Interventions aiming to reduce early retirement due to rheumatic diseases

Laires PA[1,2,3], Gouveia M[4], Canhão H[3,5]

ACTA REUMATOL PORT. 2017;42:240-248

ABSTRACT

Introduction: Aging of the population and early retirement translates into productivity losses to society. Persistence of working life is crucial to counteract this sustainability issue faced by western countries. Musculoskeletal and rheumatic diseases (RD) may cause work disability and early exit from work, including early retirement. The objective of this article is to review the current knowledge about interventions aiming to reduce early retirement due to RD.

Methods: We searched PubMed and The Cochrane Library for studies either in English or Portuguese between January 2000 and June 2016 that evaluated the impact of interventions targeting early retirement in RD patients still at work. We also searched for grey literature from Portuguese institutional repositories.

Results: We identified several published studies testing pharmacologic and non-pharmacologic vocational rehabilitation interventions. None was specifically identified for Portugal. The general low quality of the literature and its inconsistency makes it unfeasible to draw definitive conclusions. However, some broad recommendations might be outlined. An effective intervention must: 1) act upon different levels (e.g. RD patient, workplace), involving several stakeholders (e.g. rheumatologists, occupational physicians, employers); 2) prioritize the right patients (e.g. more disabling RD); and 3) consider the patients' role, for instance by including an element of patient education and support. Despite the lack of good quality evidence on this field, there seems to be a growing interest in the international scientific community with several ongoing studies promoting such interventions. This promising data will be very useful to set up effective policies.

Conclusions: This article summarizes the current knowledge about the impact of interventions to avoid or mitigate early retirement in RD patients. It highlights the demand for further research and it also contributes to aware decision-makers about the relevance of this topic, particularly in Portugal.

Keywords: Early retirement; Early exit from work; Rheumatic diseases; Vocational rehabilitation

INTRODUCTION

The world has continued to observe an increase in the life expectancy[1]. The old-age dependency ratio is rising steadily in most western countries, which are currently facing a growing economically dependent elderly population[2]. In Portugal, for instance, in 1980 there were a total of 1.8 million pensions with a ratio of 4 active age people per each Social Security old-age pensioner, but now there are over 3.6 millions pensions (including both the Social Security System and the Public Administration Retirement Fund) and a ratio of 2.6[3]. Life expectancy at 65 was 13.5 years in 1980, while now it is 19.1 years[4]. Despite the recent overall increase in the median retirement age, it has been increasing at a much slower pace than life expectancy, which leads to sustainability problems that will force all countries to take action sooner or later. In fact, a trend with early exit from employment is hardly feasible and provides a major challenge to social and health policies. In particular, Portugal is already among the oldest countries in the world, with one of the highest old-age dependency ratios and it is at the forefront of this general problem regarding premature work withdrawal[2].

1. Faculdade de Medicina da Universidade de Lisboa, Lisbon Academic Medical Center, Lisbon, Portugal
2. Centro de Investigação em Saúde Pública, Escola Nacional de Saúde Pública, Lisbon, Portugal
3. EpiReumaPt Study Group – Sociedade Portuguesa de Reumatologia, Lisbon, Portugal
4. Catolica Lisbon School of Business and Economics, Lisbon, Portugal.
5. Chronic Diseases Research Center (CEDOC), NOVA Medical School, Universidade Nova de Lisbon (NMS/UNL), Lisbon, Portugal

