



REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br



Review article

Variables related to work productivity loss in patients with ankylosing spondylitis[☆]

Renata Frauendorf*, Marcelo de Medeiros Pinheiro, Rozana Mesquita Ciconelli

Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil

ARTICLE INFO

Article history:

Received 22 January, 2012

Accepted 18 February, 2013

Keywords:

Spondylitis, ankylosing

Efficiency

Work

Risk factors

Review

Palavras-chave:

Espondilite anquilosante

Eficiência

Trabalho

Fatores de risco

Revisão

ABSTRACT

The work productivity loss due to ankylosing spondylitis (AS) has become subject of interest because of its socioeconomic impact. In addition to physical limitations, other variables seem to affect the productivity of those patients, who often withdraw early from the labor force. This review was aimed at identifying articles published in English, from January 2001 to December 2011, which assessed those variables in adult patients of both sexes diagnosed with AS, using standardized instruments to measure disease activity and work productivity. Thirty-three articles meeting the inclusion criteria were identified. The work productivity loss of patients with AS proved to be influenced by demographics, emotional, social, cultural, and occupational factors, and lifestyle. Understanding those potential risk factors may contribute to the development of preventive strategies to maintain patients with AS participating in the labor force

© 2013 Elsevier Editora Ltda. All rights reserved.

Variáveis relacionadas com perda da produtividade no trabalho em pacientes com espondilite anquilosante

RESUMO

A perda da produtividade no trabalho, como resultado da espondilite anquilosante, tem se tornado tema de interesse dado o seu impacto socioeconômico. Além das limitações físicas, outras variáveis parecem interferir na produtividade desses pacientes que muitas vezes são aposentados precocemente do mercado de trabalho. Assim, esse manuscrito de revisão buscou identificar artigos publicados na língua inglesa no período de janeiro de 2001 a dezembro de 2011 que discutissem essas variáveis por meio de estudos realizados com pacientes adultos com diagnóstico de espondilite anquilosante, de ambos os gêneros e que usaram instrumentos padronizados para a avaliação da atividade da doença e da capacidade produtiva no trabalho. Foram identificados 33 artigos atendendo aos critérios de inclusão e observou-se que a perda de produtividade no trabalho em pacientes com espondilite anquilosante é influenciada por variáveis demográficas, emocionais, socioculturais e ocupacionais, e hábitos de vida. Compreender esses possíveis fatores de risco pode

[☆] Study conducted at the Universidade Federal de São Paulo, São Paulo, SP, Brazil.

* Corresponding author.

E-mail: refrau@uol.com.br (R. Frauendorf).

colaborar para a elaboração de estratégias preventivas para a manutenção de pacientes com espondilite anquilosante no mercado de trabalho.

© 2013 Elsevier Editora Ltda. Todos os direitos reservados.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease that affects 0.1% to 1.4% of the general population, being characterized by the preferential involvement of the vertebral column and progressively impairing mobility and functional capacity.^{1,2} The disease has a relevant socioeconomic impact, because its major incidence is under the age of 40 years,³ leading to reduced working hours, missed professional opportunities, and early retirement.⁴ One of the major consequences of the disease is work productivity loss (WPL), which is mainly associated with physical limitation, chronic pain, impaired quality of life, poor self-esteem, and other emotional disorders, such as anxious and depressed mood.⁵⁻⁸

In addition to physical limitations and aspects related to the AS itself, several other variables can influence WPL, such as demographics, emotional and socioeconomic factors, life habits, and work or occupational conditions. A better understanding of those possible risk factors might provide a more adequate elaboration of preventive strategies to keep patients with AS participating in the labor force.

Thus, this review study aimed at systematically compiling studies on WPL of patients with AS, in addition to identifying and discussing the major related aspects.

Methods

A systematic bibliographic survey was conducted in the PubMed database from January 2001 to December 2011, by using the search strategy of combining the descriptor "Ankylosing Spondylitis" with the following descriptors: "Work Instability"; "Work Productivity"; "Work Disability"; and "Risk Factors".

