

## EXTENDED REPORT

## Costs of ankylosing spondylitis in three European countries: the patient's perspective

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*Ann Rheum Dis* 2003;62:741–747

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Accepted 20 January 2003

**Objective:** To assess a patient's out of pocket costs, income loss, time consumption, and quality of life (QoL) due to ankylosing spondylitis (AS) in three European countries and to assess variables predicting these outcomes.

**Methods:** 216 patients with AS from the Netherlands, France, and Belgium participated in a two year study. Health resource use, days absent from work, time lost, and quality of life (EuroQoL) were assessed by bimonthly questionnaires. AS related healthcare and non-healthcare expenditure and income loss were calculated taking into account country-specific regulations. Predictors of costs, time consumption, and QoL were analysed by Cox's regression.

**Results:** 209 patients provided data for cost analysis. Average annual healthcare and non-healthcare expenditure was €431 per patient and average annual income loss was €1371 per patient. Healthcare costs were highest for Belgian and lowest for French patients, while non-healthcare costs were highest for Dutch patients. A patient's total costs were associated with higher age and worse physical function. On average, patients with AS needed 75 minutes additional time a day because of AS. Worse physical function and higher disease activity predicted time consumption. After adjusting for baseline confounders, QoL was worse in Belgian and French than in Dutch patients. Peripheral arthritis, worse physical function, higher disease activity, and loss of income contributed to worse QoL.

**Conclusion:** AS is time consuming and associated with substantial out of pocket costs. Belgian patients incur the highest healthcare payments. Poor physical function increases patient's costs and time consumption. Loss of income is associated with lower QoL.

Traditional outcome measures aim to assess the impact of the disease on the patients themselves. However, in most economic analyses the costs of a particular disease are calculated from a point of view different from the patient's perspective, such as the societal or the health insurer's perspective. This is surprising, because not only can an illness have important economic consequences for patients, including out of pocket payments and income loss, but also the disease affects time consumption and quality of life (QoL), leading to intangible costs. Recently we performed a cost of illness study among patients with ankylosing spondylitis (AS) in three European countries, the Netherlands, France, and Belgium. Results of the productivity costs have been published previously<sup>1</sup> and the results for the direct healthcare and non-healthcare costs from a societal perspective are published in this issue of the *Annals* (see p 732). In the present analysis we determine the costs, time consumption, and quality of life (QoL) due to AS, for patients with the disease. Patient's costs, time consumption, and QoL are compared among three countries. In addition, determinants of these outcomes are explored.

## PATIENTS AND METHODS

### Patients

Patients were recruited from the rheumatology departments of four hospitals in three European countries, the University Hospital Maastricht and the Maasland Ziekenhuis Sittard in the Netherlands, Hôpital Universitaire Cochin Paris in France, and the University Hospital Gent in Belgium. For detailed description we refer to the related article on the societal costs (see p 732). Patients were included between September 1996 and March 1997 and were followed up for two years.

### Questionnaires

For the description of the type and the time points of the clinical and economic assessments see the article on the direct societal costs (p 732). In addition, patients reported in the bimonthly economic questionnaires the days on which they could not perform paid work and the hours of time per day or week lost because of AS. In the six-monthly questionnaires patients had to report changes in job, working status, and income. Also, every two months patients completed the Euro-QoL 5 dimensions (EQ-5D) questionnaire.

### Health insurance system and social security system of the three countries

A description of the healthcare system and social security system from the point of view of the patients' contributions and income loss due to sick leave or work disability can be found in Appendix 1 of the online version of the article. The three countries have an insurance based social security system. For healthcare, people in the Netherlands have higher premiums and social taxes than both the other countries, while in France and Belgium a patient's contributions for healthcare visits or procedures and a patient's contributions for drugs are considerably higher. In France, patients with a severe chronic disease (such as severe AS) can be exempted from such contributions, whereas this possibility does not exist for patients with AS in

**Abbreviations:** ANOVA, analysis of variance; AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; EQ-5D, EuroQoL 5 dimensions; HR, hazard ratio; IBD, inflammatory bowel disease; QoL, quality of life; RA, rheumatoid arthritis

