















Predictive factors for work-day loss in Behçet's syndrome: A multi-center study

Gonca Mumcu¹  | Meral Yay²  | Aysun Aksoy³  | Mehmet Nedim Taş⁴  |
Berkan Armağan⁵  | Alper Sari⁵  | Burçin Cansu Bozca⁶  | Emre Tekgöz⁷  |
Duygu Temiz Karadağ⁸  | Suade Özlem Badak⁹  | Duygu Tecer¹⁰  |
Cemal Bes¹¹  | Ali Şahin¹²  | Eren Erken⁹  | Ayşe Cefle⁸  | Muhammet Çınar⁷  |
Sedat Yılmaz⁷  | Ümit Karaçaylı¹³  | Erkan Alpsoy⁶  | Soner Şenel¹⁴  |
Şule Yaşar Bilge¹⁵  | Timuçin Kaşifoğlu¹⁵  | Ömer Karadağ⁵  | Kenan Aksu⁴  |
Gökhan Keser⁴  | Fatma Alibaz-Öner³  | Nevsun İnanç³  | Tülin Ergun¹⁶  |
Haner Direskeneli³ 

¹Faculty of Health Sciences, Marmara University, Istanbul, Turkey

²Department of Statistics, Mimar Sinan Fine Arts University, Istanbul, Turkey

³Division of Rheumatology, Medical School, Marmara University, Istanbul, Turkey

⁴Division of Rheumatology, Medical School, Ege University, Izmir, Turkey

⁵Division of Rheumatology, Medical School, Hacettepe University, Ankara, Turkey

⁶Dermatology Department, Medical School, Akdeniz University, Antalya, Turkey

⁷Gulhane Medical Faculty, Division of Rheumatology, Gulhane Education and Research Hospital, Ankara, Turkey

⁸Division of Rheumatology, Medical School, Kocaeli University, Kocaeli, Turkey

⁹Division of Rheumatology, Medical School, Cukurova University, Adana, Turkey

¹⁰Sanliurfa Mehmet Akif İnan Education and Research Hospital, Sanliurfa, Turkey

¹¹Rheumatology Clinic, Istanbul Bakırköy Dr.Sadi Konuk Education and Research Hospital, Istanbul, Turkey

¹²Division of Rheumatology, Medical School, Cumhuriyet University, Sivas, Turkey

¹³Gulhane Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Ankara, Turkey

¹⁴Division of Rheumatology, Medical School, Erciyes University, Kayseri, Turkey

¹⁵Division of Rheumatology, Medical School, Osmangazi University, Eskisehir, Turkey

¹⁶Dermatology Department, Medical School, Marmara University, Istanbul, Turkey

Correspondence

Ümit Karaçaylı, Health Science University, Gulhane Faculty of Dentistry, Department of Oral and Maxillofacial Surgery, Ankara, Turkey.

Email: ukaracayli@gmail.com

Abstract

Objective: The aim of this multi-center study was to assess predictive factors for work-day loss as an indirect cost element in Behçet's syndrome (BS).

Methods: In this cross-sectional, multi-center study, 834 BS patients (F/M: 441/393, age mean: 38.4 ± 10.9 years) were included. Data were collected by a questionnaire regarding treatment protocols, disease duration, smoking pattern, frequency of medical visits during the previous year and self-reported work-day loss during the previous year.

Results: Work-day loss was observed in 16.2% of patients (M/F: 103/32). The percentages of being a smoker (81.8%), using immunosuppressive (IS) medications (82%), and having disease duration <5 years (74%) were higher in male patients with work-day



loss ($P < .05$). The majority of males (90.9%) had more than four clinic visits during the previous year. Moreover, the mean work-day loss (30.8 ± 57.7 days) was higher in patients with vascular involvement (56.1 ± 85.9) than those without (26.4 ± 50.6 days) ($P = .046$). In addition, increased frequency of ocular involvement (25.9%) was also observed in patients with work-day loss compared to others (8.6%) ($P = .059$).

