/factors on EQ-5D. The use of mouthwash was significant (beta value = 0.149, p=0.012) and had a positive impact on the HRQoL. Using other dental hygiene product items just failed to reach significance (p=0.052) (Table IV).

The single linear regression result of tobacco consumption revealed that tobacco use was a risk factor for decreasing the EQ-5D score; beta value = - 0.72, p=0.001. Moreover, the p-value between groups (never, yes-currently, yes-in the past, yes-with cannabis) was significant (p=0.027) (Table V).

BS patient group who 'currently drink alcohol' had a significantly better EQ-5D than those who 'never drink alcohol' (p=0.030). In addition, those who 'currently drink alcohol' had significantly better EQ-5D result compared to those who 'drink in the past' (p=0.034) (Fig. 1). The amount of alcohol intake per week did not reveal any statistical significant variation with patients' EQ-5D index. Chewing paan was not statistically significant as the majority of our cohort were White British patients who traditionally do not chew paan. The interaction between number of portions of fruit and vegetables per week had no impact on the EQ-5D.

Claiming benefits and career changes of BS patients have a significant impact on their EQ-5D scores in ANOVA analysis (p=0.013 and p=0.048, respectively). Furthermore, ANOVA and LSD tests showed that adult BS patients who were not receiving any benefits and have never tried to claim any benefit in the past have significantly better

Table IV. The impact of oral hygiene factors on the EQ-5D index (n=315).

Predictors	n (yes)	Unstandardised Coefficients		Standardised Coefficients	*p*-value
		B	Std. Error	Beta	
Dental Floss	147	-0.013	0.027	-0.029	0.628
Interdens/Toothpicks/Woodsticks	91	0.024	0.029	0.048	0.407
Dental Disclosing Tablets	6	0.167	0.092	0.105	0.069
Dental Chewing Gum	22	0.075	0.050	0.088	0.136
Mouthwash	196	0.070	0.027	**0.149**	**0.012***
Interspace Toothbrush	51	0.022	0.036	0.036	0.551
Electric Toothbrush	149	-0.031	0.026	-0.068	0.245
Sensodyne or Smokers Toothpaste	94	0.038	0.029	0.077	0.187
Other Dental Hygiene Products	27	0.093	0.048	0.114	**0.052**

a. Dependent variable: EQ-5D.
Predictors: teeth cleaning times a day, interdens/toothpicks/woodsticks, dental disclosing tablets, electric toothbrush, dental chewing gum, other dental hygiene products 2014, sensodyne or smokers toothpaste, mouthwash, dental floss, interspace toothbrush.
**p*-value was significant at the level <0.05.
The use of mouthwash was significant (beta value =0.149, *p*=0.012) and had a positive impact on the HRQoL. Using other dental hygiene products item (other dental hygiene products such as: oral irrigators for orthodontic appliance or a fixed bridge, denture cleaner, tongue scraper and cleaner) was also almost significant (*p*=0.052).

Table V. The regression analysis of tobacco smoking and the EQ-5D index (n=313).

Regression results	Tobacco use (predictors variable)	EQ-5D (dependent variable)
Linear regression (beta value)		-0.72
p-value		**0.001***
number	313	289