Initially, 335 articles were identified, of which, 33 met the inclusion criteria, which comprised studies published in English and performed on adult patients of both sexes diagnosed with AS. In addition, only studies using standardized tools validated for assessing their samples were selected, such as the following: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index);⁹ BASFI (Bath Ankylosing Spondylitis Functional Index);¹⁰ HAQ-S (Health Assessment Questionnaire – Spondylitis);¹¹ BASMI (Bath Ankylosing Spondylitis Mobility Index);¹² AS-WIS (Work Instability Scale for Ankylosing Spondylitis);¹³ WPAI-SHP (Work Productivity and Activity Impairment Questionnaire: Specific Health Problem);¹⁴ WPAI:SpA (Work Productivity and Activity Impairment questionnaire in AS);¹⁵ and WLQ (Work Limitations Questionnaire).¹⁶

All 33 full articles were read, their information summarized, and the variables interfering with WPL were grouped into categories.

Results

The prevalence of permanent work disability ranges from 10% to 40%, depending on the disease stage, age at disease onset, and the characteristics of each country, such as patient's access to the health care system.^{4,6,17-20} In the United States, the annual cost related to WPL is estimated at US\$ 5,000 for each patient with AS.⁵ Although the new modalities of AS treatment contributed to reduce the impact of WPL²¹ over the past decade, some studies still show a high rate of withdrawal from work or early retirement of those patients^{22,23} and the existence of factors that can influence that phenomenon.

Table 1 summarizes the variables associated with the WPL of patients with AS reported in the articles reviewed. Those variables were subdivided according to risk and protection (Table 2).

Related to the disease itself

Activity and functionality

Most studies have shown a close correlation of WPL with higher disease activity, as well as with worse functionality¹⁷⁻²⁸ and worse mobility^{18,22,28} in patients with AS, according to the most commonly used instruments BASDAI,⁹ BASFI,¹⁰ HAQ-S¹¹ and BASMI.¹²

Table 1 – Variables associated with the WPL of patients with AS.

1. Related to the disease itself	1.1 Activity and functionality 1.2 Time since diagnosis 1.3 Pharmacological and non-pharmacological treatment 1.4 Prostheses 1.5 Comorbidities and EAM 1.6 Family history of AS
2. Demographics	2.1 Age 2.2 Sex 2.3 Educational and socioeconomic levels
3. Emotional	3.1 Coping with disease 3.2 Quality of life and global well-being 3.3 Social support
4. Life habits	4.1 Smoking 4.2 Current and regular physical activity
5. Occupational	5.1 Absenteeism 5.2 Type of professional activity 5.3 Work environment
6. Socioeconomic	6.1 Unemployment rate 6.2 Social security 6.3 Economic prosperity 6.4 Health care system

WPL, work productivity loss; AS, ankylosing spondylitis; EAM, extra-articular manifestations.

Table 2 – Variables associated with the WPL of patients with AS: risk and protective factors.

Risk factors	Protective factors
Disease activity	Socioeconomic factors
Function	Educational factors
Time since diagnosis	Coping factors
Concomitant medications	Quality of life
Arthroplasty	Global well-being
Associated diseases	Social support
Extra-articular manifestations	Regular physical activity
Age	Less physically-demanding professional activities
Smoking	Appropriate work environment
Absenteeism	Economic prosperity (lower unemployment rate and health care system)
Family history of AS	Social security system

WPL, work productivity loss; AS, ankylosing spondylitis.

Time since diagnosis

It is not surprising that long-lasting AS symptoms and diagnosis delay also contribute to increase the risk of work disability.^{4,6,17,22,27,29-33} The rate of withdrawal from work significantly increases for each year of diagnosis – from 5% in the first year to 31% for a time since diagnosis longer than 20 years. After 5 and 15 years of diagnosis, WPL increases from 13% to 23%.^{18,27}

Cakar et al.,³¹ studying 121 military personnel with AS in Turkey, have identified that those with a time since diagnosis longer than eight years were more prone to work disability,³¹ differently from those with a time since diagnosis shorter than five years.³⁰ However, it is worth noting that age at diagnosis plays an important role in that assessment.²³ Usually, the sooner the disease manifests, the greater the chance of early disability.^{8,18,25,34,35}

Treatment

Over the past 20 years several therapeutic advances were made in the clinical management of patients with AS, such as the non-pharmacological (awareness, education, exercises) and pharmacological (TNF α inhibitors) approaches, as well as advances enabling earlier diagnosis, especially magnetic nuclear resonance.^{21,36-38}

Usually, the greater the number of medications used, the greater the vulnerability to early withdrawal from the labor force, probably related to higher severity and longer duration of disease and the presence of concomitant diseases.²³

In addition to improving the symptoms and functionality of patients with AS, TNF α inhibitors have been recently proven to keep those patients participating in the labor force,³⁸⁻⁴³ or even to professionally reassign them in 10% to 25% of the cases.^{20,37,40} The major instruments to assess productive capacity or reintegration into work are AS-WIS,¹³ WPAI-SHP,¹⁴ WPAI:SpA¹⁵ and WLQ.¹⁶

Prostheses

Some studies have shown that even after arthroplasty those patients are more prone to abandon their occupational activities as compared with those who have not undergone that

procedure.^{18,23,31,33} However, it is worth noting that patients undergoing knee or hip surgery usually have greater functional impairment and more severe disease, factors that might confound the real dimension of that procedure in the WPL of patients with AS.