Conclusion: Work-day loss was associated with both vascular and ocular involvement. Close associations were observed among male gender, early period of the disease, frequent medical visits, being a smoker and treatment with IS medications in patients with work-day loss.

KEYWORDS

Behçet's disease, ocular involvement, vascular involvement, work-day loss

1 | INTRODUCTION

The costs of healthcare are categorized as direct or indirect costs. Direct costs are linked with the use of healthcare resources whereas indirect costs are various. In this perspective, work limitation as an indirect cost element is a critical issue for health policies. It has a significant impact on economic life of both employed patients and their employers.¹⁻⁵ On this basis, it is necessary to define work limitation-related factors in patients with chronic diseases to improve work performance of patients.^{2,6-16}

Behçet's syndrome (BS) is a chronic disease presenting as mild disease course regarding mucocutaneous manifestations and musculoskeletal involvement as well as severe disease course with ocular, vascular, central nervous system and gastrointestinal involvement. A severe disease course is commonly seen in males and treated with immunosuppressive medications (IS).^{17,18} Occurrence of unpredictable relapses and life-threatening conditions are crucial components of the disease pattern; workplace problems could be seen in patients with severe organ involvement, especially young males.^{9,19-32} Since workplace problems are thought to be an indicator to modify treatment protocols of employed patients for physicians, the evaluation of employment life of BS patients is critical in disease management.^{2,24,25} In this perspective, the mean sick leave days or disabled days as workdays lost for the last year were reported as 173 ± 79 for neurological involvement, 134 ± 87 for ocular involvement and 75 ± 100 for vascular involvement in BS in a previous study.²⁴ When the work performance is previously evaluated by using work productivity and activity impairment (WPAI) scale in BS patients, absenteeism, presenteeism and overall work impairment are assessed in BS patients in a 7-day short period. Weekly working hours are found to be low in BS patients with ocular involvement.² In addition, absenteeism evaluated by WPAI is found to be associated with disease activity in BS.²⁵ However, risk factors for work-day loss have not been previously studied in a long-term assessment in BS patients. Thus, we designed this multi-center study to assess predictive factors for work-day loss as a productivity measure within the previous year in BS.

Since BS has a heterogeneous clinical presentation, disease-related factors and personal factors like age, gender and work-related factors like working hours might be thought as major factors influencing long-term work limitations.² Consequently, we aimed to find out whether nature of the disease and personal factors can influence work-day loss in BS patients and also the factors that can be modified to improve the outcomes in working life of BS patients.

2 | METHODS

In this cross-sectional study, 834 BS patients from 12 centers (F/M: 441/393, age mean: 38.4 ± 10.9 years) diagnosed by the International Study Group criteria²⁶ were included. In the clinical examination, data were collected using a structured questionnaire regarding self-reported work-day loss, treatment protocols, disease duration, smoking pattern and frequency of medical visits during the previous year. Self-reported work-day loss during the previous year was noted if it was related with BS. Primary outcome was to evaluate work-day loss according to organ involvement. Associations among personal factors, smoking habits and disease-related factors on work-day loss were secondary outcomes in the study.

The inclusion criteria were: >18 years of age and being under medical control for BS. Patients with other chronic conditions leading to work impairment and/or irregular medical visits were excluded from the study.

The study was performed according to the principles of the Declaration of Helsinki. It was approved by the Ethics Committee of Marmara University Medical School (14 July 2017; No: 09.2017.497) and informed consent was taken from the study group.

2.1 | Statistical analysis

Data were analyzed by using SPSS 16.0 statistic program (SPSS Inc). Chi-square test and Mann-Whitney *U* test due to non-normal



distribution of data were used in the study. $P < .05$ was accepted as statistically significant in the study.

3 | RESULTS

In this cross-sectional study, 834 patients were included from 12 centers in Turkey. The clinical profiles of patients are presented in Table 1. Positive pathergy reaction was observed in 57.7% of the patients ($n = 481$). Treatment protocols were categorized as non-immuno-suppressive (non-IS) medications regarding colchicine, sulphasalazine, nonsteroidal anti-inflammatory drugs, antibiotics ($n = 501$, 60.07%) for mild disease course or IS medications ($n = 289$, 34.65%) such as azathioprine, corticosteroids, anti-tumor necrosis factor- α and interferon- α for severe disease course in the previous year. However, 5.27% of the group ($n = 44$) were not using any medication.

