
The economic burden of disease: comparison between rheumatoid arthritis and ankylosing spondylitis

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ABSTRACT

During the last decade the economic burden of rheumatic diseases has been increasingly recognised. Even though more studies have been published on rheumatoid arthritis (RA) than ankylosing spondylitis (AS) sufficient data is available for comparison of some economic consequences. This overview addresses mainly the societal impact of RA and AS on (1) labour force participation, on (2) the costs of healthcare consumption and reduced productivity and on (3) health in terms of QALY.

In order to examine labour force participation comparison with the general population is preferable. These studies demonstrate increased withdrawal from work in both diseases but more frequently in RA. Risk factors for reduced labour force participation in RA and AS are longer disease duration, lower education and unfavourable labour market conditions. The influence of the sex on employment depends on several factors such as the type of disease and the labour force participation of the general population.

In RA overall mean direct costs of healthcare consumption and indirect costs of reduced productivity are above that of AS, particularly after long disease duration. Out-of-pocket expenditures costs were higher in females RA patients than in males while this was less clear in AS. The main cost driver in both diseases for all type of costs was reduced physical function.

The societal valuation of health (utility) showed similar reductions of quality adjusted life years (QALYs) in RA and AS when compared with the general population.

In conclusion, while the societal valuation of the impact of both diseases on health is similar, the decrease in worker participation is more pronounced in RA and direct as well as productivity costs are higher. However, since AS starts at an earlier age, the lifetime economic

burden might be higher. There is a strong relation between physical function and each aspect of economic impact.

Introduction

To understand what 'economic burden' represents, it is informative to reflect on the etymology and definition of the word economics. The term originates from two Greek words, οἶκος (*oikos*, "house") and νόμος (*nomos*, "custom" or "law"), hence "rules of the house (-hold)". It refers to the social and behavioural science which studies the production and distribution of products that are usually limited. The aim is to maximise welfare. *Health economics* studies the supply and utilisation of healthcare in a given society with the aim to maximize health. It is important to realise that the consumers of healthcare have also an important contribution, through labour, to the economic situation of a society (Fig. 1).

Increasingly, economic sciences also study how desired distributional situations can be reached. The *economy of healthcare* studies the distributional issues of the healthcare system usually based on data derived from health economic studies.

While health economic principles usually consider the macro level, which is the society, these principles can also be applied at the meso-level (hospitals, health insurance companies, social security organisations) and the micro-level, which is level of the individual patients.

In this overview, we will address mainly the societal impact of RA and AS, two chronic rheumatological diseases, on the economy of health; this is on (1) labour force participation, (2) the costs of healthcare consumption and reduced productivity and finally (3) the effect on health in terms of QALY. First, an overview of the data on each issue for the individual disease will be provided and next data of studies that directly compared both diseases.

Competing interests: none declared.

Labour force participation

Worker participation is not a single hard endpoint, but a continuum of outcomes or states moving across normal participation, reduced participation at work (presenteeism), temporary absence (such as sick leave) and permanent absence (such as work disability) from work.

The majority of studies in RA and AS addressed the issue of permanent absenteeism (work disability and reduced employment) and a few reported on sick leave. Recently, presenteeism received more attention (1). Although presenteeism is extremely important for work related quality of life and well-being at work, it is not known whether presenteeism leads to production loss for society. The same can be said for newer outcomes such as 'work ability' and 'employability' that are nowadays used along intervention trials. While perceived ability to perform work might be important for the patient and as a predictor of future work participation, these outcomes need further validation.

A particular challenge is that figures on work participation are only meaningful when comparison with a reference population (usually the general population) can be made. Also in the 'healthy' general population, not all persons in working age are employed and differences exist across genders and age categories. Similarly, sick leave and presenteeism also occur in working subjects without a chronic illness.