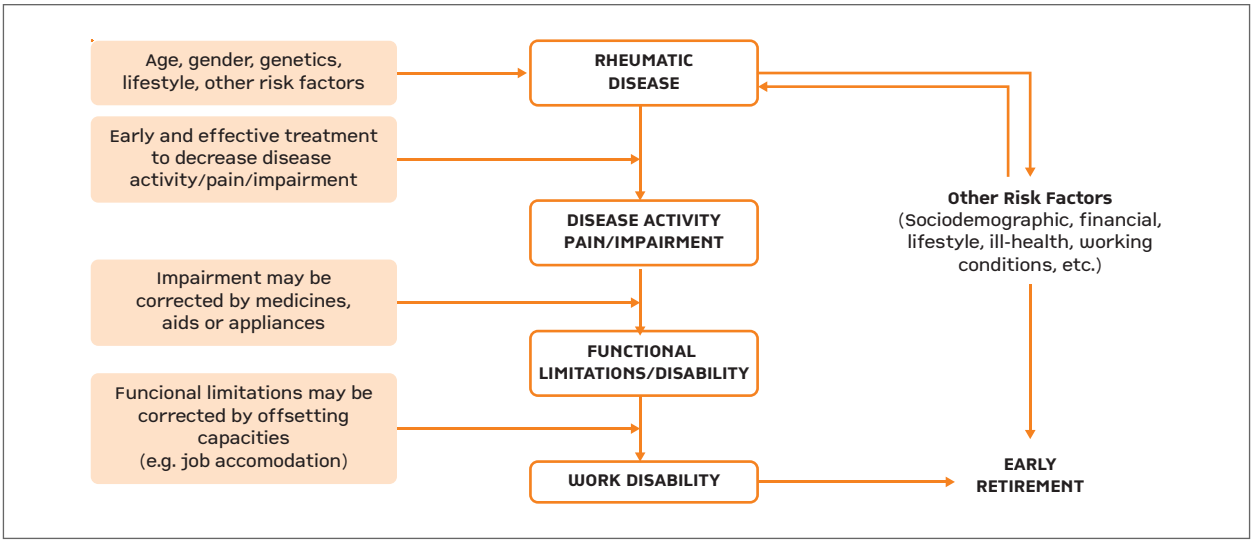

FIGURE 1. Etiological model on the relationship between RD and Early Retirement (Adapted from Nagi S[17] and Stattin M 2005[18])

Musculoskeletal and Rheumatic Diseases (RD) are highly prevalent in the western world and their clinical and functional impacts may be profound, representing major causes of disability among workers. In fact, RD may cause work disability and early exit from work, including early retirement[5-16].

RD usually generates pain and impairment, which in turn may lead to disability and ultimately to work disability and withdrawal (Figure 1 – Etiological model). In each step of this etiological model there are influencing factors, at least some of which may be changeable to some extent (e.g. pain control and disease activity). Interventions aiming to prevent RD-related job loss should target at least some step of this model, therefore its comprehension is crucial in this field.

The objective of this article is to review the current knowledge about interventions aiming to reduce early retirement due to RD.

METHODS

The information source used was PubMed, maintained by the US National Library of Medicine, and The Cochrane Library (including The Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database). We searched for studies either in English or Portuguese between January 2000 and June 2016, combining relevant keywords, such as "retirement", "job loss", "job retention", "exit from work", "work participation", "employment status", "sick leave", "work disability", "rheumatic diseases", "musculoskeletal diseases" and "arthritis". We also searched for grey literature from Portuguese institutional repositories. The objectives of this search were specified by the following framework: Population – RD adults still at work who experience, or are likely to experience, disability; Intervention – Any vocational rehabilitation intervention (pharmacologic and non-pharmacologic); Comparison – any or other intervention (including the standard practice); Outcomes – early exit from work, including early retirement.

RESULTS

Our article focuses on studies aiming to prevent employment loss (i.e. acting on the earlier steps of the etiological model) and we grouped the studies according with the main nature of the intervention approach (i.e. pharmacologic and non-pharmacologic).

PHARMACOLOGIC INTERVENTIONS

Below are some of the studies we found that tested the impact of pharmacologic interventions on early exit from work, including early retirement:

- In 2003, Yellin E et al. interviewed 497 American RA patients of working age (18–64 years) about

their employment status in the year of diagnosis and as of the study year. Among RA patients who had been employed at the time of diagnosis, those from the etanercept clinical trials were more likely to be employed at the time of survey. Moreover, the authors found that after adjustment for relevant factors having been in the etanercept clinical trials was associated with higher employment rates[9].

- In 2004, Puolakka K et al. analyzed the impact of initial aggressive drug treatment with disease-modifying anti-rheumatic drugs (DMARDs) versus therapy with a single DMARD in the prevention of work disability in patients with early RA. 195 patients were randomly assigned to receive either combination therapy with DMARDs plus prednisolone or single therapy with a DMARD with or without prednisolone. After 2 years, the drug treatment strategy was no longer restricted. At baseline, 162 patients (80 in the combination-treatment group and 82 in the single-treatment group) were still working or at least available for work. After 5 years of follow-up the authors found a positive impact with initial aggressive drug treatment in terms of lost productivity – including sick leave and employment loss, either temporary (unemployment) or permanent (disability pensions and retirement). However, this benefit was mainly due to the differences in sick leave. In fact, no statistically significant differences were seen in the take-up of disability pensions or early retirement[20].
- In the same year, Kobelt G et al. observed a slight increase in the work capacity (from 31% to 33%, based on the proportion of patients on full time work) of 160 RA patients under 65 treated during the first year with either etanercept or infliximab in four rheumatology units in southern Sweden[21].
- In 2006, Smolen JS et al. verified that the proportion of patients whose status changed from employable at baseline to unemployable at week 54 was smaller in 722 RA patients receiving methotrexate plus infliximab compared with 282 RA patients receiving methotrexate alone (8% versus 14%; p= 0.05)[22].
- In 2007, Wolfe F et al. examined the effect of anti-TNF therapy on work disability using data from the National Data Bank (NDB) for RD. They studied 3886 patients with RA who were employed at study entry, of whom 1986 received and 1900 did not receive anti-TNF therapy. After adjustment for demographics, RA severity, and comorbidity the authors did not find that anti-TNF therapy was associated with the reduction of self-reported employment loss. However, these results might be hampered by a number of limitations, including the study design (non-randomized) and the study population (<61 years old)[23].
- In 2008, Allaire S et al. using a nested, matched, case–control approach in a large cohort of rheumatoid arthritis patients (NDB) observed no protection of anti-TNF therapy against any or disease-attributed employment loss. However, a protective effect was found for users with shorter disease duration (<11 years. OR 0.4, 95% CI 0.2-0.9)[24].
- In the same year, Cole JC and colleagues, re-examined data from 2 clinical trials [one for RA methotrexate failure patients (n=652) and another for RA severe anti-TNF failure patients (n=391)] and found a significant reduction in the likelihood for early exit from work with abatacept treatment compared with placebo (at 6 months, 1 year and 2 years)[25].
- Also in 2008, Bejarano V et al. published results from a randomized controlled trial (RCT) reporting positive results on reduced employment loss for a 56-weeks period following treatment with adalimumab plus methotrexate[26].
- Similarly, a year later, Halpern MT et al. have shown in an open label extension study that patients with RA who received adalimumab experienced considerably longer periods of work and continuous employment. Thus, during a 24-month period, 158 patients who received adalimumab worked 2 months longer (95% CI 1.3-2.6) and were significantly less likely to stop working than did the 180 patients treated with DMARDs (HR 0.36, 95% CI 0.15--0.85)[27].
- In 2010, Augustsson J et al. using data from the Stockholm anti-TNF follow-up registry concluded that biological therapy is associated with increases in workforce participation in patients with RA[28]. Similar results have been obtained in another Swedish register for ankylosing spondylitis[29].
- In the same year, Verstappen SM et al. using a large British RD registry (BSRBR, British Society for Rheumatology Biologics Register) found that compared with the use of conventional DMARDs, the use of anti-TNF did not prevent patients with RA (n=3291) from not working due to ill health/disability (adjusted OR 0.80; 95% CI 0.36-1.81; p=0.596). However, RA patients in the anti-TNF group who were in remission 6 months after commencing anti-TNF therapy were less likely to exit work 3 years