In the whole group, the mean disease duration was found to be 9.03 ± 7.6 years. Since we aimed to evaluate the effects of early period of the disease,¹⁹ patients were classified into two groups; disease duration less than 5 years ($n = 334$; 40.04%) vs ≥ 5 years ($n = 484$; 58.03%) for the analysis. Yet, no information was available for 16 patients (1.92%) diagnosed in other centers. In addition, patients were also grouped according to smoking habits as current smokers ($n = 216$, 25.9%) or non-smokers regarding past smokers/never smokers ($n = 596$, 71.5%). No response was obtained from 22 patients (2.6%).

TABLE 1 Work-day losses according to organ involvement in patients with Behçet's syndrome

	Patients with work-day loss (n = 135)		Patients without work-day loss (n = 699)	
	n	%	n	%
Organ involvement				
Oral ulcer	135	100	699	100
Genital ulcer	115	85.2	595	85.1
Cutaneous	112	83.0	521	74.5
Musculo-skeletal	69	51.1	375	53.6
Ocular ^a	35	25.9	130	8.6
Vascular	20	14.8	86	12.3
Neurological	6	4.4	28	4.01
Gastrointestinal	1	0.7	12	1.7
	Mean \pm SD			
Vascular involvement (+), d ^b	56.1 \pm 85.9			
Vascular involvement (-), d	26.4 \pm 50.6			
Male, d ^c	31.7 \pm 54.2			
Female, d	27.9 \pm 68.8			

^aChi-square test, $P = .059$.

^bMann-Whitney U test, $P = .046$.

^cMann-Whitney U test, $P = .007$.

Number of medical visits of patients during the previous year was noted. Then, the cut-off point for the number of medical visits (≥ 4 medical visits [$n = 90$; 10.79%] vs < 4 visits [$n = 653$; 78.29%]) was determined according to median value. Newly diagnosed patients ($n = 91$; 10.91%) were not coded.

The ratio of employed patients was 47.48% of the total group ($n = 396$; F/M: 94/302). Self-reported work-day loss was observed in 16.18% of the group ($n = 135$; M/F: 103/32) and 34.09% of employed patients. Clinical features of patients are presented whether work-day loss was present or not during the previous year (Table 1).

The mean work-day loss was found to be 30.8 ± 57.7 days in the group. It was higher in males (31.7 ± 54.2) compared to females (27.9 ± 68.8) ($P = .007$) (Table 1). When work-day loss was analyzed according to organ involvement, increases in the work-day loss and the number of medical visits were observed in patients with vascular involvement (M/F: 19/1; 56.1 ± 85.9 days; 5.85 ± 3.6) than without vascular involvement (M/F: 84/31; 26.4 ± 50.6 days; 3.8 ± 3.1) ($P = .046$; $P = .007$, respectively). The ratio of ocular involvement was also higher in patients with work-day loss ($n = 35$; M/F: 26/9; 25.9%) compared to others ($n = 130$; M/F: 56/74; 8.6%) ($P = .059$) (Table 1).

Disease severity score was lower in the non-IS group (4.0 ± 1.47) than the IS group (5.6 ± 2.5) ($P = .000$). In the non-IS group ($n = 68$), the majority of patients had mucocutaneous manifestations and musculoskeletal involvement ($n = 58$, 85.3%) whereas the other patients had newly diagnosed ocular involvement ($n = 10$, 14.7%). Regarding these, the work-day loss was significantly higher in patients treated with IS ($n = 61$, 47.3%) compared to non-IS use ($n = 68$, 52.75%) (46.29 ± 76.82 vs 18.02 ± 29.9 days; $P = .001$).

Among patients with work-day loss, the mean age, disease duration and age at disease onset were lower ($P < .05$); whereas the number of medical visits and education years were higher than the rest ($P < .05$) (Table 2).

