Finding Rheumatoid Arthritis Impact on Life (FRAIL Study): economic burden

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ABSTRACT

Introduction: The economic impact of rheumatoid arthritis (RA) is related with the costs supported by the society. It is of the utmost importance to estimate the costs of RA in Portugal in order to access its true social impact and improve the clinical management of this disease.

Objectives: To determine the yearly direct and indirect costs of RA supported by the society in Portugal. Methods: Observational, cross-sectional study with collection of retrospective data, involving patients with RA, diagnosed accordingly to 1987 American College of Rheumatology (ACR) criteria, independently of disease stage, with attendance to a specialist visit between October and December 2009 in a Rheumatology Clinic in Portugal. Data were obtained through the fulfillment of medical and patient questionnaires. Data being covered included socio-demographic and clinical characteristics and health resources. The societal perspective was considered including direct and indirect costs. Unitary costs were obtained from official national sources. **Results:** The FRAIL study included 353 patients, 84% females, with an average age of 59 (range: 23-85 years). In the previous year: 97.2% of patients had a Rheumatology appointment (average: 4) and 35.6% a GP appointments (average: 6); 8.2% were hospitalized at least once, 9.3% had an urgency admission and 41.4% went to the day hospital. Most of the patients (96.0%) were on DMARD; 94.3% performed routine exams; 35.7% had rehabilitation treatments; 21.4% had alternative medicine treatments; 5.7% needed house adaptations; 9.3% needed prosthesis; 5.1% needed permanent home support, 2.9% partial; 31% of the patients referred sick leave because of RA. We estimate that the annual mean cost of treating one RA patient in Portugal is about $3.415 \in$, of which 77.3%, 9.6% and 11.4%, corresponds to direct medical, direct non-medical and indirect cost, respectively. Total cost of the disease increase with disease activity. RA in remission has an average cost of 2.205 \in /patient/year versus 5.634 \in in high activity RA.

Conclusions: Results of the FRAIL study allow a better understanding of the real economic impact of RA for society, which increased very significantly in the last 10 years. If we consider 35 000 patients with RA in Portugal, the annual cost would be 119 525 000 € per year.

Keywords: Rheumatoid arthritis; Direct costs; Disease burden; Disability; Disease activity; Indirect costs.

INTRODUCTION

Rheumatoid arthritis (RA) is considered the most relevant inflammatory rheumatic disease. Estimates for prevalence of RA varies between 0.3 to 1.1% and the majority of patients are in a working age (55%). Therefore its clinical impact is closely related to the economic burden to society¹. The occupational participation of patients with rheumatoid arthritis is reduced when compared to the general population, although less in man (reduction between 16-20%) than in women (reduction between 25-37%). That reduction in employability is also associated with the need for adjustments in the workplace related to the disease and/or work specifications both contributing to a reduction in income expectations^{2,3}.

The relative risk for an RA patient to be unemployed is 1.2 to 3.4 fold comparing to the general population

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and it is closely related to disease duration⁴.

RA imposes more costs to the society than many other musculo-skeletal diseases, with costs representing 2.5% of the GDP in 1992 in the United States with an equivalent impact of a moderate economic depression. We can find similar impact in European countries. In 1998, in Germany and U.K., 12 and 2.3 billion dollars were spent respectively just on RA patients⁵.

We can divide the social cost of a disease in direct, indirect and intangible costs. Directs costs are related to drugs, diagnostics, medical and other appointments as well as hospital admissions. Indirect costs can be described as costs related to loss of productivity and time in occupational, household and familiar tasks. Indirect costs in RA are responsible for two thirds of the total costs². Intangible costs are associated with pain and sufferings of patients because of a disease, which are usually measured by using the reduction in quality of life.

Treatment and management of RA and other inflammatory rheumatic diseases consume time because daily life tasks take longer in result of pain, stiffness and functional disability. Also the regular medical appointments, exams and the need for physical therapy can limit work performance in these patients. RA patients take 1.15 extra hours to do the same daily activities mostly spent on the need for more rest time. The time spent for hospital appointments and is in some studies of 1.9 hours and the global reduction of work time is of 11.6%. Co-morbidities as well as disease activity and disability are also involved in extra time spent, worse radiological status, poor functional performance, ESR and CRP but also cumulative damage all contribute for the loss of occupational and recreational time².