Comorbidities and extra-articular manifestations (EAMs)

Concomitant diseases are more common in patients with chronic disorders than in controls. In patients with AS, comorbidities are twice more common than in healthy individuals (78.7% vs. 31.5%),^{26,34} being associated with WPL,^{4,18,23,26,29,32,34} especially the psychopathological findings, such as anxiety and depression.^{4,22,26,29}

The major EAMs related to work disability were peripheral arthritis, inflammatory intestinal disease and uveitis (current or previous).^{5,18,24,28,29,33}

Family history

Some studies have found a significant association between family history of AS and WPL.^{17,32} Forejtová et al.,¹⁷ studying more than 1,000 patients with AS, have found a history of AS in first-degree relatives in 20% of the sample. In addition, they had worse health conditions and more disability, according to the BASFI and HAQ-DI scales.⁹ Work productivity loss has been attributed to greater disease intensity and severity, as well as to the worst prognosis in the family.

Demographics

Age

More advanced age is one of the most important risk factors for disability in patients with AS.^{5,6,21-24,26,28,29,39} On average, patients with permanent disability are six to ten years older.²⁰ Thus, the earlier the disease manifests or the later it is diagnosed, the higher the risk of early withdrawal from the labor force.

In addition, patients with a late diagnosis of AS can retire earlier due to their greater difficulty in adapting to other professional activities.^{8,18,25,34,35}

Sex

Studies are controversial regarding sex. Some authors have reported that work disability is more common among men,^{6,17,26,27} while others have reported it more commonly among women,^{23,25,28,33,37,39} or even no significant difference.^{18,21,29,34} One of the aspects justifying higher WPL among men is their greater frequency of structural damage and worse axial prognosis.⁶

Ward and Kuzis, however, have found that women receive twice more benefits than men, particularly in the first year, suggesting that fatigue, pain and limitations are more relevant in the female sex.³⁴

Educational and socioeconomic levels

A higher educational level is positively associated with maintenance in the labor force.^{4,21,23-25,28,32,34,37} Some aspects, such as better socioeconomic and educational levels,^{18,27,34} could explain that finding. In addition, the better capacity to adapt to new jobs and compliance with ergonomic managements can explain that correlation.^{25,34}

Emotional

Coping with the disease

Patients diagnosed with AS usually face disease chronicity, experiencing several difficulties when dealing with functional limitation, pain, expectations, dependency, adverse reactions to treatment, and prognosis. Those difficulties can impair their well-being and quality of life, interfering with their productive capacity.¹⁷

In addition, assessing the impact of pain, fatigue and work disability on life style, career, family and social life of patients with AS is not a simple task, because the magnitude of such aspects also relates to the way patients cope with their diseases.⁴ Coping strategies have been assessed in a study by Boonen et al.¹⁸ with 658 patients with AS by means of the 'Coping with Rheumatic Stressors' (CORS) questionnaire, which measures eight coping styles directed at the disease (three related to pain, three related to the limitations on daily activities, and two related to dependence). Those authors reported that the higher the number of coping strategies of patients, the greater their capacity to cope with the disease and to keep themselves productive at work. In the sample analyzed, 36% of the patients had unfavorable scores for those coping strategies, reflecting more passive attitudes. Thus, the behavioral difficulties of coping with AS represent an elevated risk for productive disability.^{18,23}

Barlow et al.,⁴ in a qualitative approach, have reported that patients with AS associate work with economic independence as an essential aspect of life, and emphasized that their major challenge was to cope with daily fatigue and the direct interference with physical, psychic and social well-being.