**p*-value was significant at the level <0.05.

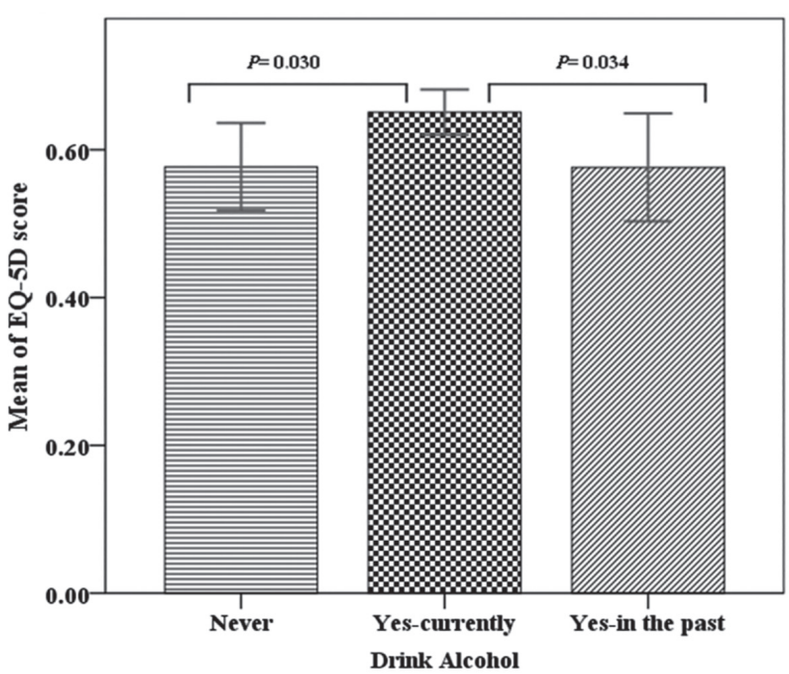

Fig. 1. ANOVA test for alcohol consumption per week of BS patients and its impact on the EQ-5D index (n=296).
BS patients 'currently drink alcohol' group had a significantly better EQ-5D than those who 'never drink alcohol' (*p*=0.030). Moreover, those who 'currently drink alcohol' had significantly higher EQ-5D scores compared to those who 'drink in the past' (*p*=0.034).

EQ-5D than those who were receiving DSA (mean differences = 0.130 and *p*=0.001) (Table VI). Also patients not receiving any benefits tended to have a better HRQoL but the statistical analysis just failed to reach significance compared with patients who had benefits in the past. There were no significant differences in the EQ-5D index between other groups in the claiming benefits variables.

The multiple comparison between the variables of *career changes* as a result of BS revealed that BS patients who had to give up work as a result of BS have significantly worse EQ-5D than BS patients who were in work (mean differences= 0.074 and *p*=0.024) (Table VII). There were no statistical significant differences between the other groups.

Discussion

Although most of the studies of BS have focused on assessing HRQoL of patients at the time of study (cross-sectional study), less attention has been devoted to regular monitoring of HRQoL in BS patients over a period of time or after receiving different interventions. To our knowledge, this is the first study of BS patients to review the role of health related lifestyles and employment status on QoL using the EQ-5D index.

Our findings demonstrate that patients' gender had a significant association with most variables in this study such as ethnicity, education level, BS symptoms, and employment status. A low EQ-5D Utility score was observed in the married as opposed to the single respondents. This was similar to the results seen in the 2009 cohort (11). At first, this appears to be at variance with established data about other chronic diseases where marriage seems to have a protective and positive role on HRQoL (20, 21). However in BS, the additional burden of orogenital and skin lesions have a negative impact on patients' social and sexual behaviour and hence the outcome of HRQoL (22, 23). In addition, the EQ-5D of BS males and females was significantly higher in patients with high level of education attainment (undergraduate

Table VI. Claiming benefits by BS patient and the EQ-5D index (n=315).

Multiple comparisons						
LSD (I) benefit claim	(J) Benefit Claim	Mean difference (I-J)	Std. error	*p*-value	95% Confidence interval	
					Lower value	Upper value
No benefit claim	Yes (Receive DLA)	**0.13037**	0.03165	**0.001***	0.0681	0.1927
	Yes (Receive ESA)	0.06703	0.03556	0.060	-0.0030	0.1370
	Yes (Receive AA)	0.11920	0.06620	0.073	-0.0111	0.2495
	No (Unsuccessful in claiming DLA)	0.06478	0.06887	0.348	-0.0708	0.2003
	No (Unsuccessful in claiming ESA)	0.09848	0.11099	0.376	-0.1200	0.3169
	Not now but have received benefits in the past	0.11122	0.05823	0.057	-0.0034	0.2258

Post hoc test (LSD) to compare between variable and the EQ-5D.
*p-value was significant at the level <0.05.
DLA:disability living allowance; AA: attendance allowance; ESA: Employment and Support Allowance.
BS patients not receiving any benefits and have never tried to claim any benefit in the past have significantly better EQ-5D than those who were receiving DSA (p=0.001). Also patients not receiving any benefits had almost significant result comparing with patients who had benefits in the past.

and post graduate degree) than those with lower level. This finding is similar to the results in other studies (24, 25), where patients with lower level of education attainment may require support services to improve their HRQoL. These findings highlight the importance of socio-demographic factors in HRQoL of BS patients.