after inclusion in the register[30].

- Still in 2010, van Vollenhoven RF et al. showed that the likelihood of gaining/ retaining employment over 2 years treatment in early RA patients was greater for the combination therapy of abatacept plus methotrexate (n=219) than for the methotrexate alone (n=214. OR 1.53, 95% CI 1.04–2.26)[31].
- In 2013, Eriksson JK et al. in a randomized controlled open-label trial observed radiological superiority of biological compared with conventional combination therapy which did not translate into better work loss outcomes (i.e. monthly sick leave and disability pension days 21 months after randomization) in patients with early RA who had experienced an insufficient response to methotrexate[32].
- More recently, in 2016, the same author and colleagues compared the long-term employment loss in methotrexate-refractory early RA patients randomized to addition of infliximab or conventional combination treatment. Of 210 working age patients, 109 were randomized to infliximab and 101 to conventional treatment. After over 7 years of follow-up in real world clinical practice, the authors observed that, compared to the year before randomization, exit from employment of these patients improved significantly, with the largest improvement during the first 3 years. However, no difference was detected between strategies, and the level of work loss days remained twice that observed in the general population[33].
- In the same year, Olofsson T et al. using the Swedish Biologics Register, after 5 years of follow-up, observed a substantial decrease in work loss (i.e. mean monthly days lost and accumulated employment loss) of RA patients with high and moderate disease activity treated with anti-TNF[34].

Many other studies explored other work-related outcomes (e.g. surrogate markers) in RD following pharmacologic interventions[35-50].

NON-PHARMACOLOGIC INTERVENTIONS

A vast amount of studies focused on non-pharmacologic interventions aiming to facilitate return to work after sickness absence of employees with low back pain. However, there is already some data for other RD and with other occupational outcomes as well, such as early retirement. Below we listed the most relevant studies performed in this area (some studies also have a pharmacologic intervention):

- In 2003, Allaire SH et al. made a RCT with 48 months of follow-up undertaken to determine the efficacy of vocational rehabilitation, which consisted of 3 components: job accommodation, vocational counseling and guidance, and education and self-advocacy. The job accommodation component consisted of an assessment of possible health-related work place barriers to job performance and development of solutions to the barriers that participants had identified. In the vocational counseling and guidance component, the counselor and participant evaluated the individual's job in light of his or her RD. If problems were foreseen, possible job alternatives, requirements, and relevant resources were identified. In the education and self-advocacy component, information about legal rights and responsibilities, guidance regarding disclosure issues, and skills training to increase the participant's ability to request a job accommodation in an appropriate manner were provided. The counselors also gave the participants in the experimental group documentation about how to manage health-related employment problems and about other available resources. A total of 242 patients with RD residing in Massachusetts, USA at risk for job loss were recruited, 122 for the experimental group and 120 for the control one. Employment withdrawal was delayed in the experimental group compared with the control group. After adjustment for potential confounders, participation in the experimental group was found to be protective against temporary or permanent work loss (OR 0.58, 95% CI 0.34–0.99)[51].
- In 2005, Abásolo L et al. analyzed the effect of a specific program, run by rheumatologists in Spain, in which care was delivered during regular visits and included 3 main elements: education, protocol-based clinical management, and administrative duties. Thus, the visits were structured following specific proceedings for the different diagnoses, which included education (e.g. instructions about the diagnosed RD and due self-management), pharmacologic and non-pharmacologic treatment, and timing of diagnostic tests in a stepwise manner. 13,077 patients were included in this RCT, 7805 in the control group and 5272 in the intervention group. The program was highly efficacious in several occupational outcomes. In particular, fewer participants in the intervention group were permanently work disabled or took early retirement after 4 years[52,53].
- In 2005, de Buck PD et al. conducted a RCT within the region of Leiden, the Netherlands, to investigate