The majority of the patients with work-day loss were males (76.3%). Moreover, smoking habits, treatment protocol, frequency of visits and disease duration were observed to be risk factors for work-day loss ($P < .05$) (Table 3). Then, these factors were analyzed according to gender. The presence of having more than four visits during the previous year (90.9%) as well as being a smoker (81.8%), using IS medications (82%), and having disease duration < 5 years (74%) were higher in male patients with work-day loss ($P < .05$) (Table 4) (Figure 1).

4 | DISCUSSION

Absenteeism, loss of productivity and unemployment due to illness may be variable in chronic diseases.² In the present study, work-day loss-associated factors were assessed according to patient characteristics like age, gender, treatment protocols, disease duration, smoking habits and frequency of medical visits during the previous year. Male gender was found to be a risk factor for work-day loss. Male gender is a critical prognostic factor in BS, as neutrophils



TABLE 2 Socio-demographic properties and frequency of medical visits in Behçet's syndrome patients with work-day loss

	Patients with work-day loss (n = 135)	Patients without work-day loss (n = 699)	P ^a
	Mean ± SD	Mean ± SD	
Age, y	34.3 ± 8.4	39.2 ± 11.2	.000
Disease duration, y	7.04 ± 6.04	9.4 ± 7.8	.000
Age of disease onset, y	27.2 ± 7.4	29.7 ± 8.8	.009
Number of medical visit/previous year	4.2 ± 3.2	2.9 ± 2.1	.000
Education year	10.1 ± 4.03	8.4 ± 3.9	.000

^aMann-Whitney *U* test was used in the analysis.

TABLE 3 Gender and disease-related factors in Behçet's syndrome patients with work-day loss

		Patients with work-day loss (n = 135)		Patients without work-day loss (n = 699)		P ^a
		n	%	n	%	
Gender	Male	103	76.3	290	41.5	.000
	Female	32	23.7	409	58.5	
	Total	135	100	699	100	
Smoking habits	Non-smoker	78	58.6	518	76.3	.000
	Current Smoker	55	41.4	161	23.7	
	Total	133	100	679	100	
Treatment protocols	Non-IS	68	52.7	433	65.5	.007
	IS	61	47.3	228	34.5	
	Total	129	100	661	100	
Examination period/ previous year	<4 visits	97	74.6	556	90.7	.000
	≥4 visits	33	25.4	57	9.3	
	Total	130	100	613	100	
Disease duration	<5 y	73	54.1	261	38.2	.001
	≥5 y	62	45.9	422	61.8	
	Total	135	100	683	100	

Abbreviation: IS, immunosuppressants.

^aChi-square test was used in the analysis.

implicated in the pathogenesis could be activated by testosterone, the primary sex hormone in men.^{17,18,22,27,28} Vascular and ocular involvements were found to be related to increased work-day loss in male patients. As expected, the use of IS medications were higher among these male patients. Thus male patients with major organ involvement requiring IS use were the risk group for increased work loss.

The work-day loss among those with vascular complaints reaches to almost 2 months during the preceding year. Vasculitis as a primary pathologic feature affects both arterial and venous systems with all sized vessels in BS and venous involvement is reported to be more common in young male patients.²⁹ Since vascular involvement is a severe health problem leading to mortality and morbidity,^{17,19} the primary goal of treatment protocols for vascular disease is to control disease-related symptoms, increase survival and to prevent relapses

in BS. Systemic IS medications are used to reduce inflammation and endothelial damage leading to the formation of thrombus. Since venous stasis, leg pain, ulcers on the leg, limitation in walking capacity and mobility are critical problems affecting daily life of patients with vascular involvement,²⁹ increase in work-day loss could be predicted.