When we applied the same statistical methods as those used in 2009 study the results showed that the BS symptoms which had the most impact on patients' HRQoL were arthropathy, headache, other neurological problems, pathergy reaction and skin problems in decreasing order. This was similar to the finding in 2009, where the greatest impact of BS symptoms on patients' HRQoL were arthropathy, neurological problems, pathergy reaction and gastrointestinal symptoms (11). Interestingly, 85.4% of BS patients had fatigue. However, symptom of fatigue did not have impact on their HRQoL. This supports the notion that BS patients are less likely to cope with chronic symptoms which are usually more severe, than with the more frequent symptoms such as ulcers and fatigue (11, 26, 27).

The distribution of patients' symptoms found in this study was comparable to the 2009 (particularly for arthropathy, gastrointestinal, and neurological) (11). However, this was considerably higher when compared to other studies of BS patients (28-30). The reasons may be that these were anonymised self-reported questionnaires, which meant that no medical records could be inspected to exclude comorbidities which may share similar symptoms with BS.

Gastrointestinal symptoms are not significant in this study compared to the findings in 2009. This may be due to the increased use of topical oral medication as opposed to systemic oral medication causing irritation of the bowel lining, and the introduction of medication requiring intramuscular and intravenous infusion. Additionally, enhancing oral hygiene and oral health using topical bespoke steroid based mouthwash in the past five years has resulted in a reduction in the use of systemic medication. Similarly, the use

Table VII. Career changes of BS patient and theEQ-5D index (n=315).

Multiple comparisons						
LSD (I) Career changes	(J) Career changes	Mean difference (I-J)	Std. error	*p*-value	95% Confidence interval	
					Lower value	Upper value
No change in the career	Yes (reduced my working hours)	0.02091	0.03949	0.597	-0.0568	0.0986
	Yes (changed to a less stressful job)	0.08333	0.05478	0.129	-0.0245	0.1911
	Yes (have had to give up work)	**0.07420**	0.03269	**0.024***	0.0099	0.1385
Yes (reduced my working hours)	No	-0.02091	0.03949	0.597	-0.0986	0.0568
	Yes (changed to a less stressful job)	0.06242	0.05617	0.267	-0.0481	0.1730
	Yes (have had to give up work)	0.05329	0.03498	0.129	-0.0155	0.1221
Yes (changed to a less stressful job)	No	-0.08333	0.05478	0.129	-0.1911	0.0245
	Yes (reduced my working hours)	-0.06242	0.05617	0.267	-0.1730	0.0481
	Yes (have had to give up work)	-0.00913	0.05162	0.860	-0.1107	0.0925
Yes (have had to give up work)	No	-**0.07420**	0.03269	**0.024***	-0.1385	-0.0099
	Yes (reduced my working hours)	-0.05329	0.03498	0.129	-0.1221	0.0155
	Yes (changed to a less stressful job)	0.00913	0.05162	0.860	-0.0925	0.1107

Post hoc test (LSD) to compare between variable and the EQ-5D.
*p-value was significant at the level <0.05.
BS Patients who had to give up work as a result of BS have a significantly worse EQ-5D than patients who were in work (p=0.024).

of diagnostic tests (*e.g.* calprotectin) as a marker for bowel inflammation (IBD) in the Behçet's clinics has led to the earlier treatment of gastrointestinal inflammation and hence, with consequent earlier symptom relief from distressing bowel symptoms.