Quality of life and global well-being

Considering that quality of life is the individuals' perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns,^{44,45} some studies have shown the relevant impact of WPL and the worse quality of life of patients with AS.^{25,26,38}

The major instruments used to measure quality of life in those patients were SF-36 (*Medical Outcomes Study short form*)⁴⁶ and BAS-G (*Bath Ankylosing Spondylitis Global health index*)⁴⁷ for measuring global well-being, as demonstrated by Chorus et al.^{18,23} Those authors have reported that the worst well-being was significantly associated with the early retirement of patients with AS.

Social support

Social support is considered a protective measure for WPL, because it involves the emotional support of friends and family in the behavioral reinforcement of better life habits, compliance with treatment, and coping with the disease.^{22,29}

Healthy habits

Smoking

Some studies have demonstrated that the smoking habit is a relevant risk factor for WPL.^{29,32,34} A reduction in the pulmonary and cardiac capacity can interfere directly with the work

performance of patients with AS,²⁹ and determine a worse response to clinical treatment.⁴⁸

Current physical activity

The practice of physical activity is usually recommended to patients with AS. Exercises reduce symptoms, contribute to a better posture, improve mobility, help to preserve function, and reduce the use of non-steroidal anti-inflammatory drugs (NSAIDs). Thus, those patients become better prepared to perform their work activities.^{17,29,34}

It is worth noting that the regularity and frequency of exercises are more important than the modality of physical activity.^{17,29,34}

Occupational

Absenteeism

Work absenteeism is frequent in patients with AS, particularly in the periods of higher disease activity.^{25,26} Annually, the number of days lost ranges from 8 to 46 days for each patient, according to the studies reviewed,^{5,19,27,37,49} a rate three times greater than that observed in the general population.¹⁸

According to the prospective study conducted by Ramos-Remus et al.,²¹ the absenteeism rate of patients with AS decreased over the last 15 years (from 77%, in 1993, to 53%, in 2007), similarly to the number of lost work days and the proportion of individuals with permanent disability (from 3% to 2.1%). That illustrates the reduction in the impact of AS on productive capacity, probably reflecting the advance of treatment.^{21,37,44} Nevertheless, other aspects need to be better explored, such as financial needs, social health system, educational level and satisfaction at work.^{37,50}

Type of professional activity

Usually, decisions about the professional career, such as workload and type of activity, are individualized and depend on each patient's peculiarities.^{4,34} In 2001, Barlow et al.⁴ reported that 15% of the patients make professional changes according to the AS activity, especially a reduction in worked hours and adaptations at the workplace.

For patients with AS, the risk of permanent or temporary WPL increases with the increase in physical effort, mainly for physically demanding activities (kneeling, reaching, bending, crawling), with the increase in manual jobs related to agriculture, industry, transport, and civil construction, and with excessive worked hours.^{5,18,25,34} Less physically demanding activities, such as administrative and management services, help maintaining patients with AS participating in the labor force.^{5,28}

Because of the disease, patients with AS engage in more passive and sedentary activities, decrease the number of hours worked and frequently engage in autonomous activities. The major negative aspects of such changes relate to loss of independence, of self-esteem and of professional satisfaction, and frustrations. However, they can dedicate more time to family and treatment.⁴

Workplace

The work environment most affected by the WPL of patients with AS is the industrial sector,²³ particularly because of dif-

faculties in accessing the workplace,²³ ergonomic inadequacy^{23,51} and lack of cooperation of colleagues³⁴ and superiors.²³

Work reconditioning is extremely important as a policy of human resources at a firm, because about 70% of the patients with AS, out of the work force due to the disease, could continue employed if changes in the work environment had been carried out, such as a reduction in monotonous activities that impair posture and adjustments in temperature.²³

Socioeconomic

When the possibility of early retirement needs to be discussed at the workplace, socioeconomic variables, especially the peculiarities of the social security policies, unemployment rates, prosperity, and the health system of each country, need to be considered.^{5,20} Boonen et al.⁵ have reported that disability, absenteeism and the productivity costs of patients with AS are higher in the Netherlands than in France and Belgium, due to the benefits offered by the Dutch government to individuals at a prolonged leave of absence. In Denmark, approximately 30% of the patients with AS are considered permanently disabled for work after 20 years of disease.¹⁸ However, that prevalence is much lower (13%) in the United States, even for a similar disease duration.³⁴

Discussion

The rate of the WPL of patients with AS has varied in different studies because of the several factors involved, such as those directly inherent in the disease (duration, activity and severity) and in life habits, and in other aspects, such as demographics, socioeconomic, psychological, and cultural factors, social security, type of work, and the country of residence.