**Table 1** Characteristics of patients completing the study

|                                     | Total<br>(n=209) | The Netherlands<br>(n=130) | France<br>(n=53) | Belgium<br>(n=26) |
|-------------------------------------|------------------|----------------------------|------------------|-------------------|
| Male (%)                            | 70.3             | 70.8                       | 67.9             | 73.1              |
| Age (years), mean [range]*          | 43.1 [18–77]     | 45.6 [23–77]               | 37.4 [19–67]     | 41.9 [18–74]      |
| Education ≤12 years (%)*            | 71.8             | 82.8                       | 48.1             | 65.4              |
| Disease duration (years), mean (SD) | 11.1 (8.9)       | 11.9 (9.2)                 | 9.2 (7.4)        | 10.8 (10.3)       |
| IBD (%)*                            | 7.2              | 10.0                       | 0.0              | 7.7               |
| Peripheral arthritis (%)            | 25.4             | 28.5                       | 26.4             | 8.7               |
| BASFI baseline, mean (SD)*          | 3.3 (2.6)        | 3.9 (2.4)                  | 2.5 (2.9)        | 2.6 (2.3)         |
| BASDAI baseline, mean (SD)          | 3.3 (2.1)        | 3.7 (2.1)                  | 2.8 (2.3)        | 3.1 (1.9)         |
| Time averaged EQ-5D, mean (SD)      | 0.67 (0.19)      | 0.68 (0.16)                | 0.63 (0.23)      | 0.67 (0.14)       |

\*p Value for difference among countries <0.05 (tested by  $\chi^2$  for proportions and ANOVA for continuous variables).

IBD, inflammatory bowel disease; BASFI, Bath Ankylosing Spondylitis Functional Index (range 0–10, higher values indicating worse function); BASDAI, Bath Ankylosing Spondylitis Disease Activity Index (range 0–10, higher values indicating higher disease activity); EQ-5D, EuroQol 5 dimensions (0 equals death and 1 perfect health).

Belgium. For sick leave and work disability the benefits in the Netherlands are in general more favourable than in both other countries.

### Healthcare resource use and time consumption

AS related healthcare and non-healthcare resource use, absence from paid work due to sick leave or chronic work disability, and time consumed due to AS were assessed. Effects of spinal and extraspinal (peripheral arthritis, inflammatory bowel disease, psoriasis, uveitis) manifestations of AS and of the side effects of drugs were included. Patients received extensive instruction on how to complete the questionnaires, especially how to interpret AS related and non-AS related resource use at the start of the study and with each repeat questionnaire. For detailed description of resources included in *healthcare use* and in *non-healthcare use* see the article on direct societal costs (p 732). In addition, *absence from paid work* due to sick leave (expressed as number of working days absent from paid work) was assessed in the bimonthly economic questionnaires, and changes in working hours, work disability, and income were assessed in the six-monthly economic questionnaires. Finally, *time loss because of disease* comprised the number of hours the patients spent daily in resting and exercising at home, time lost because of in- or outpatient health care, time lost because of participation in group physical exercise or swimming group, and time lost because of AS related absence at paid work. If a patient mentioned admission to hospital or healthcare visits and reported at the same time absence from paid work, the time absent from work was subtracted from the total loss of time. Resource use, absence from work, and time consumption were not ascertained by comparison with other data sources.

### Definition and sources of costs

Costs were calculated from the patient's perspective. Expenditures for healthcare related resources are called *healthcare patient costs*. Expenditures for non-healthcare resources are called *non-healthcare patient costs* and *income loss* refers to loss of income because of days absent from paid work (sick leave) or chronic work disability. *Total patient costs* comprise the sum of healthcare, non-healthcare patient costs, and income loss.

For the *healthcare patient costs* the official country-specific patient contributions were used for each unit of healthcare resource.<sup>2–9</sup> Specific national regulations on reimbursement of costs were taken into account. For example, Dutch and Belgian patients with AS can be granted reimbursement for physiotherapy for an unlimited number of sessions a year. For alternative medicine, we assumed that patients only visited recognised doctors for which there is reimbursement for a regular visit. During the period of our study, Dutch patients had to pay the first €45.45 per year of healthcare costs and €3.6

per day in hospital. A patient's out of pocket costs were not corrected for differences in social contributions among countries. Patients with additional private insurance had difficulty in reporting the additional premium because this was often included in the total premium for the entire family. Moreover, the kind and level of additional financial advantage for the patient (complete reimbursement, reimbursement higher or lower than a maximum limit, reimbursement of provisions not included such as alternative medicine or extra number of physiotherapy sessions) was very variable. Therefore we proposed that the premium for the private insurance would balance out the exemption from personal contributions.