This study also examined the impact of tobacco smoking, the intake of alcohol, diet and oral hygiene measures on HRQoL in BS patients. Tobacco smoking and the use of mouthwash were found to have a significant effect on QoL measured by EQ-5D. Smoking had a negative impact on HRQoL which is probably compounded by the effects of stress and depression in BS patients, causing increased smoking especially during periods of BS flare. Stress itself has been confirmed to impact negatively on QoL which may be the reason for this finding in our study (31). Smoking is also an established risk factor not only for cancer but also for cardiac and vascular diseases. However, a case series study of five BS ex-smoker patients showed that both smoking and nicotine-replacement therapy had beneficial effects on mucocutaneous lesions of BS patients (32).

The use of mouthwash was found to significantly impact positively on HRQoL in this study. This might be because medications in the form of mouthwashes are now used as first line drugs in the management of BS in UK centres to control the disease activity. This will invariably reduce symptoms and improve QoL of the patients. Moreover, this cohort of patients has been educated on the importance of improving their oral health through regular use of mouthwashes. This intervention has helped improve their oral health and as such, improve their QoL. New research which has found a strong link between BS activity and oral health (33-35) further supports this finding.

Interestingly, patients in this study who 'currently drink alcohol' had a positive perception about their QoL. Whereas in the other patient groups ('never drank alcohol' and 'used to drink alcohol but in the past'), their EQ-5D did not relation to drink alcohol. It is possible that the finding that the 'currently drink' alcohol is the patient personal perception as those who drink alcohol are more likely to socialise and report having a good QoL.

Although portions of fruits and vegetables eaten per week were not found to significantly impact on HRQoL in this study, the importance of eating adequate amount of fruits and vegetables (5 portions/day) as recommended in healthy eating guidelines cannot be overemphasised. Only 10% of this study's respondents reported eating the recommended amount of 5 portions of fruits and vegetables per day (35 portions per week). Given the health benefits of a diet rich in fruits and vegetables (36), more should be done to encourage adequate consumption in BS patients. It may be possible that the acidic nature of some fruits and vegetables aggravate the symptoms of oral ulcers in BS patients helps to explain the low level of consumption. Hence, while encouraging adequate intake of fruit and vegetables in BS patients, a selection of fruits and vegetables that will not aggravate the symptoms of ulcers should be identified and recommended.

The health impact of redundancy and unemployment on health have been increasingly investigated since the period of high unemployment in the 1930s (37). Numerous studies have shown that ill health may itself lead to a greater risk of unemployment and benefits claims. Similarly, for people in poor health, who recognise that their chances of re-employment are reduced, job insecurity is a stressful life event (38). Similarly, our findings revealed that patients who had to stop working because of their BS have a worse EQ-5D than BS patients who were in work. In addition, patients who were not receiving any benefit and have never tried to claim any benefit in the past were significantly healthier than patients who were receiving disability living allowance.

The employment status and health related lifestyles measures including smoking and use of topical mouthwash have a significant impact on HRQoL of BS patients. Supporting BS patients with appropriate treatment resulting in good symptom control and it enables them to cope in their working environment which will improve their QoL. Continuous monitoring of HRQoL of BS patients is also recommended.

The low levels of both fruit and vegetable consumption in this study cohort emphasises the need for dietary intervention. Eating a well-balanced diet rich in daily recommended portions of fruit and vegetables can also boost BS patients' health and enhance their QoL. Smoking in this study was shown to have a significantly negative impact on the EQ-5D score. This highlights the importance of smoking cessation advice to patients with BS. In addition, a dedicated smoking cessation service intervention is essential tool for promoting good HRQoL in BS patients.

In this study, the questionnaire compared the results with a similar study carried out in 2009 on the same cohort of BS. Both questionnaires specifically asked whether they had experienced the symptoms as a result of BS. However, there are some limitations related to the questionnaire. Firstly the questionnaire was entirely patients reported perception of their symptoms with no ability to investigate whether the comorbidity was being reported as a BS. Other limitations are that the question related to the patients' symptoms would need greater clarification. The addition of further questions should be included to find out more about the disease severity and the comorbidities. This is particularly important in both our cohorts of 2009 and 2014 where a large number of patients were in their mid-forties and over.