Results regarding sex are controversial. Work productivity loss was believed to be more common among men, because they are more frequently affected by AS and have a worse prognosis as compared with women. However, several authors have reported a higher disability rate among women. In addition, compared to men, women receive twice more benefits due to disability. The major explanations for that fact relate to financial, motivational and cultural factors. Apparently, men have a lower chance of permanent work disability, because they usually are the family's financial providers and do not easily accept disablement. However, women have increasingly participated more actively in the labor force, more often assuming their family's livelihood and their professional satisfaction, which might make women equally vulnerable to WPL.

In addition to the worse prognosis of heredity as a risk factor for WPL, another hypothesis relates to the apprehended behavioral archetype, because the transmission of beliefs, values and habits from parents to children induce similar thoughts and actions.

Although the higher number of associated diseases and of concomitant medications is known to associate with a greater likelihood of WPL, their real impact on the work disability of patients with AS is little known. In addition, which health conditions would affect the work disability of patients with AS are yet to be fully clarified. Nevertheless, it is worth

emphasizing that psychological disorders seem to be significantly associated, although a causality relationship between those events still lacks. Some researchers question whether they are consequence of work withdrawal or whether they are the actual risk factors. Those findings indicate the need for a multiprofessional assessment in that scenario.

To minimize the effect of the occupational variables that represent a risk for disability, those patients should be instructed to perform tasks that require less physical effort and working hours, and partnership among peers should be encouraged. In addition, awareness inside the companies should be encouraged, comprising ergonomic adaptation to the work environment and establishment of human resources policy that could meet the need of patients with AS, providing them with more autonomy, support and professional satisfaction. Another interesting strategy would be promoting counseling and professional planning programs to guide the career and keep the productive capacity as adequate as possible.

The different criteria for granting benefits due to work disability make the comparison of the work status in different countries difficult. In addition, the unemployment rates, economic prosperity and health care system functioning of each country might interfere with the productivity of patients with AS, either encouraging or not their participation in the labor force. So far, few data have been found to solve or clarify that question.

It is worth emphasizing that some results of this review should be carefully analyzed, because of limitations, such as the difficulty in accessing rheumatology services, delay in diagnosis, heterogeneous characteristics of the different populations studied, and the non-adjustment to confound factors, as well as the interaction between all those variables. In addition, those patients are usually discriminated and excluded from the major scientific studies, even in developed countries.

Much of the information was obtained from studies that considered only the total work disability of withdrawal from the official labor force. Many patients are known to have withdrawn from the labor force due to AS, but continue to unofficially engage in paid activities, even receiving retirement due to disability or sick leave. Similarly, some epidemiological studies about risk factors for the WPL of patients with AS have a cross-sectional descriptive design, which makes the analysis of the cause-effect relationship of those associations difficult. Thus, further longitudinal studies are required to assess the progression of the predictive variables of WPL of patients with AS.

This systematic review of the literature indicates that WPL is one of the major consequences of AS. In addition, there are variables that can contribute to that phenomenon, such as those associated with the disease itself and life habits, and those associated with socioeconomic, demographic, emotional, cultural and occupational factors.

The work disability of patients with AS is multifactorial, involving not only work loss. Work productivity loss involves social, emotional and economic drawbacks that might hinder promotion opportunities and cause concern about one's future and autonomy, impairing the quality of life of patients with AS.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