Literature review of AS and RA of studies comparing data with the general population

Rheumatoid arthritis

Geuskens *et al.* reviewed studies that report employment and work disability in RA compared with the general population. In five cross-sectional studies the risk of reduced employment was 2.0 to 2.7 fold and in eight studies the odds of being work disabled varied between 1.2

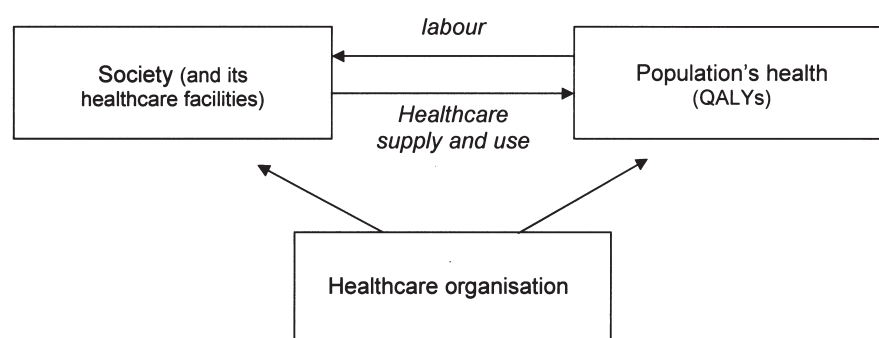


Fig. 1. Health economics weights the population's health against the provision and utilisation of healthcare, taking account of possible returns in terms of productivity. The healthcare organisation system aims to control and regulate this relation.

to 3.4 (2). Longitudinal data suggested that withdrawal from work occurs already early, one third withdrawing in the first two years, but continues constantly in longstanding disease (2). Also compared with the general population, the risk of decreased employment was steadily increasing with advancing disease duration (3). Chung *et al.* demonstrated in RA the strong influence of the social security system by revealing higher withdrawal from work withdrawal rates in Finland opposed to USA despite better health (4). In countries with lower labour force participation decrease in employment in RA women was more important than males but in countries with high labour force participation the opposite was seen (5). Burton suggested that the apparent decrease in recent years in withdrawal for work in RA is related to a decrease in physically demanding work rather than to changes in the epidemiology of RA (6). Within patients with RA, inception cohorts showed that older age at onset, having physical loading jobs and worse HAQ are associated with future work disability (6-8). Improvement in HAQ was strongly associated with maintenance of work status (9).

Sick leave in early disease occurred in 53 to 82% of patients with paid work and patients had 46 days sick leave compared to 11 days in the general working

population (2). Sick leave in early RA was shown to predict later work disability (10) and explains why in early disease sick leave is more important while in later disease work disability better reflects the impact of RA (11).

Two studies reported that employed patients with RA have a decrease in productivity and would need an increase of about 5.1 to 6% of working hours to compensate. Fatigue, HAQ, mental and physical component subscore of the SF-36 were associated with reduced productivity at work (12, 13).

Ankylosing spondylitis

In AS two cross-sectional studies, one in The Netherlands and another in Germany showed that the chance of being employed was decreased in males (0.80 to 0.92) but not in female patients (0.92 to 0.97) when compared to the general population (14, 15). Withdrawal from work was three times increased. (16) Surprisingly, despite better employment, female AS patients were at higher risk to be work disabled (OR: 4.0; 3.2-4.9) compared to male patients (OR: 2.8; 2.5-3.1) in the Dutch study, likely because the Dutch social security system allows to have partial work disability while remaining half time in labour force (14). A case control study in Argentina reported work disability of 9% in patients opposed to 0% in controls

normal productivity ↔ presenteeism ↔ temporary absenteeism ↔ permanent absenteeism

Fig. 2. Worker productivity is a continuum of states where the return from permanent absenteeism to other states is more difficult than going back and forth among the other work-states.

and patients worked less often full time than controls (71% opposed to 87%) (17). However, in Germany, a country with a different social security system and availability of part-time jobs, no increase of part-time employment was found compared to the population (15). The risk of work-disability compared to the general population occurred mainly immediately after diagnosis and was especially pronounced in younger persons and in those with manual work (18, 19). Within patients, pain, worse physical function, education or manual occupations, co-morbidity, avoiding coping strategies and depression were associated with withdrawal (16, 17, 20). Sick-leave occurred in up to 50% of patients yearly. The total number of days annual sick leave compared with the general working population was slightly higher (7 and 12 days opposed to 6 and 9 days in the population) in some countries and markedly increased in other studies (22 opposed to 12 days) (21). Invariably, the majority of days sick leave were attributable to AS. Sick leave occurred more frequent in patients with more physical demanding jobs, those with higher disease activity, with peripheral arthritis or inflammatory bowel disease. It was also shown that the type of social security system of a country or the unemployment rate influenced work participation. An abstract on presenteeism in AS indicated a decrease in at-work productivity of about 8%.