The novelty of this study lies in the follow up of the QoL of a cohort of patients using the EQ-5D 4 years later and 2 years after of the introduction of a new 'one stop shop' model of care for BS patients in the UK. It shows that BS symptoms continue to have an effect on the patients' QoL, also factors such as the patients' lifestyle and employment status which may have a considerable impact on the HRQoL of BS patients.

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References

1. SAVEY L, RESCHE-RIGON M, WECHSLER B: Ethnicity and association with disease manifestations and mortality in Behçet's disease. *Orphanet J Rare Dis* 2014; 9: 42.
2. KUROKAWA MS, SUZUKI N: Behçet's disease. *Clin Exp Med* 2004; 4: 10-20.
3. DEUTER CM, KÖTTER I, WALLACE GR, MURRAY PI, STÜBIGER N, ZIERHUT M: Behçet's disease: Ocular effects and treatment. *Prog Ret Eye Res* 2008; 27: 111-36.
4. JADAD AR, O'GRADY L: How should health be defined? BMJ 2008; 337: a2900.
5. JAKOB R, ÜSTÜN B, MADDEN R, SYKES C: The WHO family of international classifications. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2007; 50: 924-31.
6. GILWORTH G, CHAMBERLAIN MA, BHAKTA B, HASKARD D, SILMAN A, TENNANT A: Development of the BD-QoL: a quality of life measure specific to Behçet's disease. *J Rheumatol* 2004; 31: 931-7.
7. BODUR H, BORMAN P, OZDEMIR Y, ATAN C, KURAL G: Quality of life and life satisfaction in patients with Behçet's disease: relationship with disease activity. *Clin Rheumatol* 2006; 25: 329-33.
8. MUMCU G, INANC N, ERGUN T *et al*.: Oral health related quality of life is affected by disease activity in Behçet's disease. *Oral Dis* 2006; 12: 145-51.
9. SENUSI A, SEOUDI N, BERGMEIER LA, FORTUNE F: Genital ulcer severity score and genital health quality of life in Behçet's disease. *Orphanet J Rare Dis* 2015; 10: 117.
10. ALDER MN, FISHER M, YAZICI Y: Behçet's syndrome patients have high levels of functional disability, fatigue and pain as measured by a Multi-dimensional Health Assessment Questionnaire (MDHAQ). *Clin Exp Rheumatol* 2008; 26 (Suppl. 50): S110-3.
11. BERNABÉ E, MARCENES W, MATHER J, PHILLIPS C, FORTUNE F: Impact of Behçet's syndrome on health-related quality of life: influence of the type and number of symptoms. *Rheumatology* 2010; 49: 2165-71.
12. MUMCU G, NIAZI S, STEWART J *et al*.: Oral health and related quality of life status in patients from UK and Turkey: a comparative study in Behçet's disease. *J Oral Pathol Med* 2009; 38: 406-9.
13. SADETSKY N, HUBBARD A, CARROLL PR: Predictive value of serial measurements of quality of life on all-cause mortality in prostate cancer patients: data from CaPSURE™ (cancer of the prostate strategic urologic research endeavor) database. *Qual Life Res* 2009; 18: 1019-27.
14. TSAI SY, CHI LY, LEE C, CHOU P: Health-related quality of life as a predictor of mortality among community-dwelling older persons. *Eur J Epidemiol* 2007; 22: 19-26.
15. KROENKE CH, KUBZANSKY LD, ADLER N: Prospective change in health-related quality of life and subsequent mortality among middle-aged and older women. *Am J Public Health* 2008; 98: 2085-91.
16. BROOKS R, GROUP EQ: EuroQol: the current state of play. *Health Policy* 1996; 37: 53-72.
17. GROUP TEQ: EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy* 1990; 16: 199-208.