the effectiveness of a multidisciplinary job-retention vocational rehabilitation program in RD patients at risk for job loss, consisting of a systematic assessment followed by education, vocational counseling, guidance, and medical or non-medical treatment. The program was delivered by a multidisciplinary team comprising a rheumatologist, a social worker, a physical therapist, an occupational therapist and a psychologist. Depending on the specific problems of the individual patient, the intervention further consisted of education, counseling and guidance, or treatment. All patients made at least 2 visits to the hospital in connection with the job-retention vocational rehabilitation program and the total duration of the intervention varied, and lasted 4 to 12 weeks. A total of 140 patients with a chronic rheumatic condition were randomly assigned to either this vocational rehabilitation program or usual outpatient care. In contrast with the previous studies the authors observed no difference between the 2 groups regarding the proportion of patients having lost their employment at any time point, with 24% and 23% of the patients in the vocational rehabilitation program and outpatient care groups, respectively, having lost their work after 24 months. This could be at least partly explained by the studied population being composed by ~40% of patients already on sick leave at baseline, many of them longer than 6 weeks. Long-term sick leave usually indicates substantial limitations in work capacity and often precedes permanent work disability. Of note, this study found significant less fatigue in the intervention group, which in turn is expected to lead to more employment maintenance in the long run[54]. The authors emphasized that there was still plenty rationale for the future development and evaluation of vocational rehabilitation programs, in particular the need for early identification of RD patients at risk for work disability, namely through the broad implementation in the clinical setting of rheumatologic care of instruments to measure work disability[55].

- In 2011, Varekamp I et al. studied the effect of an employment maintenance program for employees with chronic disease (25% with RD). This group--training program consisted of six three-hour sessions every two weeks, with a seventh session two months after the sixth. This was combined with three individual counseling sessions. It had an empowerment perspective with the aim of enhancing the knowledge, self-awareness and skills of the individuals, in order to help them solve problems at work. Participants were randomly assigned to the intervention (N=64) or control group (N=58) and after 24 months of follow-up no statistical differences were observed regarding employment maintenance, which remained high in the whole group resulting in too low power to show any significant changes. Alike de Buck PD et al[55] the authors observed less fatigue in the intervention group[56].

The overall quality of these studies is low, namely due to risk of bias, inconsistency and imprecision[57], which also highlights the need for further research on this important topic. Other studies are currently ongoing to evaluate the effectiveness of specific interventions on employment retention of RD patients[58-59].

On the other hand, some studies have already reported the effect of non-pharmacologic interventions in more temporary occupational outcomes, such as sick leave[60], or surrogate markers of early retirement, such as assessments of function and work ability[61-67]. Some scales have been developed specifically to measure work ability in RD patients[68].

DISCUSSION

Many studies have been conducted about interventions aiming to achieve successful outcomes in terms of return to work of workers with RD, however emphasis has shifted towards employment maintenance rather than the more likely irreversible exit from work. This article focuses on interventions to avoid early retirement while RD patients are still at work. There seems to be more consistent data on the positive effects of pharmacologic interventions than on the non-pharmacologic ones. Many reasons may explain this, namely the very nature of the interventions themselves. Non--pharmacologic activities vary immensely and its effectiveness may be difficult to replicate in different settings. Pharmacologic interventions may lower RD activity and cease pain and impairment, which in turn interfere with work disability and early retirement. It is therefore of the utmost importance that RD patients are effectively treated with the most appropriate pharmaceutical approach. Obviously, this judgment must always be done by the rheumatologist who needs to decide on a case-by-case basis among the available treatment options. On this regard, the current trend to expand the rheumatology referral network in Portugal may bring significant productivity gains by allowing

the system to effectively address the problems systematized in the etiologic model presented in this article and thereby avoiding early retirement caused by RD. Unquestionably, in order to ensure optimization of this network, effective identification and referral of RD patients at risk of job loss requires alignment with the primary care (i.e. general practitioner and occupational physicians).