When individuals were classified according to organ involvement, it was also observed that ocular involvement was higher in patients with work-day loss. Ocular involvement is a chronic sight-threatening manifestation with a relapsing pattern in BS. Prevention of visual loss, improvement of visual outcomes and decrease in flares of uveitis are the main treatment goals with IS and biologics. Yet, loss of visual acuity could be seen in spite of aggressive therapy protocols.³⁰⁻³⁴ Although limited information is available for work limitation in BS, weekly working hours is found to be lower in patients with ocular involvement in our previous study.²



		Patients with work-day loss (n = 135)		Patients without work-day loss (n = 699)		P ^a
		n	%	n	%	
Current smokers	Male	45	81.8	96	59.6	.003
	Female	10	19.2	65	40.4	
	Total	55	100	161	100	
Immunosuppressant treatment protocols	Male	50	82	123	53.9	.000
	Female	11	18	105	46.1	
	Total	61	100	228	100	
≥4 medical visits/previous year	Male	30	90.9	25	43.9	—
	Female	3	9.1	32	56.1	
	Total	33	100	57	100	
Disease duration < 5 y	Male	54	74	115	41.1	.000
	Female	19	26	146	55.9	
	Total	73	100	261	100	

TABLE 4 Work-day loss-related factors in Behçet's syndrome patients according to gender

^aChi-square test was used in the analysis.

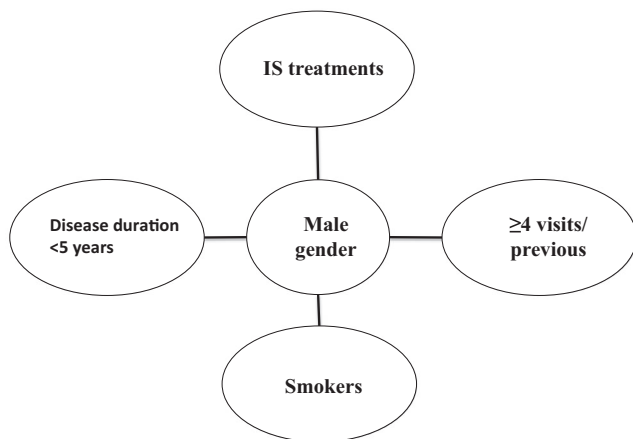


FIGURE 1 Work-day loss-related factors in patients with Behçet's syndrome

An association with frequent visits (≥4 visits during the last year) was found to be a predictive factor for work-day loss, especially in males. Frequency of visits reflects healthcare utilization in the disease management. Multiple visits from different experts are needed in patients with severe disease course such as ocular, vascular, neurological and gastrointestinal involvement due to mortality and morbidity risks.^{17,19,20} Therefore, the close relationship between increase in the number of visits and work-day loss could be predicted in the severe disease spectrum.

In the present study, disease duration <5 years and being young were associated with work-day loss. Disease manifestations may not be controlled sufficiently in the early period of the disease following the diagnosis. New vascular events could be seen in one-third of the patients at 5 years.¹⁹ Therefore, exacerbations and remissions of

clinical manifestations as well as response to treatments are unpredictable in this period.³⁵

Smoking was found to be another risk factor for work-day loss in our study in male patients. Smoking is a well-known risk factor for cardiovascular disease, cancer, infections, various respiratory diseases, intestinal ischemia and renal failure.³⁶⁻³⁸ It has a significant impact on direct costs regarding healthcare resource usage as well as indirect costs associated with the decrease in work productivity. Since smoking cessation improves both health status and working life of patients,³⁹ it could be thought as being a part of the disease management process. Increase in weekly hours worked could be achieved by using integrated disease management programs in heterogeneous clinical manifestations.³

As an interesting observation, the education year was higher in patients with work-day loss. Both health problems and work environment may affect work performance.⁵ Patients could be unemployed or change their jobs due to reduced work effectiveness. However, work-day loss may also be less due to "fear of job loss" although patients may feel unhealthy and do not work at full capacity.³⁻⁵

In chronic disease management, effective disease control aims to fulfill both the complex needs of patients as well as to reduce hospitalization and unplanned emergency visits from a health policy perspective.⁴⁰ In this perspective, patient-centered⁴¹ and evidence-based effective management programs as well as patient's empowerment improve outcomes in patients with chronic diseases.⁴⁰ This study addressed that organ involvement, treatment protocols, disease duration and smoking pattern of employed patients are needed in clinical practice to evaluate working performance, because better outcomes in working lives are achieved by disease management and is an aspect of health policy.²⁵ BS patients with severe organ involvement

have problems with continuous employability and become an economic burden on society due to increases in work-day losses. More aggressive treatment protocols at acceptable medical cost levels, the modification of life-style and patient empowerment may be options to overcome this problem. In addition multidisciplinary dedicated centers providing patient care maybe helpful.