Besides the deterioration in quality of life of the patients and their families occupational disability has major impact with direct implications to patients and society. Several studies demonstrate that rheumatoid arthritis as well as other musculo-skeletal diseases can reduce in 3 to 4 years the work potential, reducing also the potential income of these patients⁶.

RA is an increasing cause of disability and is responsible for more than two thirds of patients with disability (37.6%), with an expectable increase of 21.4 million to 41.4 million of patients by 2030. If eliminated, one in four cases of disability would be prevented⁷.

The profile of occupational disability in RA is not a constant variable; it rises from 15% in the first year to

20 to 40% in the following three years and achieving 50 to 60% in 10 years of disease. In the later years, the disease is still very important with 60 to 70% of occupational disability at 15 years rising to 80% at 20 years and to 90% at 30 years. Globally that impact on working ability is dramatically different from the general population as well as from other chronic conditions^{1,3,8-12}.

In RA, early diagnosis is crucial because at the end of the first 3 years of the disease the percentage of patients already in retirement is near one third. Therefore, a clear strategy to control RA is also important in order to reduce occupational disability. But apart from retirement, RA reduces the ability to get an income that is usually 27% and 48% less in man and women with RA in comparison to healthy workers and 40% less than before becoming ill^{1,8}.

OBJECTIVES

The objectives of this study were to estimate direct and indirect costs of RA in a Portuguese RA patient population and to evaluate its association with functional class status (American College of Rheumatology), disease activity and disability evaluated by Disease Activity Score 28 (DAS28) and Health Assessment Questionnaire (HAQ), respectively.

METHODS

STUDY DESIGN

This was an observational cross-sectional study conducted in a rheumatology clinic setting, between October and December 2009, in Portugal. The main objective was to access the impact and annual costs associated with the treatment and management of RA in patients in various stages of the disease. A consent form validated by the centre ethical commission and the Portuguese national data protection entity was signed by the patients that accepted to participate in the study.

PATIENTS

RA patients fulfilling ACR classification criteria, attending a specialist rheumatology clinic in the eight weeks of the recruitment that were older than 18 years and that were willing and able to participate in the study.

DATA COLLECTION

Data was collected in two paper questionnaires specifi-

cally designed for this study: a) A questionnaire for the rheumatologist that included ACR functional class status, DAS28 parameters¹³, number and type of radiological, laboratory and other complementary exams performed in the previous 12 months as well as prescribed medication; b) A patient self-questionnaire that included socio-demographic data, health resources consumption (medical appointments, hospital admissions, hospital emergency admissions and day hospital sessions), non-medical expenses (transportation, rehabilitation programmes, nonconventional medicine, technical help, and domiciliary support), and days lost due to RA; a validated Portuguese version of the Health Assessment Questionnaire (HAQ)14 was included in the questionnaire and according to its score (from 0 to 3), patients were classified as mildly disabled with a score of 0-1, moderately disabled with a score of 1.01-2, and severely disabled with a score >2¹⁵; the EuroQol quality of life questionnaire (EQ-5D) was also applied and utilities were estimated through a regression model^{16,17}. Although the questionnaire was self-reported, it was supervised by trained staff as a support help.

COSTS

The costs were calculated from the society perspective including direct medical costs (hospitalizations, urgency admissions, outpatient visits, exams, drugs, physiotherapy), direct non-medical costs (transportation, home adaptation, domiciliary support, non-conventional medicine) and also indirect costs (workdays lost, medical absenteeism related to the disease or to medical appointments or similar, workdays lost of the family members to support medical activities). Unitary drug costs were extracted from INFARMED IP18 (ambulatory prices) or from the Catalogue of Health Procurement¹⁹ (hospital prices). Hospitalizations and exams were valued at the prices published by the Portuguese Health Ministry²⁰. Costs for urgency admissions, outpatient visits and day hospital were estimated by medical speciality based mainly on the Public Finance Report of the National Health Service Hospitals²¹. Whenever necessary, costs were updated for 2010 prices considering an annual inflation rate for Portugal according to UNECE22. All costs were expressed in 2010 Portuguese euros. The unitary cost for each item is reported in Table I.