Despite the overall inconsistence and low quality of information, some studies have already shown promising results for the non-pharmacologic interventions. For instance, the work done by Lydia Abásolo and colleagues[52] is being highlighted by the Fit for Work Europe initiative, which produced estimates about the effects of repeating this intervention in other European countries[69]. The ultimate occupational outcome from successful interventions might be so large that justifies on the one hand further research on the topic and on the other to take the risk to intervene even when uncertainty still remains about its effectiveness. The inertia on this field is already too costly and certainly the early retirement scenario is not going to improve if nothing is done otherwise. Of course, the decision should always depend on the budget required to implement a given job vocational program and due opportunity costs. On this regard, taking advantage of geographically or historically closed stakeholders might be a key success factor, by sharing costs and leveraging synergies and economies of scale. For instance, job vocational programs agreed upon by large employers and the nearest rheumatology department in a certain region could be a cost-effective starting point – to build the proof-of-concept of a given protocol and to pilot a broader national policy targeting early retirement in RD patients. Surely, such programs, if possible, should go along with longitudinal prospective studies in order to measure the occupational outcomes and their levels of cost-effectiveness.

In order to increase the likelihood of success of such interventions, some guidance can be drawn from the current literature. First, well-planned interventions should aim different levels (e.g. RD patient, workplace) and should foster lean communication and alignment of all involved actors (e.g. rheumatologists, occupational physicians, employers). A coordinator could integrate all aspects of such multilevel and multidisciplinary intervention in order to better guarantee the person-environmental fit by orchestrating distinct roles and responsibilities; second, prioritizing the right patients can substantially increase the likelihood of success of a given intervention. RD patients at risk of job loss (e.g. longer duration of disease, high self-reported pain and disability measured by the health assessment questionnaire) can be prioritized leading to better and faster occupational outcomes; third, interventions should consider the patients' role and include an element of patient education, coaching and support to enable them to play an active part in the management of their condition in the workplace and also improve their self-efficacy perception.

Some steps have been taken in Portugal regarding this issue, namely the Portugal Apto.PT (Fit for Work Portugal)[70], however more political engagement should take place to ensure impactful nationwide policies and interventions targeting RD-related retirement. Hopefully, this article can also contribute to make politicians and other relevant decision-makers aware of the relevance of this topic and the possible solutions that can be, at least partially, replicated in Portugal.

CORRESPONDENCE TO
Pedro Laires
Sociedade Portuguesa de Reumatologia.
Av. de Berlim, 33 B 1800-033
Lisbon, Portugal
E-mail: laires.pedro@gmail.com

REFERENCES

1. Mortality Data. Geneva, World Health Organization, 2013 (http://www.who.int/gho/mortality_burden_disease/life_tables/en/index.html.
2. United Nations, Department of Economic and Social Affairs, Population Division (2011). World Population Prospects: The 2010 Revision, Volume I: Comprehensive Tables. ST/ESA/SER.A 313.
3. PORDATA – CGA/MTSSS, IGFSS/MSESS (until 1998) | ISS/MSESS (as from 1999).http://www.pordata.pt/en/Portugal/Pensions+total++Social+Security+and+Public+Administration+Retirement+Fund-851
4. INE – https://www.ine.pt/xportal/xmain?xpgid=ine_main&xpid =INE
5. Lacaille D, Hogg RS. The effect of arthritis on working life expectancy. J Rheumatol 2001; 28:2315-2319.
6. Lund T, Csonka A. Risk factors in health, work environment, smoking status, and organizational context for work disability. Am J Ind Med 2003; 44:492-501.
7. Karpansalo M, Manninen P, Kauhanen J, Lakka TA, Salonen JT. Perceived health as a predictor of early retirement. Scand J Work Environ Health 2004; 30:287-292.
8. Solomon C, Poole J, Palmer KT, Coggon D. Health-related job loss: findings from a community-based survey. Occupational and environmental medicine 2007; 64:144-149.
9. Westhoff G, Buttgereit F, Gromnica-Ihle E, Zink A. Morning stiffness and its influence on early retirement in patients with recent onset rheumatoid arthritis. Rheumatology (Oxford) 2008; 47:980-984.
10. Schofield DJ, Shrestha RN, Passey ME, Earnest A, Fletcher SL.