18. ASSOCIATION WM: World Medical Association "Declaration of Helsinki. Ethical principles for medical research involving human subjects". *Bull World Health Organ* 2001; 79: 373-4.
19. RABIN R, DE CHARRO F: EQ-5D: a measure of health status from the EuroQol Group. *Ann Med* 2001; 33: 337-43.
20. HSU PC, KRAJDEN M, YOSHIDA EM, ANDERSON FH, TOMLINSON GA, KRAHN MD: Does cirrhosis affect quality of life in hepatitis C virus-infected patients? *Liver Int* 2009; 29: 449-58.
21. ORR JG, HOMER T, TERNENT L *et al*.: Health related quality of life in people with advanced chronic liver disease. *J Hepatol* 2014; 61: 1158-65.
22. ERTAM I, KITAPCIOGLU G, AKSU K, KESER G: Quality of life and its relation with disease severity in Behçet's disease. *Clin Exp Rheumatol* 2009; 27: S18.
23. KOÇAK M, BAŞAR MM, VAHAPOĞLU G: The effect of Behçet's disease on sexual function and psychiatric status of premenopausal women. *J Sex Med* 2009; 6: 1341-8.
24. REGIDOR E, BARRIO G, DE LA FUENTE L, DOMINGO A, RODRIGUEZ C, ALONSO J: Association between educational level and health related quality of life in Spanish adults. *J Epidemiol Community Health* 1999; 53: 75-82.
25. BARBARESCHI G, SANDERMAN R, LEEGTE I, VELDHUISEN DJ, JAARSMA T: Educational level and the quality of life of heart failure patients: a longitudinal study. *J Card Fail* 2011; 17: 47-53.
26. SAKANE T, TAKENO M, SUZUKI N, INABA G: Behçet's Disease. *N Engl J Med* 1999; 341: 1284-91.
27. YURDAKUL S, YAZICI H: Behçet's syndrome. *Best Pract Res Clin Rheumatol* 2008; 22: 793-809.
28. BANG D, LEE J, LEE E *et al*.: Epidemiologic and clinical survey of Behçet's disease in Korea: the first multicenter study. *J Korean Med Sci* 2001; 16: 615-8.
29. YAZICI H, TÜZÜN Y, PAZARLI H, YURDAKUL S: Influence of age of onset and patient's sex on the prevalence and severity of manifestations of Behçet's syndrome. *Ann Rheum Dis* 1984; 43: 783-9.
30. GÜRLER A, BOYVAT A, TÜRSEN Ü: Clinical Manifestations of Behçet's Disease: An Analysis of 2147 Patients. *Yonsei Med J* 1997; 38: 423-7.
31. PARROTT AC: Does cigarette smoking cause stress? *Am Psychol* 1999; 54: 817.
32. CIANCIO G, COLINA M, CORTE R *et al*.: Nicotine-patch therapy on mucocutaneous lesions of Behçet's disease: a case series. *Rheumatology* 2010; 49: 501-4.
33. DURHAM J, FRASER H, MCCRACKEN G, STONE K, JOHN M, PRESHAW P: Impact of periodontitis on oral health-related quality of life. *J Dent* 2013; 41: 370-6.
34. HAYRAN O, MUMCU G, INANC N, ERGUN T, DIRESKENELI H: Assessment of minimal clinically important improvement by using Oral Health Impact Profile-14 in Behçet's disease. *Clin Exp Rheumatol* 2009; 27 (Suppl. 53): S79-84.
35. MUMCU G, ERGUN T, INANC N *et al*.: Oral health is impaired in Behçet's disease and is associated with disease severity. *Rheumatology* 2004; 43: 1028-33.
36. LAMPE JW: Health effects of vegetables and fruit: assessing mechanisms of action in human experimental studies. *Am J Clin Nutr* 1999; 70 (Suppl.): 475s-90s.
37. MARMOT MG BM, DAVEY SMITH G: Explanations for social inequalities in health. 1995.
38. FERRIE JE, SHIPLEY MJ, MARMOT MG, STANSFELD S: Health effects of anticipation of job change and non-employment: longitudinal data from the Whitehall II study. *BMJ* 1995; 311: 1264-9.