A yearly cost was estimated per patient summing the following components: a) drug cost, obtained multiplying the unitary cost of drugs (prescribed by the rheumatologist) by its daily dose; b) hospitalization, urgency admissions, outpatient visits, day hospital and exams cost, obtained multiplying number of events per year by corresponding unitary cost; c) cost supported by the patient per year regarding rehabilitation, transportation to outpatient visits, domiciliary support, non-conventional medicine, technical help and home adaptations (cost self-reported); d) indirect cost calculated on the basis of the human capital method, through the multiplication of lost work days (by the patient and others in support of the patient) by the mean daily earning extrapolated from the official mean monthly national base gross salary²².

Statistical analysis of the collected data and calculation of costs was performed using IBM SPSS version 16.0.

RESULTS

A total of 353 patients were included in the study. Socio-demographic and clinical characteristics are shown in Table II. As expected most of the patients were female with a mean age of 59 years (SD 12.7, ranging from 23 to 85 years old); the majority lived with their spouses and/or children. Approximately one-third of the sample was employed and more than half had the minimum school years. Disease duration on average was 8.2 (SD 8.6) years with a mean diagnostic gap of 3 years (time between the first complain and the medical diagnosis). The majority had functional class ACR II to IV and almost two thirds had a moderate or severe disease activity by the DAS 28 score. One in five patients was severely disabled according to HAQ. Mean (SD) utility by HAQ class was estimated in 0.761 (0.177), 0.552 (0.261) and 0.311 (0.343) for mildly, moderately and severely disabled patients, respectively.

Health resource consumption related with direct medical costs is presented in Table I. We find important to point out that the number of patients attending acute care (emergency room or acute hospitalization) was relatively low, respectively 9.3% and 8.2%. The majority of the patients (97.2%) had a mean of 4 (SD 2) rheumatologist visits and one third (35.6%) had 6 (SD 4) general practitioner visits in one year.

A high percentage of patients (41.4%) had appointments in the day hospital/ biologics clinic, not only for specific evaluations but also for biologic or other intravenous medication treatment (ex. bisphosphonates). Almost every patient had diagnostic tests

	% of patients	Average number/year	Unitary cost
Hospitalizations	8.2%	2.0	1.495 €
Urgency admission	9.3%	4.1	149€
Outpatient visits			
General practitioner	36.5%	6.2	32 €
Rheumatology	97.2%	4.0	153 €
Orthopedics	4.8%	3.5	60 €
Physiatrist	7.4%	3.8	157 €
Ophthalmology	15.6%	2.9	62 €
Endocrinology	2.5%	2.4	107 €
Cardiology	8.5%	2.9	118€
Pneumology	1.4%	3.2	152 €
Psychiatry	0.9%	2.7	55€
Otorrinolaringologyst	1.4%	2.0	62€
Nutrition	0.8%	4.0	32€
Gynecology	0.3%	2.0	94 €
Hematology	0.3%	2.0	201€
Nephrology	0.3%	2.0	123€
Surgery	0.3%	6.0	98€
Podiatry	1.1%	2.5	32 €
Day hospital	41.4%	3.7	121€
Exams			
X-ray	67.4%	4.7	23 €
СТ	15.3%	1.2	79€
MRI	1.4%	2.8	138€
Bone densitometry	43.1%	1.0	27 €
Upper GI endoscopy	2.3%	1.1	39€
Capillaroscopy	3.1%	1.0	21 €
Sonography	22.7%	1.3	62 €
Blood analysis	87.8%	3.6	26 €
Physiotherapy	35.7%	-	_
	% of patients	Daily average dosage	Cost*/mg
Drugs			
Ledertrexate	73.7%	16 mg/w	0,039 €
Hydroxychloroquine	21.8%	301 mg	0,001 €
Sulfasalazine	24.4%	1.9 g	0,294 €/g
Leflunomide	3.4%	17.5 mg	0,125€
Cyclosporine	1.4%	120 mg	0,014 €
Azathioprine	2.5%	50 mg	0,004 €
SC/ IM Ledertrexate	8.5%	18.7 mg/w	2,01 €
Etarnercept	1.1%	50 mg 2/2 w	4,74 €
Adalimumab	2.0%	40 mg 2/2 w	17,88 €
Infliximab	0.8%	184 mg 2/2 w	7,09 €
Prednisolone	52.4%	6.6 mg	0,009 €
Deflazacort	17.6%	6.6 mg	0,103 €
		0	,