Chronic disease and labour force participation among older Australians. Med J Aust 2008; 189:447-450.
11. Alavinia SM, Burdorf A. Unemployment and retirement and ill-health: a cross-sectional analysis across European countries. International archives of occupational and environmental health 2008; 82:39-45.
12. Pit SW, Shrestha R, Schofield D, Passey M. Partial and complete retirement due to ill-health among mature age Australians. Public Health 2013; 127:561-571.
13. Kivimäki M, Ferrie JE, Hagberg J, Head J, Westerlund H, Vahtera J, Alexanderson K. Diagnosis-specific sick leave as a risk marker for disability pension in a Swedish population. J Epidemiol Community Health 2007; 61:915-920.
14. Jensen LD, Ryom PK, Christensen MV, Andersen JH. Differences in risk factors for voluntary early retirement and disability pension: a 15-year follow-up in a cohort of nurses' aides. BMJ Open 2012; 12;2-6.
15. Li Ranzi T, d'Errico A, Costa G. Association between chronic morbidity and early retirement in Italy. International archives of occupational and environmental health 2013; 86:295-303.
16. Leijten FR, de Wind A, van den Heuvel SG, Ybema JF, van der Beek AJ, Robroek SJ, Burdorf A. The influence of chronic health problems and work-related factors on loss of paid employment among older workers. J Epidemiol Community Health 2015; 69:1058-1065.
17. Nagi S. Disability concepts revisited: implications for prevention. In: Pope AM, Tarlov AR, eds. Disability in America: Toward a National Agenda for Prevention. Washington, DC: National Academy Press; 1991:309-327
18. Stattin M. Retirement on grounds of ill health. Occup Environ Med 2005; 62:135-140.
19. Yelin E, Trupin L, Katz P, Lubeck D, Rush S, Wanke L. Association between etanercept use and employment outcomes among patients with rheumatoid arthritis. Arthritis Rheum 2003; 48:3046-3054.
20. Puolakka K, Kautiainen H, Mottonen T, et al. Impact of initial aggressive drug treatment with a combination of disease-modifying anti-rheumatic drugs on the development of work disability in early rheumatoid arthritis: a five-year randomized follow-up trial. Arthritis Rheum 2004; 50:55–62.
21. Kobelt G, Eberhardt K, Geborek P. TNF inhibitors in the treatment of rheumatoid arthritis in clinical practice: costs and outcomes in a follow up study of patients with RA treated with etanercept or infliximab in southern Sweden. Ann Rheum Dis 2004; 63:4–10.
22. Smolen JS, Han C, van der Heijde D, Emery P, Bathon JM, Keystone E, Kalden JR, Schiff M, Bala M, Baker D, Han J, Maini RN, St Clair EW. Infliximab treatment maintains employability in patients with early rheumatoid arthritis. Arthritis Rheum 2006; 54:716-722.
23. Wolfe F, Allaire S, Michaud K. The prevalence and incidence of work disability in rheumatoid arthritis, and the effect of antitumor necrosis factor on work disability. J Rheumatol 2007; 34:2211–2217.
24. Allaire S, Wolfe F, Niu J, et al. Evaluation of the effect of antitumor necrosis factor agent use on rheumatoid arthritis work disability: the jury is still out. Arthritis Rheum 2008; 59:1082--1089.
25. Cole JC, Li T, Lin P, MacLean R, Wallenstein GV. Treatment impact on estimated medical expenditure and job loss likelihood in rheumatoid arthritis: re-examining quality of life outcomes from a randomized placebo-controlled clinical trial with abatacept. Rheumatology (Oxford) 2008; 47:1044-1050.
26. Bejarano V, Quinn M, Conaghan PG, Reece R, Keenan AM, Walker D, Gough A, Green M, McGonagle D, Adebajo A, Jarrett S, Doherty S, Hordon L, Melsom R, Unnebrink K, Kupper H, Emery P. Effect of the early use of the anti-tumor necrosis factor adalimumab on the prevention of job loss in patients with early rheumatoid arthritis. Yorkshire Early Arthritis Register Consortium. Arthritis Rheum 2008; 59:1467-1474.
27. Halpern MT, Cifaldi MA, Kvien TK. Impact of adalimumab on work participation in rheumatoid arthritis: comparison of an open-label extension study and a registry-based control group. Ann Rheum Dis 2009; 68:930-937.
28. Augustsson J, Neovius M, Cullinane-Carli C, Eksborg S, van Vollenhoven RF. Patients with rheumatoid arthritis treated with tumour necrosis factor antagonists increase their participation in the workforce: potential for significant long-term indirect cost gains (data from a population-based registry). Ann Rheum Dis 2010; 69:126-131.
29. Kristensen LE, Petersson IF, Geborek P, Jöud A, Saxne T, Jacobsson LT, Englund M. Sick leave in patients with ankylosing spondylitis before and after anti-TNF therapy: a population--based cohort study. Rheumatology (Oxford) 2012; 51:243--249.
30. Verstappen SM, Watson KD, Lunt M, McGrother K, Symmons DP, Hyrich KL; BSR Biologics Register. Working status in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis: results from the British Society for Rheumatology Biologics Register. Rheumatology (Oxford) 2010; 49:1570-1577.
31. van Vollenhoven RF, Cifaldi MA, Ray S, Chen N, Weisman MH. Improvement in work place and household productivity for patients with early rheumatoid arthritis treated with adalimumab plus methotrexate: work outcomes and their correlations with clinical and radiographic measures from a randomized controlled trial companion study. Arthritis Care Res (Hoboken) 2010; 62:226-234.
32. Eriksson JK, Neovius M, Bratt J, Petersson IF, van Vollenhoven RF, Geborek P, Ernestam S. Biological vs. conventional combination treatment and work loss in early rheumatoid arthritis: a randomized trial. JAMA Intern Med 2013; 173:1407-1414.
33. Eriksson JK, Wallman JK, Miller H, Petersson IF, Ernestam S, Vivar N, van Vollenhoven RF, Neovius M. Infliximab versus Conventional Combination Treatment and 7-Year Work Loss in Early RA: Results of the Randomized Swefot Trial. Arthritis Care Res (Hoboken) 2016; 68:1758-1766.
34. Olofsson T, Johansson K, Eriksson JK, van Vollenhoven R, Miller H, Petersson IF, Askling J, Neovius M. Does disease activity at start of biologic therapy influence work-loss in RA patients? Rheumatology (Oxford) 2016; 55:729-734.
35. van der Burg LR, Ter Wee MM, Boonen A. Effect of biological therapy on work participation in patients with ankylosing spondylitis: a systematic review. Ann Rheum Dis 2012; 71:1924-1933.
36. ter Wee MM, Lems WF, Usan H, Gulpen A, Boonen A. The effect of biological agents on work participation in rheumatoid arthritis patients: a systematic review. Ann Rheum Dis 2012; 71:161-171.
37. Barkham N, Coates LC, Keen H, Hensor E, Fraser A, Redmond A, Cawkwell L, Emery P. Double-blind placebo-controlled trial of etanercept in the prevention of work disability in ankylosing