Direct comparisons of RA and AS

Evidence of direct comparisons on the impact of each disease on worker participation is much stronger, but limited to only two studies in Germany. Compared with the general population,

the overall standardised employment ratios in RA patients were 0.76 in females and 0.78 in males as opposed to 0.97 and 0.92 in females and males with AS (15). Also after adjustment for sex, education, and region of residence the chance of employment was higher in AS compared to RA: 11% and 42% higher participation after 5 and 10 years disease duration, respectively. The stratification by age and sex shows a slightly earlier peak of new work disability pensions in male AS patients aged 50-54 years (42.5 per million) compared to females with AS (15.5 per million in the age group 55-59 years) and to all RA patients (age group 55-59 years: 89.6 per million men, 180.7 per million women, respectively) (22, 23). The higher risk of work disability in RA compared to AS (particularly in women) is confirmed by incidence rates from the annual statistical report of the compulsory German pension insurance in all age groups (Table I) (22, 23). In female RA patients with less than 10 years of school education and living in regions with high unemployment rates the lowest standardised employment ratios of 0.55 were found compared to 0.70 in females with similar education but residence in areas with more favourable labour market conditions. In higher educated women with RA the respective ratios were 0.76 and 0.82 (15).

Cost-of-illness studies

Cost-of-illness studies provide insight into the financial consequences of resource utilisation and loss of paid productivity for society. As such they are a necessary starting point for full health economic analyses. When considering the societal perspective, all resources used and all productivity lost for society

is important and the monetary value is the true market value of the resource or production lost. This is different for the perspective of the insurance perspective, for which tariffs are relevant, or the perspective of the patients, for whom the out-of-pocket costs are important.

Review of the literature on societal costs

Original studies reporting costs of RA or AS were searched systematically and revealed 26 studies in RA and 7 studies in AS. The detailed methodology and results of this review can be found in this issue (24). Overall mean costs of RA (€14,906 per year) were above that of AS (€9,374 per year), while the relative distribution of costs over cost domains was approximately similar (Table II).

One third of the outpatient costs were medication costs in both diseases. Remarkable were the higher costs for rheumatology nurse, psychologists consultations and emergency department visits in RA opposed to higher costs for physiotherapist visits in AS. Home care services and societal costs of informal care were the main cost drivers within the patient and family costs in RA as well as AS. For both diseases, productivity costs based on the human capital approach (considering costs of absenteeism from the first day until return, retirement because of age or death) were 3 to 10 times higher than based on the friction costs (considering costs of absenteeism until replacement from the free market occurred which is estimated on average at 3 months) and accounted for more than half the total costs of both diseases (24). None of these studies included costs of presenteeism.

The majority of these studies reported

Table I. Annual incidence rates (no. per 1 million persons) of work disability due to RA/ AS in 2007 among 35.253.500 members of the compulsory German pension insurance (22, 23).

Diagnosis (ICD-10-code)	Sex	Age groups (yrs.)							total
		< 35	35-39	40-44	45-49	50-54	55-59	≥ 60	
RA (M05/ 06)	females	6.0	22.7	34.4	59.4	139.3	180.7	48.6	52.2
	males	1.6	9.9	11.3	24.4	57.8	89.6	37.3	23.7
AS (M45)	females	0.5	4.5	4.8	9.2	12.5	15.5	3.6	8.8
	males	1.6	11.4	15.6	27.4	42.5	38.5	10.1	16.8

costs specifically as the consequence of the rheumatologic disease. In RA, the COI of RA without co-morbid disease were compared to COI of RA with depression (7% of patients) or cardiovascular disease (5.9%) or both comorbidities in a large database registering medical consumption. (25) Patients with RA and cardiovascular (CV) disease had the highest medical COI (US\$14,145), followed by RA and CV disease and depression (US\$ 13,513), RA and depression (US\$12,225) and RA alone (US\$11,404). In a study among AS patients in the USA, AS-related costs direct costs accounted for 66% of the total costs with especially higher costs for medications and hospitalizations for the non-AS-related costs (26). For 50% of patients the direct cost of AS accounted for 90% of the all-cause direct costs. Another study reported that patients with IBD as AS related co-morbidity occurred higher costs than patients without IBD (27).