TABLE I. UNITARY COSTS AND CONSUMPTION OF HEALTH RESOURCES RELATED TO DIRECT MEDICAL COSTS

6.6 mg

0,063€

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5.9%

Deflazacort generic

	% of patients	Daily average dosage	Cost*/mg
Lepicortinole	8.2%	6.5 mg	0,011 €
Paracetamol	7.4%	1.1 g	0,132 €/g
Paracetamol + tramadol	5.1%	1.8 pills	0,260 €/pill
Paracetamol + tiocolchicoside	2.8%	2.4 pills	0,174 €/pill
Paracetamol + codeine	2.0%	2.3 pills	0,129 €/pill
Clonixin	1.4%	600 mg	0,001 €
Metamizole magnesium	4.2%	1.8 pills	0,171 €/pill
Tramadol	0.8%	83.3 mg	0,004 €
NSAID	76.5%	Varies	-
Folic acid	61.8%	11.3 mg	0,019 €
Proton pump inhibitor	58.9%	Varies	_

TABLE I. UNITARY COSTS AND CONSUMPTION OF HEALTH RESOURCES RELATED TO DIRECT MEDICAL COSTS (continuation)

Note: Cost of hospitalizations, visits to general practitioner/nutrition/podiatry, exams - Portuguese Health Ministry, Decree n.º 132/2009; cost of urgency admission, other visits, day hospital – Finance Report of Portuguese Hospital 2006; drug costs – INFARMED 2010 and Catalogue of Health Procurement 2010.

*Cost was obtained considering the market drug name referred by the patient.

(94.3%), mostly blood and urine analysis (87.8%), x-rays (67.4%) and 35.7% had at least a physiotherapy program in the last year. Regarding medication methotrexate was the most frequently prescribed drug (73.7%) followed by prednisolone (52.4%), non-steroidal anti-inflammatory drugs (NSAIDs) (76.5%) and proton pump inhibitors (58.9%).

Regarding non-medical resources the majority of patients spent money on traveling to the get to the rheumatologist, general practitioner or to the physiotherapy unit. Only a small percentage of patients reported expenditures on other non-medical resources (home adaptation, technical aids, home support, and non-conventional medicine).

The mean annual cost per patient was $3.498 \in (SD 3.944 \in)$, in which 77.3% were direct medical costs (Figure 1). From this expense the most relevant were medication and medical appointments respectively 34.4% and 22.8% of the total of annual cost (Table IV).

Figure 2 describe the mean values obtained according to functional class and disability. There seems to be no direct relation between costs and the ACR functional class. However we can see an increase from class I to II with a decrease from class II to III-IV. Sub-analysis of the costs revealed that the indirect costs are responsible for this result because they are relatively low in classes III and IV (due to a lower rate of working patients in this class). When we analyse disease activity using DAS28, there is an increase in the total costs with the disease activity. The average cost of a patient in remission is 2.205 € versus 5.634 € in a high disease activity patient. Regardless of the type of the cost, we can find an almost linear relation between costs and disability evaluated by HAQ. This is very relevant, with mildly disabled patients spending on average 2.487 €/year and patients with severe disability spending on average 4.773 €/year.

DISCUSSION

In RA, the economic impact can be important even in short term disease duration, which can be even more relevant on the long term due to the chronic and potentially disabling character of the disease. A study in the US showed that RA patients could reduce their incomes by 20 000 dollars when compared to age matching workers¹¹.

As we review the literature we can find a reduction in working capacity as soon as in 2 years with 62% patients with RA with 1,8 years of disease duration suffering some degree of disability in work performance, and 42% getting unemployed. Of the patients that still worked 38% had no restrictions, but 75% had to have some work adjustments in the workplace. After 4 years only 10% have the same job with no restrictions or adjustments. We can see that sick leave is more frequent in the first year of the disease and with a stabilization