For the *non-healthcare patient costs*, a patient's reported financial contributions were used whenever available. If these were missing, costs as reported by other patients from the same country for the same resource were used. For travel costs the variable costs per kilometre, based on the country-specific mean fuel prices over the period studied, were used. For help from private paid household help, the country-specific mean wage of a female manual worker was used as reported for 1998 by Eurostat (€11.00 per hour in the Netherlands; €10.25 per hour in France, and €12.00 per hour in Belgium).<sup>10</sup> All known sources of reimbursement to the patient were taken into account.

Where applicable, taxes were included in the costs prices. All costs were expressed in euros (31 December 1998 currency). The currency of one euro was set at NLG 2.20, FF 6.56, and BEF 40.34. On the same date €1.00 was worth \$1.17.

An overview of the sources used to calculate a patient's out of pocket costs can be found in Appendix 2 of the online version of this article.

### Statistical analyses

Results are analysed for patients who completed two years' follow up and who filled out at least nine of 12 bimonthly questionnaires. For missing values of healthcare resource use in the bimonthly questionnaires, the mean for the same patient of the completed questionnaires was imputed. Demographic and disease characteristics are presented using descriptive statistics. The EQ-5D questionnaire was calculated using the patients' ratings and transformed into a utility scale ranging from zero (death) to one (perfect health) by applying the York weighting.<sup>11</sup> To better represent the overall QoL during the two year follow up, the time averaged EQ-5D was used in the analysis. Differences in the variables among countries were assessed by  $\chi^2$  for proportions and by analysis of variance (ANOVA) for continuous variables. For healthcare resource use, firstly, the proportion of patients who had used this resource over the period studied was assessed, next the mean annual number of units of each resource was ascertained, and finally, the annual out of pocket costs or time consumed per