In RA, clearly disease activity DAS but especially HAQ were associated with higher costs (28). In AS, patient global disease activity and physical function (BASFI) were related to all type of costs. In addition, gender was associated with patient and family costs and disease duration with productivity costs (20, 21, 26, 29, 30).

Direct comparisons of RA and AS

Few studies performed direct comparisons of cost-of-illness studies in patients with AS and RA using similar inclusion criteria and similar approaches to assess the costs. In the large national rheumatology database in Germany patients of working age (<65 years) were compared (31). Overall, mean annual direct and indirect costs were higher in RA than in AS (Table III). In RA patients' costs were higher in females than in males whereas the opposite was found in AS. Remarkably, within the first 10 years of the disease, both direct and indirect costs were similar, but after more than 10 years they were higher in RA than in AS. Functional status had the largest impact on costs: in patients with moderate to severe limitations costs were higher in RA compared to AS.

Table II. Summary of societal cost-of-illness in RA and AS for the different subcategories of costs from a systematic literature review.

	Rheumatoid arthritis		Ankylosing spondylitis	
	Weighted mean	IQR	Weighted mean	IQR
<i>Direct healthcare and non healthcare costs</i>				
Healthcare costs	4170	(2756–4561)	1992	(1359–2474)
Outpatient costs	2981	(1754–3660)	1400	(1114–1419)
Inpatients costs	1243	(446–1649)	592	(245–983)
Patient & family costs	2284	(628–3092)	1104	(541–1431)
<i>Costs of paid productivity loss</i>				
Costs sick leave	2770	(855–2378)	913	(388–1079)
Productivity costs (HCA)	8452	(4144–11,566)	6278	(5111–7725)
Productivity costs (FCA)	1441	(702–1307)	2271	(1572–2970)

HCA: Human Capital approach; FCA: Friction costs approach.

Table III. Direct comparison of costs of illness in outpatients aged 18–65 years with RA (n=4351) and AS (n=827) in the national database of the German collaborative arthritis centres in 2002 (31).

	RA		AS	
	Direct costs (€/patient/year)	Productivity costs (€/patient/year)	Direct costs (€/patient/year)	Productivity costs (€/patient/year)
Sex				
Men	4236	16187 (HC) 7769 (FC)	3726	13904 (HC) 7426 (FC)
Women	4874	15479 (HC) 7921 (FC)	3630	12812 (HC) 6783F
Disease duration				
< 5 years	4137	10190 (HC) 6757F	4165	10712 (HC) 7815 (FC)
5–10 years	4163	13118 (HC) 6806F	4273	10412 (HC) 6994 (FC)
> 10 years	5563	21222 (HC) 9409F	3385	15046 (HC) 7030F
Functional status (FFbH / HAQ)*:				
> 70 / < 1.2	3225	8811 (HC) 4832 (FC)	3799	8214 (HC) 5384 (FC)
50–70 / 1.2–1.7	5661	21580 (HC) 10892F	3865	17791 (HC) 9480 (FC)
<50 / > 1.7	8403	34915 (HC) 19024 (FC)	4590	29647 (HC) 14396 (FC)

* Disability recorded by the Hannover Functional Status Questionnaire (FFbH), which is highly correlated with the Health Assessment Questionnaire (HAQ) ($r=0.87$); HC: human capital approach; FC: friction cost approach (the friction period of 58 days).

Patient out-of-pocket costs

Although it was shown that in patients with arthritis out-of-pocket expenditures (OOPE) are substantial and are increasing at a rate higher than the inflation rate despite better health (32), only few studies examined OOPE in RA or AS. One study presented a direct comparison, and reported slightly higher mean annual OOPE in RA (€559) than in AS (€517) (31). Other investigators

studied OOPE in both diseases separately. In Germany, OOPE accounted for 12–15% of the total direct costs in RA patients (31, 33) and for 14–20% in patients with AS (31, 34). In Belgium the mean annual OOPE were €1098 per patient per year in longstanding RA (>12 years), opposed to €469 per patient per year in early RA (<1 year). The largest component of OOPE (about 45%) were co-payments for medication (35). In

Australia, OOPe in RA were AU\$1523 with higher costs for females than males and for patients older than 65 years (36). In the USA, it was found that, compared with the population, income losses in RA were between US\$2319 (9.3%) and 3406 (10.9%) (12). In AS, out of pocket costs in 1998 were estimated at €432 (sd:172) but income loss due to sick leave or work disability were €1372 per patient per year (37). OOPe clearly increases with disability in both RA and AS (31, 37, 38). Also female patients incurred higher OOPe. In the US, it was shown that compliance with etanercept and adalimumab was lower for RA patients with the highest copayments or coinsurance (39).