- Russell AS. Ankylosing spondylitis: history. In: Klippel JH, Dieppe PA, editors. *Rheumatology*. 2 ed. London: Mosby. 1998;14:1-2.
- Boonen A, van der Linden SM. The burden of ankylosing spondylitis. *J Rheumatol*. 2002;78:4-11.
- Boonen A. Socioeconomic consequences of ankylosing spondylitis. *Clin Exp Rheumatol*. 2002;20(Suppl 28):S23-6.
- Barlow JH, Wright CC, Williams B, Keat A. Work disability among people with ankylosing spondylitis. *Arthritis Rheum*. 2001; 45(5):424-9.
- Boonen A, van der Heijde D, Landewé R, Spoorenberg A, Schouten H, Rutten-van Mólken M, et al. Work status and productivity costs due to ankylosing spondylitis: comparison of three European countries. *Ann Rheum Dis*. 2002;61(5):429-43.6.
- Ariza-Ariza R, Hernández-Cruz B, Collantes E, Batlle E, Fernández-Sueiro JL, Gratacós J, et al. Work disability in patients with ankylosing spondylitis. *J Rheumatol*. 2009;36(11):2512-6.
- Torres TM, Ciconelli RM. Instrumentos de Avaliação em Espondilite Anquilosante. *Rev Bras Reumatol*. 2006;46(Suppl.1):52-59.
- Ward M, Kuzis S. Functional disability in patients with ankylosing spondylitis. *J Rheumatol*. 2001;28(2):315-21.
- Garrett S, Jenkinson T, Kennedy G, 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(12):2286-91.
- Calin A, Garrett S, Whitelock H, Kennedy LG, O'Hea J, Mallorie P, 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(12):2281-5.
- Daltroy LH, Larson MG, Roberts NW, Liang MH. A modification of the health assessment questionnaire for the spondyloarthropathies. *J Rheumatol*. 1990;17(7):946-50.
- Jenkinson T, Malloric PA, Whitchlock HC, Kennedy LG, Garrett SL, Calin A. Defining spinal mobility in ankylosing spondylitis: The Bath Ankylosing Spondylitis Metrology Index (BASMI). *J Rheumatol*. 1994;21(9):1694-8.
- Gilworth G, Emery P, Barkham N, Smyth MG, Helliwell P, Tennant A. Reducing work disability in Ankylosing Spondylitis - development of a work instability scale for AS. *BMC Musculoskeletal Disorders*. 2009;10(68):1-7.
- Prasad M, Wahlqvist P, Shikhar R, Shih YC. A review of self-reported instruments measuring health-related productivity. *Pharmacoeconomics*. 2004;22(4):225-44.
- 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(4):812-9.
- Lerner D, Amick BC, Rogers WH, Malspeis S, Bungay K, Cynn D. The Work Limitations Questionnaire. *Med Care*. 2001;39(1):72-85.
- Forejtová S, Mann H, Stolfa J, Vedral K, Fenclová I, Némethová D, et al. Factors influencing health status and disability of patients with ankylosing spondylitis in the Czech Republic. *Clin Rheumatol*. 2008;27(8):1005-13.
- Boonen A, Chorus A, Miedema H, van der Heijde D, Landewé, H Schouten, et al. Withdrawal from labour force due to work disability in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2001;60(11):1033-9.
- 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(4):353-8.
- Jacobs P, Bissonnette R, Guenther LC. Socioeconomic burden of immune-mediated inflammatory diseases - focusing on work productivity and disability. *J Rheumatol Suppl*. 2011;88:55-61.
- Ramos-Remus C, Hernandez-Rios G, Duran-Barragan S, Sanchez-Ortiz A, Aceves-Avila FJ, Castillo-Ortiz JD, et al. Fifteen-year trends of long-term disability and sick leaves in ankylosing spondylitis. *Clin Rheumatol*. 2011;30(3):361-7.
- 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(1):34-40.
- Chorus AMJ, Boonen A, Miedema HS, van der Linden SJ. Employment perspectives of patients with ankylosing spondylitis. *Ann Rheum Dis*. 2002;61(8):693-9.
- Tam LS, Chan KY, Li EK. The influence of illness and variables associated with functional limitations in Chinese patients with ankylosing spondylitis. *J Rheumatol*. 2007;34(5):1032-9.
- Montacer Kchir M, Mehdi Ghannouchi M, Hamdi W, Azzouz D, Kochbati S, Saadellaoui K, et al. Impact of the ankylosing spondylitis on the professional activity. *Joint Bone Spine*. 2009;76(4):378-82.
- Marengo MF, Schneeberger EE, Citera G, Cocco JA. Work status among patients with ankylosing spondylitis in Argentina. *J Clin Rheumatol*. 2008;14(5):273-7.
- 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(5):1056-62.
- Bakland G, Gran JT, Becker-Merok A, Nordvåg BY, Nossent JC. Work disability in patients with ankylosing spondylitis in Norway. *J Rheumatol*. 2011;38(3):479-84.