**Table 2** Comparison among countries of the annual healthcare resource use and annual out of pocket costs per patient

| Resource categories                                | Annual healthcare resource use per patient; mean [median] |                        |                        | Annual costs in €/pt/yr; mean [median] (% of health and non-healthcare costs) |                             |                             |                              |
|--|---|------------------------|------------------------|---|-----------------------------|-----------------------------|------------------------------|
|  | The Netherlands (n=130)                                   | France (n=53)          | Belgium (n=26)         | The Netherlands   | France                      | Belgium                     | All countries                |
| General practitioner*†‡§                           | 1.4 [0.5] visits  | 2.2 [1.0] visits       | 4.0 [1.1] visits       | 0 [0] (0)   | 1.5 [0] (0.6)               | 17 [5] (4.5)                | 3 [0] (0.7)                  |
| Rheumatologist*†‡§                                 | 1.7 [1] visits  | 1.6 [0.5] visits       | 2.6 [2.4] visits       | 0 [0] (0)   | 2 [0] (0.8)                 | 23 [21] (6)                 | 3 [0] (0.7)                  |
| All specialists*†‡§                                | 2.6 [1.5] visits  | 2.6 [1.0] visits       | 3.3 [2.7] visits       | 0 [0] (0)   | 4 [0] (1.6)                 | 27 [21] (7)                 | 5 [0] (1)                    |
| Physiotherapist*†‡§                                | 18.3 [6.5] visits   | 17.4 [4.4] visits      | 26.6 [14.3] visits     | 0 [0] (0)   | 17 [0] (6.7)                | 102 [55]                    | 17 [0] (4)                   |
| Spa therapy†‡                                      | 0.008 [0] treatments                                      | 0.04 [0] treatments    |                        | 4 [0] (0.8)   | 23 [0] (9)                  | 0 [0] (0)                   | 8 [0] (2)                    |
| All physical therapy*†‡§                           |   |                        |                        | 4 [0] (0.8)   | 40 [0] (16)                 | 102 [55] (26)               | 25 [0] (6)                   |
| Other care providers†                              | 0.4 [0] visits  | 0.6 [0] visits         | 6.9 [0] visits         | 0 [0] (0)   | 1 [0] (0.5)                 | 1 [0] (0.5)                 | 0.3 [0] (0.1)                |
| Drugs*†‡§  | 1.2 [1] kind of drugs                                     | 2.0 [2] kind of drugs  | 1.4 [1] kind of drugs  | 0 [0] (0)   | 25 [0] (10)                 | 72 [61] (18)                | 15 [0] (3)                   |
| Technical procedures*†‡§                           | 4.5 [2.7] examinations                                    | 4.1 [2.5] examinations | 4.6 [5.6] examinations | 0 [0] (0)   | 8 [0] (3)                   | 46 [33.78] (12)             | 8 [0] (2)                    |
| Inpatient care§                                    | 2.6 [0] days  | 2.7 [0] days           | 0.3 [0] days           | 6 [0] (1.2)   | 3 [0] (1)                   | 4 [0] (1)                   | 1 [0] (0.5)                  |
| Aids and adaptations†‡§                            | 0.3 aids  | 0.1 aids               | 0.02 aids              | 48 [0] (9)  | 18 [0] (7)                  | 0 [0] (0)                   | 34 [0] (9)                   |
| Formal help  | 17.1 [0] hours  | 3.9 [0] hours          | 8.0 [0] hours          | 36 [0] (7)  | 8 [0] (3)                   | 28 [0] (7)                  | 28 [0] (7)                   |
| <b>Patient's healthcare costs†‡</b>                |   |                        |                        | <b>142 [50] (28%)*</b>  | <b>110 [0] (44%)</b>        | <b>296 [224] (75%)</b>      | <b>153 [0] (35%)</b>         |
| Swim and exercise group*†‡§                        | 15.6 [4.8] sessions                                       | 6.17 [1.0] sessions    | 5.36 [0.8] sessions    | 51 [54] (10)  | 14 [2] (6)                  | 6 [2] (1.5)                 | 36 [6.5] (8)                 |
| Contributions*†‡§                                  |   |                        |                        | 8 [0] (2)   | 1 [0] (0.5)                 | 0 [0] (0)                   | 5 [0] (1)                    |
| Private help†‡§                                    | 22.6 [0] hours  | 5.9 [0] hours          | 0.00 [0] hours         | 249 [0] (49)  | 60 [0] (24)                 | 0 [0] (0)                   | 170 [0] (39)                 |
| Transport  | 527.9 [174.59] km   | 451.5 [96.0] km        | 776.9 [406.6] km       | 61 [24] (12)  | 67 [26] (27)                | 92 [52] (23)                | 66 [0] (15)                  |
| <b>Patient's non-healthcare costs*†</b>            |   |                        |                        | <b>369 [115] (72%)</b>  | <b>142 [47] (56%)</b>       | <b>98 [54] (25%)</b>        | <b>278 [77] (65%)</b>        |
| <b>Patient's health- and non-healthcare costs*</b> |   |                        |                        | <b>510 [181] (100%)</b>   | <b>252 [109] (100%)</b>     | <b>394 [265] (100%)</b>     | <b>431 [172] (100%)</b>      |
|  |   |                        |                        | <b>[95% CI 364 to 689]</b>  | <b>[95% CI 136 to 417]</b>  | <b>[95% CI 269 to 551]</b>  | <b>[95% CI 331 to 551]</b>   |
| Patient's income loss†                             | 43%   | 45%                    | 42%                    | 1663 [0]  | 1034 [0]                    | 595 [0]                     | 1371 [0]                     |
| <b>Total patient's cost†*</b>                      |   |                        |                        | <b>2172 [1697]</b>  | <b>1286 [197]</b>           | <b>988 [303]</b>            | <b>1795 [351]</b>            |
|  |   |                        |                        | <b>[95% CI 1781 to 2557]</b>  | <b>[95% CI 664 to 2048]</b> | <b>[95% CI 459 to 1640]</b> | <b>[95% CI 1490 to 2121]</b> |

\*Bootstrapped difference between the Netherlands and France statistically significant; †bootstrapped difference between the Netherlands and Belgium statistically significant; ‡bootstrapped difference between France and Belgium statistically significant; §Difference in resource use among countries significant (p<0.05) in multivariate regression analysis after adjusting for baseline confounders; ¶Includes the annual out of pocket payment for the first €45.45, independent of the type of healthcare resource; CI, bootstrapped 95% confidence interval.