TABLE II. PATIENTS' SOCIO-DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

	Total (n=353)
Female †	295 (84%)
Age, years	59.3 (12.7)
With whom live †	
Alone	54 (15.6%)
Relatives / friends	30 (8.7%)
Spouse / sons	262 (75.7%)
Professional situation †	
Active	121 (35.6%)
Retired	170 (50.0%)
Disability Pension	49 (13.9%)
Education †	
No education	26 (7.9%)
1-4 y	168 (51.1%)
5-8 y	33 (10.0%)
9-12 y	80 (24.3%)
> 12 y	22 (6.7%)
Years in school	6.1 (4.2)
Duration of disease, years	8.2 (8.6)
Delay in diagnosis, years	3.1 (5.0)
ACR functional class †	
Ι	114 (32.4%)
II	216 (61.4%)
III	21 (6.0%)
ĪV	1 (0.3%)
Rheumatoid factor positive †	262 (75.9%)
Tender joints (physician evaluation)	5.8 (6.8)
(n) (0-28)	
Swollen joints (physician evaluation)	2.4 (3.8)
(n) (0-28)	
ESR, mm/hr	23.6 (18.4)
CRP, mg/l	1.5 (3.1)
Disease activity by the patient	44.9 (23.1)
(VAS 0-100)	
Disease activity score (DAS28, 0-10)	3.9 (1.4)
DAS28 class †	
Remission (<2.6)	66 (19.9%)
Low disease activity (2.6 - 3.1)	48 (14.5%)
Moderate disease activity (3.2 - 5.1)	149 (44.9%)
High disease activity (5.2 - 10)	69 (20.8%)
Functional disability score (HAQ, 0-3)	1.3 (0.7)
HAQ class †	
Mildly disabled $(0 - 1)$	114 (32.6%)
Moderately disabled (1.01 – 2)	161 (46.0%)
Severely disabled (> 2)	75 (21.4%)
Utility (EQ-5D score)	0.57 (0.3)

NOTE: The values presented are averages (standard deviation) except in categorical variables (†) where n (%) are presented

of the disease we can achieve a lower incidence of sick leave. An early intervention by a rheumatologist with a more aggressive approach to the disease is related also to a reduction of days on sick leave^{2,4,5,10,24,25}. In our study several of the possible conclusions are different because of a high diagnostic gap (3 years on average) and the time lost to referral to a rheumatologist.

It is not only the absence from the workplace that influences the work performance of an RA patient, these patients tend to socialise less, to spend less time outdoors, to search less for jobs. There are two barriers that RA patients tend to consider regarding job satisfaction, leaving their house (morning stiffness, ability to do morning tasks) and the need to workplace adaptation both can cause discomfort and can even be responsible for job cessation²⁶.

We can find in the literature that, in opposition to our findings, indirect costs are 2 to 3 times higher than direct cost, but that seems to be changing with the introduction with biological drugs in the 90's and with the use of combination DMARD s¹¹. That can be partially explained by the high level of retired patients that contributes to lower sick leave or disability pension related to RA. In other studies drugs are responsible for 8-24% of the total of medical costs, medical appointments to the rheumatologist to 8-21% and hospitalization 17-88%^{10,24,}25. Drugs are responsible to 6-17% of direct costs and 2-5% of the total of costs with RA. Our findings report a different view to the role of drug and medical appointments costs in the total of the cost with RA²⁴⁻²⁶. That can be explained by the different types of health and social security services as well as the type of patients²⁴⁻²⁶. We found a high percentage of retired patients, an important diagnostic gap and a low education and with jobs with lower salaries of our group. If we add a universal health system and a state reimbursement on drugs that alone can explain if not totally at least partially the differences obtained with our work.

The amount considered as direct cost from RA differs from study to study and some consider direct costs around \$5.425 with indirect costs of \$ 9.744 with a total of \$15.238 and that amount is very different from our work and from previous Portuguese studies⁵.

In Portugal, it seems that there has been an increase in the disease cost in the last years. From $1.151 \in$ to $2556.6 \in$ in 2002 to $2966.6 \in$ in 2006^{27-29} . However, different study designs and approach to the costs considered cannot allow a direct comparison of these costs. It is nevertheless expected with inflation and the use of

THE LAST YEAR		
	% of	Average
	patients	number/year*
Direct non-medical resources paid by the patient**		
Travelling expenses to attend outpatient appointments	86.4%	
Travelling expenses to attend physiatrist treatments	17.0%	
Investment in adaptations made to the house	5.7%	
Investment in prosthesis	9.3%	
Investment in domiciliary support	4.5%	
Investment in alternative medicine	6.5%	
Productivity loss		
Days of active work lost because of absences/ leaves***	8.8%	139.8 (133.5)
Working active hours lost to attend doctor appointments***	28.3%	19.3 (20.6)
Days of active work lost by the companion (ex. spouse)	16.4%	1.9 (0.3)

TABLE III. RESOURCES CONSUMPTION RELATED TO DIRECT NON-MEDICAL COSTS AND INDIRECT COSTS WITHIN THE LAST YEAR

*The values presented are averages (standard deviation).