spondylitis. Ann Rheum Dis 2010; 69:1926-1928.
38. Furuya H, Kasama T, Isozaki T, Umemura M, Otsuka K, Isojima S, Tsukamoto H, Tokunaga T, Yanai R, Takahashi R. Effect of TNF antagonists on the productivity of daily work of patients with rheumatoid arthritis. J Multidiscip Healthc 2013; 6:25-30.
39. Emery P, Smolen JS, Ganguli A, Meerwein S, Bao Y, Kupper H, Chen N, Kavanaugh A. Effect of adalimumab on the work-related outcomes scores in patients with early rheumatoid arthritis receiving methotrexate. Rheumatology (Oxford) 2016; 55:1458-1465
40. Herenius MM, Hoving JL, Sluiter JK, Raterman HG, Lems WF, Dijkmans BA, Tak PP, Nurmohamed MT, Voskuyl AE, Frings-Dresen MH Improvement of work ability, quality of life, and fatigue in patients with rheumatoid arthritis treated with adalimumab. J Occup Environ Med 2010; 52:618-621.
41. Hoving JL, Bartelds GM, Sluiter JK, Sadiraj K, Groot I, Lems WF, Dijkmans BA, Wijbrandts CA, Tak PP, Nurmohamed MT, Voskuyl AE, Frings-Dresen MH. Perceived work ability, quality of life, and fatigue in patients with rheumatoid arthritis after a 6-month course of TNF inhibitors: prospective intervention study and partial economic evaluation. Scand J Rheumatol 2009; 38:246-250.
42. Mittendorf T, Dietz B, Sterz R, Cifaldi MA, Kupper H, von der Schulenburg JM. Personal and economic burden of late-stage rheumatoid arthritis among patients treated with adalimumab: an evaluation from a patient's perspective. Rheumatology (Oxford) 2008; 47:188-193.
43. Zhang W, Bansback N, Guh D, Li X, Nosyk B, Marra CA, Anis AH. Short-term influence of adalimumab on work productivity outcomes in patients with rheumatoid arthritis. J Rheumatol 2008; 35:1729-1736.
44. Anis A, Zhang W, Emery P, Sun H, Singh A, Freundlich B, Sato R. The effect of etanercept on work productivity in patients with early active rheumatoid arthritis: results from the COMET study. Rheumatology (Oxford) 2009; 48:1283-1239.
45. Kavanaugh A, Smolen JS, Emery P, Purcaru O, Keystone E, Richard L, Strand V, van Vollenhoven RF. Effect of certolizumab pegol with methotrexate on home and work place productivity and social activities in patients with active rheumatoid arthritis. Arthritis Rheum 2009; 61:1592-1600.
46. Farahani P, Levine M, Gaebel K, Wang EC, Khalidi N.J Rheumatol. Community-based evaluation of etanercept in patients with rheumatoid arthritis 2006; 33:665-670.
47. van der Heijde D, Han C, DeVlam K, Burmester G, van den Bosch F, Williamson P, Bala M, Han J, Braun J. Infliximab improves productivity and reduces workday loss in patients with ankylosing spondylitis: results from a randomized, placebo--controlled trial. Arthritis Rheum 2006; 55:569-574.
48. Kavanaugh A, Antoni C, Mease P, Gladman D, Yan S, Bala M, Zhou B, Dooley LT, Beutler A, Guzzo C, Krueger GG. Effect of infliximab therapy on employment, time lost from work, and productivity in patients with psoriatic arthritis. J Rheumatol 2006; 33:2254-2259.
49. Listing J, Brandt J, Rudwaleit M, Zink A, Sieper J, Braun J. Impact of anti-tumour necrosis factor alpha treatment on admissions to hospital and days of sick leave in patients with ankylosing spondylitis. Ann Rheum Dis 2004; 63:1670-1672.
50. Maksymowych WP, Gooch KL, Wong RL, Kupper H, van der Heijde D. Impact of age, sex, physical function, health-related quality of life, and treatment with adalimumab on work status and work productivity of patients with ankylosing spondylitis. J Rheumatol 2010; 37:385-392.
51. Allaire S, Anderson J, Meenan R. Outcomes from the job-raising program, a self-improvement model of vocational rehabilitation, among persons with arthritis. Journal of Applied Rehabilitation Counseling 1997; 28:26–31.
52. Abásolo L, Blanco M, Bachiller J, Candelas G, Collado P, Lajas C, Revenga M, Ricci P, Lázaro P, Aguilar MD, Vargas E, Fernández-Gutiérrez B, Hernández-García C, Carmona L, Jover JA. A health system program to reduce work disability related to musculoskeletal disorders. Ann Intern Med 2005; 143:404-414.