Despite the fact that our results give some clues about work limitations in BS patients, the study had some limitations. First, the work performance was evaluated by questions on patients' perspective. Second, recall bias may occur due to underestimation or overestimation of self-reported work-day loss in the 1-year period. Third, cultural differences could also affect the gender balance of employed patients. In the perspective of these limitations, further longitudinal studies are necessary to understand how the working life of patients with severe disease course is preserved with coordinated care in different patient populations with BS.

In conclusion, work-day loss as an indirect cost element was associated with vascular and ocular involvement in BS patients. Male gender, early period of the disease, frequent medical visits, being a smoker and treatment with IS medications were more frequently associated with work-day loss in patients with BS.

ORCID

Gonca Mumcu  <https://orcid.org/0000-0002-2280-2931>
 Meral Yay  <https://orcid.org/0000-0003-1857-8719>
 Aysun Aksoy  <https://orcid.org/0000-0002-8218-7109>
 Mehmet Nedim Taş  <https://orcid.org/0000-0002-6818-6409>
 Berkan Armağan  <https://orcid.org/0000-0003-4409-059X>
 Alper Sarı  <https://orcid.org/0000-0002-3286-0940>
 Burçin Cansu Bozca  <https://orcid.org/0000-0001-7907-5037>
 Emre Tekgöz  <https://orcid.org/0000-0002-0866-1503>
 Duygu Temiz Karadağ  <https://orcid.org/0000-0002-5891-2032>
 Suade Özlem Badak  <https://orcid.org/0000-0002-9545-5811>
 Duygu Tecer  <https://orcid.org/0000-0002-8816-6181>
 Cemal Bes  <https://orcid.org/0000-0001-7100-3610>
 Ali Şahin  <https://orcid.org/0000-0002-1351-2385>
 Eren Erken  <https://orcid.org/0000-0001-6902-624X>
 Ayşe Cefle  <https://orcid.org/0000-0002-3273-7969>
 Muhammet Çınar  <https://orcid.org/0000-0002-6150-3539>
 Sedat Yılmaz  <https://orcid.org/0000-0002-4691-3417>
 Ümit Karaçaylı  <https://orcid.org/0000-0001-9588-8898>
 Erkan Alpsoy  <https://orcid.org/0000-0001-7049-0170>
 Soner Şenel  <https://orcid.org/0000-0001-9311-8179>
 Şule Yaşar Bilge  <https://orcid.org/0000-0002-0783-1072>
 Timuçin Kaşifoğlu  <https://orcid.org/0000-0002-9941-5884>
 Ömer Karadağ  <https://orcid.org/0000-0002-3443-3117>
 Kenan Aksu  <https://orcid.org/0000-0001-8889-2688>
 Gökhan Keser  <https://orcid.org/0000-0001-7289-1816>
 Fatma Alibaz-Öner  <https://orcid.org/0000-0002-6653-1758>
 Nevsun İnanç  <https://orcid.org/0000-0003-2862-0562>
 Tülin Ergun  <https://orcid.org/0000-0002-9935-6298>
 Haner Direskeneli <https://orcid.org/0000-0003-2598-5806>