Health forgone for society: utilities and QALYs

Bansback reviewed utilities in rheumatologic disease. In 14 studies in RA, the average utility was between 0.5 and 0.75 and was -0.1 to -0.3 when compared to population norms. Physical function, disease activity, income, education and treatment were all associated with utility. In AS, five studies were available and average utility was between 0.53 and 0.69. Similar as in RA the decrease with the general population was estimated to be between -0.1 and -0.3. Physical function and disease activity were reported to be the main contributors associated with utility in AS (40). No direct comparisons of utilities or QALYs were found.

Conclusions

When comparing the socio-economic impact of RA and AS, a striking difference was found in the number of publications for each of the diseases. For all the socio-economic domains explored in this article; worker participation, costs of illness and quality adjusted life years, many more data were available for RA than AS. Not only the higher prevalence of RA, but also the natural inclination of clinicians towards treatable diseases can explain this discrepancy. More important than the difference in the quantity of studies, is the scarcity of studies directly comparing the socio-economic impact of both diseases, challenging the correct interpretation

of comparisons. Indirect comparisons risk that differences between diseases can be entirely explained by different sampling, instruments and methods of analyses. Notwithstanding, it seems possible to make some clear conclusions while at the same time formulate a research agenda of issues that need further exploration.

When compared to the general population, employment was clearly more decreased in RA than in AS, also when correcting for differences in disease duration and education. Striking was that in RA the decreased employment was more pronounced in women, especially when they had a lower educational level, while in AS the decrease was more pronounced in men. In both diseases the employment rates decrease with advancing disease duration. In longitudinal studies withdrawal of one third of RA patients occurs in the first two years, but continues constantly in longstanding disease. However, in AS the data are more conflicting since one study in The Netherlands employment rates in different strata of disease duration were adjusted for age and gender with employment rates in the population and saw a sudden decrease in employment immediately after diagnoses. A specific challenge when comparing worker participation is the influence of contextual factors. While disease activity but especially limitations in functioning and comorbidity are the variables with the strongest association with restrictions in worker participation in both diseases, there is an important contribution of personal factors, especially coping strategies, and environmental factors, such as job characteristics or the economic environment (social security system and regional unemployment) to worker participation.

Direct as well as productivity costs were higher for RA than AS. The study that compared both diseases directly, suggested that the costs of illness of RA and AS are actually comparable in the first 10 years after diagnosis and diverge from then onward with higher cost for RA. The distribution of costs were similar in RA and AS. Within the direct costs, medication cost and costs of informal care giving were the most

important component of the healthcare and non-healthcare costs respectively in both diseases. Productivity costs as a consequence of work disability largely exceeded the costs due to sick-leave in both diseases. In both diseases, functional limitations, but also disease activity and comorbidity are strongly associated with higher costs. Indirect costs are also associated with lower educational level or manual jobs. The impact of educational level on direct costs was less clear.

In contrast to the societal costs, out-of-pocket expenditures (OOPe) and income loss were only marginally higher for RA than AS. It should be noted that only few studies looked into this aspect. Interestingly, women incurred higher OOPe, mainly due to the more frequent need for informal caregiving.

Although the impact on work participation and costs-of-illness in cross-sectional studies or cross-sectional cohorts were higher in RA than in AS, it should be realised that the average age of onset of AS is 15 years earlier than RA. This implies that the lifetime costs of AS might exceed the lifetime costs of RA and this issue merits more attention.

Society's aim of production and consumption of 'healthcare' is to maximise society's health. On this line, society values reported health (utility) equally decreased in both conditions but no direct comparisons are available. Again, given the earlier onset of disease in AS, the loss in quality adjusted life year, which integrate the utility over time, in AS might be more substantial than in RA.

In summary, while the societal valuation of the impact of both disease on health is similar, the decrease in worker participation is more pronounced in RA and direct as well as productivity costs are higher. In both diseases, disease activity and functional impairments seem the most important variables associated with worse economic outcome. When considering worker participation, there is additional strong influence of contextual factors in both diseases.

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