**Resources supported by the patient.

***Considering only active patients.

newer and more expensive drugs that the trend for direct costs is to increase.

The relation between HAQ score and the cost was also seen in other studies as well as quality of life with an increase of the cost with the worsening of HAQ and short form 12 (SF-12)³⁰.

Gross domestic product (GDP) can influence the impact of diseases and RA as well, it is known that in countries with lower GNP the impact of RA is higher and also that there is a tendency for chronic diseases before 65 years occur in people with lower incomes³¹.

There is no solid way to compare studies on the cost of RA in different countries because of social end economical differences but also because of the methodology of each study. For example in Germany the annual cost of RA was $21.700 \in$ and in France was $15.600 \in$ with indirect costs respectively 70 and 24%. In a recent review Xie et al found differences in the indirect cost of RA between 60 dollars in Thailand and 32.155 dollars in the US.

Like in our study several other studies link disability with higher costs of the disease with variations of increase between 2 to 5 fold in the cost depending on HAQ score³²⁻³⁷.

Disease activity is also found as a determinant of and increase cost of RA even in early arthritis, and we can see a high increase between moderate and high disease activity³⁸. In our study we consider remission as an endpoint to RA and we proved that patients on remission

can cost less 2.5 fold in comparison to high activity patients witch reinforces the need for an aggressive and patient focussed treatment strategy that as remission or low disease activity as a valid clinical endpoint.

LIMITATIONS

Our study has some limitations that should be highlighted. The RA patients group was not representative of the Portuguese RA patient's populations. There were limitations due to low understanding of the questionnaire by a minority of the patients. The data on costs of medication, appointments or exams are scarce and



FIGURE 1. Total cost distribution

	Yearly average cost/patient	Proportion of
	(n=353)	total cost
Direct medical costs	2.698 € (3.127)	77.3%
Hospitalizations	246 € (822)	7.0%
Urgency admissions	58 € (225)	1.6%
Outpatient appointments	796 € (468)	22.8%
Day Hospital	184 € (252)	5.3%
Auxiliary methods of diagnosis	206 € (141)	5.9%
Medications	1.200 € (2.881)	34.4%
Physiotherapy*	10 € (60)	0.3%
Direct non-medical costs*	339 € (1.203)	9.7%
Transports	71 € (180)	2.0%
Investment in adaptations made to the house	80 € (482)	2.3%
Investment in prosthesis	11 € (67)	0.3%
Investment in domiciliary support	127 € (1.007)	3.6%
Investment in alternative medicine	51 € (284)	1.5%
Indirect cost	452 € (1.795)	13.0%
Total cost	3.489 € (3.944)	100.0%

TABLE IV. ESTIMATES OBTAINED FOR AVERAGE YEARLY COSTS PER PATIENT

NOTE: The values are averages (standard deviation) *Only the cost supported by the patient is presented.



FIGURE 2. Total average yearly cost per patient by functional class, disease activity and disability

were obtained in several places. Retrospective data is always based on patient recollection and it is a bias to consider.

However a large population was evaluated and there was a support by investigators regarding data collec-

tion. Several experienced rheumatologists were involved and the clinical data was performed by the patients attending rheumatologists.

With our work we tried to prove that there is very relevant impact of rheumatoid arthritis in our country and that there is solid relationship between disability, disease activity and direct and indirect cost of the disease.

A global strategy to reduce the disease impact on the society has to be focused on the diagnostic gap but also in achieving remission or low disease activity. Our country social network, workplace support, occupational rehabilitation and people life expected income should be consider as a starting point to a strategy that could reduce the large amount of people that reaches specialized care already retired from work. A good network of rheumatology hospital departments and the need for early diagnostics can also provide that RA can live healthier and more productive lives.

In this study we can observe that it is relevant to treat patients in order to obtain remission not only for obvious clinic purposes but also because overall we are achieving better social and economic results. We should perform the DAS 28 and HAQ, among other possible outcome measures in order to design a strategy that can improve our patient's clinical results but

also can save some of the important economic burden of rheumatoid arthritis.

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