REFERENCES

- Nakata K, Tsuji T, Vietri J, Jaffe DH. Work impairment, osteoarthritis, and health-related quality of life among employees in Japan. *Health Qual Life Outcomes*. 2018;16:64.
- Mumcu G, Lehimci F, Fidan O, et al. The assessment of work productivity and activity impairment in Behcet's disease. *Turk J Med Sci*. 2017;47:535-541.
- Schultz AB, Chen CY, Edington DW. The cost and impact of health conditions on presenteeism to employers: a review of the literature. *Pharmacoeconomics*. 2009;27:365-378.
- Johns G. Presenteeism in the workplace: A review and research agenda. *J Organ Behav*. 2010;31:519-542.
- Schultz AB, Edington DW. Employee health and presenteeism: a systematic review. *J Occup Rehabil*. 2007;17:547-579.
- Sreih AG, Alibaz-Oner F, Easley E, et al. Health-related outcomes of importance to patients with Takayasu's arteritis. *Clin Exp Rheumatol*. 2018;36:51-57.
- Alibaz-Oner F, Can M, Ilhan B, Polat O, Mumcu G, Direskeneli H. Presence of fibromyalgia in patients with Takayasu's arteritis. *Intern Med*. 2013;52:2739-2742.
- Yilmaz-Oner S, Ilhan B, Can M, et al. Fatigue in systemic lupus erythematosus : Association with disease activity, quality of life and psychosocial factors. *Z Rheumatol*. 2016;76(10):913-919.
- Mumcu G, Inanc N, Taze A, Ergun T, Direskeneli H. A new mucocutaneous activity index for Behcet's disease. *Clin Exp Rheumatol*. 2014;32:S80-S86.
- Yilmaz N, Can M, Oner FA, et al. Impaired quality of life, disability and mental health in Takayasu's arteritis. *Rheumatology (Oxford)*. 2013;52:1898-1904.
- Khan NA, Spencer HJ, Nikiphorou E, et al. Intercentre variance in patient reported outcomes is lower than objective rheumatoid arthritis activity measures: a cross-sectional study. *Rheumatology (Oxford)*. 2017;56:1395-1400.
- Gron KL, Ornbjerg LM, Hetland ML, et al. The association of fatigue, comorbidity burden, disease activity, disability and gross domestic product in patients with rheumatoid arthritis. Results from 34 countries participating in the Quest-RA program. *Clin Exp Rheumatol*. 2014;32:869-877.
- Khan NA, Spencer HJ, Abda EA, et al. Patient's global assessment of disease activity and patient's assessment of general health for rheumatoid arthritis activity assessment: are they equivalent? *Ann Rheum Dis*. 2012;71:1942-1949.
- Mehta P, Ambrose N, Haskard DO. Work-related disability in Behcet's syndrome: a British case series. *Clin Exp Rheumatol*. 2014;32:S173-S174.
- Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993;4:353-365.
- Ilhan B, Can M, Alibaz-Oner F, et al. Fatigue in patients with Behcet's syndrome: relationship with quality of life, depression, anxiety, disability and disease activity. *Int J Rheum Dis*. 2016;21:2139-2145.
- Yazici H, Seyahi E, Hatemi G, Yazici Y. Behcet syndrome: a contemporary view. *Nat Rev Rheumatol*. 2018;14:107-119.
- Direskeneli H. Behcet's disease: infectious aetiology, new autoantigens, and HLA-B51. *Ann Rheum Dis*. 2001;60:996-1002.
- Alibaz-Oner F, Karadeniz A, Yilmaz S, et al. Behcet disease with vascular involvement: effects of different therapeutic regimens on the incidence of new relapses. *Medicine*. 2015;94:e494.
- Alibaz-Oner F, Mumcu G, Kubilay Z, et al. Unmet need in Behcet's disease: most patients in routine follow-up continue to have oral ulcers. *Clin Rheumatol*. 2014;33:1773-1776.
- Merkel PA, Aydin SZ, Boers M, et al. Current status of outcome measure development in vasculitis. *J Rheumatol*. 2014;41:593-598.
- Hatemi G, Ozguler Y, Direskeneli H, et al. Current status, goals, and research agenda for outcome measures development in