**Table 3** Determinants of patient's out of the pocket costs assessed by Cox's regression analyses

|                                       | Healthcare patient's costs |         | Non-healthcare patient's costs |         | Income loss         |         | Total patient's costs |         |
|---------------------------------------|----------------------------|---------|--------------------------------|---------|---------------------|---------|-----------------------|---------|
|                                       | HR [95% CI]                | p Value | HR [95% CI]                    | p Value | HR [95% CI]         | p Value | HR [95% CI]           | p Value |
| France as opposed to the Netherlands  | 0.65 [0.46 to 0.91]        | 0.01    | 0.69 [0.49 to 0.99]            | 0.04    | 0.93 [0.67 to 1.37] | 0.7     | 0.99 [0.51 to 1.41]   | 0.9     |
| Belgium as opposed to the Netherlands | 1.64 [1.02 to 2.63]        | 0.04    | 0.65 [0.39 to 1.07]            | 0.09    | 0.79 [0.49 to 1.26] | 0.3     | 1.04 [0.64 to 1.72]   | 0.9     |
| Belgium as opposed to France          | 2.65 [1.54 to 4.17]        | 0.0003  | 0.93 [0.56 to 0.55]            | 0.8     | 0.84 [0.50 to 1.39] | 0.5     | 1.05 [0.63 to 1.75]   | 0.8     |
| Gender                                |                            | NS      | 1.47 [1.04 to 2.08]            | 0.03    |                     | NS      |                       | NS      |
| Age                                   |                            | NS      |                                | NS      |                     | NS      | 1.03 [1.01 to 1.04]   | 0.0007  |
| BASFI                                 |                            | NS      | 1.09 [1.02 to 1.20]            | 0.02    | 1.18 [1.09 to 1.25] | <0.0000 | 1.28 [1.20 to 1.37]   | <0.0000 |
| BASDAI                                |                            | NS      | 1.09 [0.98 to 1.20]            | NS      |                     | NS      |                       | NS      |

NS, not significant; BASFI, Bath Ankylosing Spondylitis Functional Index (range 0–10, higher values indicating worse function); BASDAI, Bath Ankylosing Spondylitis Disease Activity Index (range 0–10, higher values indicating higher disease activity); HRs >1 indicate higher costs.

resource were calculated. Because the distribution of costs and time was skewed not only means but also medians are presented to provide a better illustration of the distribution. Bootstraps with 10 000 replications were computed to assess the 95% confidence of the costs and to assess the 95% confidence interval of the difference in the costs among the three countries.<sup>12</sup>

Determinants of costs, time consumption, and QoL were explored by Cox's proportional hazard regression analyses with out of pocket costs, time consumption, or QoL as dependent variable. As independent variables several sociodemographic and baseline disease characteristics were chosen: gender, age, disease duration since diagnosis, educational level (dichotomised into  $\leq 12$  years' or  $> 12$  years' formal education), presence of peripheral arthritis, presence of inflammatory bowel disease (IBD), the Bath Ankylosing Spondylitis Functional Index (BASFI; range 0–10) measuring physical function, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; range 0–10) measuring disease activity, and country (dummy). When assessing determinants of the EQ-5D utility score, time averaged BASFI and time averaged BASDAI were used within the independent variables. Because differences of the outcomes among the countries were our primary interest, the dummy country was entered into a first block and all other variables in a second block using a backward elimination likelihood procedure. Interactions between the variables of the final model and country were explored. Cox's proportional hazard regression analysis is a semiparametric statistical analysis and was chosen because cost and time data had a skewed distribution. Reported hazard ratios (HRs)  $> 1$  indicate that the independent variable is associated with an adverse outcome (higher costs, more time lost, or worse quality of life). For example, an HR of 1.5 of a dichotomous variable, indicates a 1.5 times increase in (median) costs or decrease in (median) QoL. All regression analyses were repeated by eliminating patients with extreme values and by including and excluding patients with extraspinal disease.

Bootstraps were performed in Excel and all other statistical analyses in SPSS 9.0.

## RESULTS

### Patients

In total 216 (135 Dutch, 54 French, and 27 Belgian) patients with AS fulfilled modified New York criteria and started the study. In the course of the follow up five Dutch, one French, and one Belgian patient dropped out. All patients who completed the follow up had filled out at least nine of 12 questionnaires. The proportion of patients with one, two, or three missing bimonthly questionnaires was 84%, and the proportion of missing questionnaires was 10%, of which 25% were missing at random because some patients had not received one of the bimonthly economic questionnaires owing to an administrative error. Table 1 presents, for each country separately, the sociodemographic characteristics of patients who completed the study. A comparison of patient characteristics among countries showed that Dutch patients were older, had on average a lower educational level, and reported worse physical function (BASFI). None of the French patients had concomitant IBD. Of the Dutch patients, 77% had public insurance and 23% private. Of the French patients, 72% were completely reimbursed by the Sécurité Sociale (Social Security System) and 4% had additional private insurance. Of the Belgian patients, 4% had additional insurance for costs of hospital admissions.