- Ward MM. Predictors of the progression of functional disability in patients with ankylosing spondylitis. *J Rheumatol*. 2002;29(7):1420-5.
- Dincer U, Cakar E, Kiralp MZ, Dursun H. Diagnosis delay in patients with ankylosing spondylitis: possible reasons and proposals for new diagnostic criteria. *Clin Rheumatol*. 2008; 27(4):457-62.
- Cakar E, Taskaynatan MA, Dincer U, Kiralp MZ, Durmus O, Ozgül A. Work disability in ankylosing spondylitis: differences among working and work-disabled patients. *Clin Rheumatol*. 2009;28(11):1309-14.
- Ward MM, Weisman MH, Davis JC Jr, Reveille JD. Risk factors for functional limitations in patients with long-standing ankylosing spondylitis. *Arthritis Rheum*. 2005;53(5):710-7.
- Robertson LP, Davis MJ. A longitudinal study of disease activity and functional status in a hospital cohort of patients with ankylosing spondylitis. *Rheumatology (Oxford)*. 2004;43(12):1565-8.
- Ward MM, Kuzis S. Risk factors for work disability in patients with ankylosing spondylitis. *J Rheumatol*. 2001;28(2):315-21.
- Rkain H, Allali F, Bentalha A, Lazrak N, Abouqal R, Hajjaj-Hassouni N. Socioeconomic impact of ankylosing spondylitis in Morocco. *Clin Rheumatol*. 2007;26(12):2081-8.
- Zochling J, van der Heijde D, Burgos-Vargas R, Collantes E, Davis JC Jr, Dijkmans B, et al. ASAS/EULAR recommendations for the management of ankylosing spondylitis. ASessment in AS International working group; European League Against Rheumatism. *Ann Rheum Dis*. 2006;65(4):442-52.
- 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(2):5-92.
38. Keat AC, Gaffney K, Gilbert AK, Harris C, Leeder J. Influence of biologic therapy on return to work in people with work disability due to ankylosing spondylitis. *Rheumatology*. 2008;47(4): 481-3
 39. Gorman JD, Sack KE, Davis JC Jr. Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor alpha. *N Engl J Med*. 2002;346(18):1349-56.
 40. Barkham N, Coates LC, Keen H, Hensor E, Fraser A, Redmond A, et al. Double-blind placebo-controlled trial of etanercept in the prevention of work disability in ankylosing spondylitis. *Ann Rheum Dis*. 2010;69(11):1926-8.
 41. van der Heijde D, Han C, DeVlam K, Burmester G, van den Bosch F, Williamson P, et al. Infliximab Improves Productivity and Reduces Workday Loss in Patients With Ankylosing Spondylitis: Results From a Randomized, Placebo-Controlled Trial. *Arthritis Rheum*. 2006;55(4):569-74.
 42. Verstappen SMM, Watson KD, Lunt M, McGrother K, Symmons DPM, Hyrich KL. Working status in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis: results from the British Society for Rheumatology Biologics Register. *Rheumatology*. 2010;49(8):1570-7.
 43. Listing J, Brandt J, Rudwaleit M, Zink A, Sieper J, Braun J. Impact of anti-tumour necrosis factor α treatment on admissions to hospital and days of sick leave in patients with ankylosing spondylitis. *Ann Rheum Dis*. 2004;63(12):1670-2.
 44. van Lankveld W, vant Pad Bosch P, van de Putte L, Naring G, van der Staak C. Disease-specific stressors in rheumatoid arthritis: coping and well-being. *Br J Rheumatol*. 1994;33:1067-73.
 45. THE WHOQOL GROUP. The World Health Organization Quality of Life assessment (WHOQOL): Position paper from the World Health Organization Soc Sci Med. 1995;41(10): 1403-9.
 46. McHorney CA, Ware JE Jr, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care*. 1994;32(1):40-66.
 47. Jones SD, Steiner A, Garrett SL, Calin A. The Bath ankylosing spondylitis patient global score (BASG). *Br J Rheumatol*. 1996;35(1):66-71.
 48. Kaan U, Ferda O. Evaluation of clinical activity and functional impairment in smokers with ankylosing spondylitis. *Rheumatol Int*. 2005;25(5):357-60.
 49. Boonen A, Severens JL. Ankylosing spondylitis: what is the cost to society, and can it be reduced? *Best Pract Res Clin Rheumatol*. 2002;16(4):691-705.
 50. Boonen A. A review of work-participation, cost-of-illness and cost-effectiveness studies in ankylosing spondylitis. *Nat Clin Pract Rheumatol*. 2006;2(10):546-53.
 51. Boonen A, Chorus A, Landewé R, van der Heijde D, Miedema H, van der Tempel H, et al. Manual jobs increase the risk of patients with ankylosing spondylitis withdrawing from the labour force, also when adjusted for job related withdrawal in the general population. *Ann Rheum Dis*. 2002;61(7):658.