- Behcet syndrome: report from OMERACT 2014. *J Rheumatol.* 2015;42:2436-2441.
23. Hatemi G, Merkel PA, Hamuryudan V, et al. Outcome measures used in clinical trials for Behcet syndrome: a systematic review. *J Rheumatol.* 2014;41:599-612.
 24. Sut N, Seyahi E, Yurdakul S, Senocak M, Yazici H. A cost analysis of Behcet's syndrome in Turkey. *Rheumatology (Oxford).* 2007;46:678-682.
 25. Atas N, Varan O, Babaoglu H, et al. Work productivity in patients with Behçet disease and its association with disease activity and quality of life. *Br J Occup Ther.* 2019;82(6):376-382.
 26. ISG. Criteria for diagnosis of Behcet's disease. *Lancet.* 1990;335:1078-1080.
 27. Yavuz S, Ozilhan G, Elbir Y, Tolunay A, Eksioglu-Demiralp E, Direskeneli H. Activation of neutrophils by testosterone in Behcet's disease. *Clin Exp Rheumatol.* 2007;25:S46-51.
 28. Yavuz S, Akdeniz T, Hancer V, Bicakcigil M, Can M, Yanikkaya-Demirel G. Dual effects of testosterone in Behcet's disease: implications for a role in disease pathogenesis. *Genes Immun.* 2016;17:335-341.
 29. Alibaz-Oner F, Aldag B, Aldag M, et al. Post-thrombotic syndrome and venous disease-specific quality of life in patients with vascular Behcet's disease. *J Vasc Surg Venous Lymphat Disord.* 2016;4:301-306.
 30. Fabiani C, Vitale A, Rigante D, et al. Predictors of sustained clinical response in patients with Behcet's disease-related uveitis treated with infliximab and adalimumab. *Clin Rheumatol.* 2018;37:1715-1720.
 31. Celiker H, Kazokoglu H, Direskeneli H. Conventional immunosuppressive therapy in severe Behcet's Uveitis: the switch rate to the biological agents. *BMC Ophthalmol.* 2018;18:261.
 32. Namba K, Goto H, Kaburaki T, et al. A major review: current aspects of ocular Behcet's disease in Japan. *Ocul Immunol Inflamm.* 2015;23(Suppl 1):S1-23.
 33. Bulur I, Onder M. Behcet disease: new aspects. *Clin Dermatol.* 2017;35:421-434.
 34. Urruticoechea-Arana A, Cobo-Ibanez T, Villaverde-Garcia V, et al. Efficacy and safety of biological therapy compared to synthetic immunomodulatory drugs or placebo in the treatment of Behcet's disease associated uveitis: a systematic review. *Rheumatol Int.* 2018;39:47-58.
 35. Hamuryudan V, Hatemi G, Sut N, Ugurlu S, Yurdakul S, Yazici H. Frequent oral ulceration during early disease may predict a severe disease course in males with Behcet's syndrome. *Clin Exp Rheumatol.* 2012;30:S32-S34.
 36. McEvoy JW, Nasir K, DeFilippis AP, et al. Relationship of cigarette smoking with inflammation and subclinical vascular disease: the Multi-Ethnic Study of Atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2015;35:1002-1010.
 37. Kakafika AI, Mikhailidis DP. Smoking and aortic diseases. *Circ J.* 2007;71:1173-1180.
 38. Carter BD, Abnet CC, Feskanich D, et al. Smoking and mortality—beyond established causes. *N Engl J Med.* 2015;372:631-640.
 39. Suwa K, Flores NM, Yoshikawa R, Goto R, Vietri J, Igarashi A. Examining the association of smoking with work productivity and associated costs in Japan. *J Med Econ.* 2017;20:938-944.
 40. Wagner EH. Chronic disease management: what will it take to improve care for chronic illness? *Eff Clin Pract.* 1998;1:2-4.
 41. Institute of Medicine (US) Committee on Quality of Health Care in America. *Crossing the Quality Chasm: A New Health System for the 21st Century.* Washington, DC: National Academies Press; 2001.

How to cite this article: Mumcu G, Yay M, Aksoy A, et al. Predictive factors for work-day loss in Behçet's syndrome: A multi-center study. *Int J Rheum Dis.* 2020;23:240–246. <https://doi.org/10.1111/1756-185X.13771>