### Healthcare resource use and patient's costs

The overall mean total annual patient's costs (healthcare costs, non-healthcare costs, and income loss combined) were €1795 (median €351) per patient (table 2). Income loss accounted for 76% of the total patient costs. For healthcare and non-healthcare costs combined, the non-healthcare costs were the



**Table 4** Annual time consumption (hours per patient) due to AS for different categories of time loss

| Time category                      | % Patients with time loss | Mean (median) [% of total time] Hours per patient per year |
|------------------------------------|---------------------------|--|
| Visits to healthcare providers     | 81                        | 9.94 (4.36) [2%]   |
| Attending technical procedures     | 90                        | 4.97 (3.00) [1%]   |
| Visits to physiotherapy            | 60                        | 18.87 (0) [4%]   |
| Attending group exercises          | 56                        | 20.43 (0) [4%]   |
| Rest at home                       | 71                        | 242.96 (72.00) [53%]                                       |
| Exercise at home                   | 63                        | 118.23 (29.40) [26%]                                       |
| Inpatient care                     | 9                         | 39.74 (0) [9%]   |
| <b>Medical patient's time loss</b> |                           | <b>455.15 (215.43) [100%]</b>                              |
| Time loss due to sick leave        | 27                        | 55.37 (0)  |
| <b>Total patient's time lost*</b>  |                           | <b>506.44 (278.00)</b>                                     |

\*When patients with a paid job were admitted to hospital or received outpatient health care and had reported at the same time absence from work, the hours sick leave were subtracted from the total time loss.

cost drivers, comprising 40% of the out of pocket expenditure for private household help, 15% for transportation costs, and 9% for contributions to societies or exercise or swimming groups. In univariate analysis, total patient's costs and non-healthcare costs were higher in the Netherlands than in France and Belgium. The Belgian patients had the lowest non-healthcare costs and the highest healthcare patient's contributions, reflecting the higher resource use but also the higher patient copayments for these cost categories in this country. In multivariate analysis, country was the only variable significantly contributing to the variation in a patient's healthcare out of pocket costs (table 3). Higher patient's non-healthcare costs could be predicted by living in the Netherlands but also by female gender and worse physical function (table 3). The association between female gender and non-healthcare costs could be explained by the high costs due to private household help in female patients (data not shown separately). Income loss was associated with worse physical function (BASFI). Finally, total patient costs were associated with worse physical function (BASFI) but also with higher age (table 3). After eliminating from the regression analyses the patients with extreme values or patients with extraspinal disease, the regression coefficients did not change importantly (data not shown separately).

### Time consumption

Table 4 illustrates the amount of time patients with AS lose because of disease for different time categories. Excluding the time lost because of sick leave, patients with AS lose on average 1.25 hours a day because of the disease. More than 75% of this time loss is due to time needed for additional daytime rest and time to exercise; 71% of patients reported taking regular rest at home and on average patients rest for 40 minutes a day; 62% of patients reported exercising regularly at home and on average a patient exercises for 19 minutes a day. An average

visit to a healthcare provider consumes two hours of a patient's time, a visit to the physiotherapist one hour, and attending group physical exercises takes on average two hours. Technical procedures last on average one hour. It is of note that travel and waiting time are included, if applicable. There were no important differences in the amount of disease related time consumption across countries. Worse physical function (BASFI) (HR=1.12; 95% CI 1.03 to 1.20) and higher disease activity (BASDAI) (HR=1.15; 95% CI 1.04 to 1.27) were predictors of the amount of total time lost. In addition to personal time lost, 7.6% of patients reported needing regular help from family or friends. Time invested in AS by family or friends was 4.6 minutes a day if averaged over all patients with AS, but 60 minutes (median 35) a day if averaged over patients requiring this type of help (in each country 7.5% of patients).