53. Gignac MA, Jetha A, Bowring J, Beaton DE, Badley EM. Management of work disability in rheumatic conditions: a review of non-pharmacological interventions. Best Pract Res Clin Rheumatol.2012; 26:369-386.
54. van Amelsvoort LG, Kant IJ, Beurskens AJ, Schroer CA, Swaen GM. Fatigue as a predictor of work disability. Occup Environ Med 2002; 59:712–713.
55. de Buck PD, le Cessie S, van den Hout WB, Peeters AJ, Ronday HK, Westedt ML, Breedveld FC, Vliet Vlieland TP. Randomized comparison of a multidisciplinary job-retention vocational rehabilitation program with usual outpatient care in patients with chronic arthritis at risk for job loss. Arthritis Rheum 2005; 53:682-690.
56. Varekamp I, Verbeek JH, de Boer A, van Dijk FJ. Effect of job maintenance training program for employees with chronic disease – a randomized controlled trial on self-efficacy, job satisfaction, and fatigue. Scand J Work Environ Health 2011; 37:288-297.
57. Hoving JL, Lacaille D, Urquhart DM, Hannu TJ, Sluiter JK, Frings-Dresen MH. Non-pharmacological interventions for preventing job loss in workers with inflammatory arthritis. Cochrane Database Syst Rev 2014; Nov 6;(11):CD010208.
58. Carruthers EC, Rogers P, Backman CL, Goldsmith CH, Gignac MA, Marra C, Village J, Li LC, Esdaile JM, Lacaille D. "Employment and arthritis: making it work" a randomized controlled trial evaluating an online program to help people with inflammatory arthritis maintain employment (study protocol). BMC Med Inform Decis Mak 2014; 21:14-59.
59. Keysor J. Efficacy of a Modified Vocational Rehabilitation Intervention for Work Disability. Ongoing study Ongoing. 2013 (unpublished)
60. Fleten N, Johnsen R. Reducing sick leave by minimal postal intervention: a randomised, controlled intervention study. Occupational and Environmental Medicine 2006; 63: 676–682.
61. Hammond A, Young A, Kidao R. A randomised controlled trial of occupational therapy for people with early rheumatoid arthritis. Ann Rheum Dis 2004; 63:23-30.
62. Ince G, Sarpel T, Durgun B, Erdogan S. Effects of a multimodal exercise program for people with ankylosing spondylitis. Phys Ther 2006; 86:924-935.
63. Macedo AM, Oakley SP, Panayi GS, Kirkham BW. Functional and work outcomes improve in patients with rheumatoid arthritis who receive targeted, comprehensive occupational therapy. Arthritis Rheum 2009; 61:1522-1530.
64. Baldwin D, Johnstone B, Ge B, Hewett J, Smith M, Sharp G. Randomized prospective study of a work place ergonomic intervention for individuals with rheumatoid arthritis and osteoarthritis. Arthritis Care Res (Hoboken) 2012; 64:1527-1535.
65. Saltychev M, Laimi K, Pentti J, Kivimäki M, Vahtera J. Short- and long-term changes in perceived work ability after interdisciplinary rehabilitation of chronic musculoskeletal disorders:

prospective cohort study among 854 rehabilitants. Clin Rehabil 2014; 28:592-603.
66. van Eren M, Boot CR, Twisk JW, Steenbeek R, Voskuyl AE, van Schaardenburg D, Anema JR. One Year Effects of a Workplace Integrated Care Intervention for Workers with Rheumatoid Arthritis: Results of a Randomized Controlled Trial. J Occup Rehabil. 2016 Apr 7. [Epub ahead of print]
67. van Vilsteren M, Boot CR, Twisk JW, van Schaardenburg D, Steenbeek R, Voskuyl AE, Anema JR. Effectiveness of an integrated care intervention on supervisor support and work functioning of workers with rheumatoid arthritis. Disabil Rehabil 2016; 21:1-9. [Epub ahead of print]
68. AlHeresh R, Vaughan M, LaValley MP, Coster W, Keysor JJ. Critical appraisal of the quality of literature evaluating psychometric properties of arthritis work outcome assessments: A systematic review. Arthritis Care Res (Hoboken) 2016; 68: 1354-1370.
69. http://www.fitforworkeurope.eu/
70. http://www.portugalapto.pt/