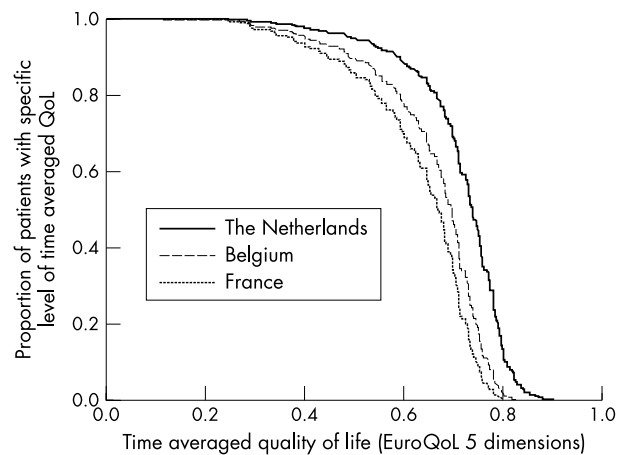
### Relation with QoL

There was no difference in time integrated QoL (assessed by EQ-5D) in univariate analysis across the countries. However, after adjusting for sociodemographic and disease characteristics, QoL was worse in France and Belgium than in the Netherlands. As can be seen in table 5, lower education, presence of peripheral arthritis, worse physical function, and higher disease activity were additional determinants of a worse quality of life. An interaction was seen between educational level and country and also between the presence of peripheral arthritis and country. The effect of education on QoL was stronger in the Netherlands and the effect of peripheral arthritis on QoL was stronger in France. When the different categories of patient's costs, time consumption, or income were added one by one to the independent variables of the regression model, only higher income loss (HR for occurring income loss 1.41; 95% CI 1.04 to 1.92) was significant, with a small but significant deterioration in QoL. No interactions between the variables of the final model and QoL were found. Cox's analysis permitted computation of survival curves and

**Table 5** Determinants of time integrated quality of life assessed by time averaged EuroQoL-5 dimensions assessed by Cox's regression analyses

|                                       | HR [95% CI]         | p Value |
|---------------------------------------|---------------------|---------|
| France as opposed to The Netherlands  | 2.94 [1.99 to 4.43] | <0.0001 |
| Belgium as opposed to The Netherlands | 2.03 [1.30 to 3.17] | 0.002   |
| Belgium as opposed to France          | 0.69 [0.41 to 1.15] | 0.5     |
| ≤12 Years' education                  | 1.92 [1.33 to 2.75] | 0.0005  |
| Peripheral arthritis                  | 1.46 [1.02 to 2.09] | 0.04    |
| BASFI (time averaged)                 | 1.34 [1.21 to 1.49] | <0.0001 |
| BASDAI (time averaged)                | 1.28 [1.13 to 1.44] | 0.0001  |

IBD, inflammatory bowel disease; BASFI, time averaged Bath Ankylosing Spondylitis Functional Index (range 0–10, higher values indicating worse function); BASDAI, time averaged Bath Ankylosing Spondylitis Disease Activity Index (range 0–10, higher values indicating higher disease activity); HRs >1 indicate worse quality of life.



**Figure 1** Survival curve illustrating the proportion of patients reporting a specific level of quality of life (QoL) for each country separately.

visualisation of the difference in QoL among the countries. Figure 1 illustrates, for example, that a QoL of 0.7 or better is reported by 60% of Dutch patients as compared with 30% of French patients.

## DISCUSSION

For the patients, AS is a time consuming disease and associated with substantial out of pocket costs and loss of income. On average, patients with AS need 75 minutes additional time per day because of their disease. Seventy eight per cent of this time is spent on daytime rest and exercises at home. Patients with a worse physical function, higher disease activity, and peripheral arthritis lose more time. Among 84 Dutch patients with rheumatoid arthritis (RA) the average time consumption was 110 minutes a day within the first six years of disease.<sup>13</sup> As in our study, this could be mainly attributed to the need for additional rest but also to extra time needed to perform usual daily activities, a type of time loss not registered in our study. Similarly, worse physical function was associated with more time consumption.

Apart from time consumption, patients also have considerable out of pocket expenditure because of their disease and substantial income loss. The mean total annual patient's costs amounted to €1795 (median €351) per patient, of which 76% were due to income loss because of work disability or sick leave. The inventory of out of pocket costs was rather conservative because some personal extra expenditure, such as extra costs for heating the house and for extra clothing (for example, sportswear), were not included in the questionnaires. Also, we assumed that patients out of pocket costs for alternative medicine equalled a contribution for a regular visit to a doctor. This will possibly be an underestimation of these costs.

Important differences in patient out of pocket payments among the three European countries were noted. Owing to the characteristics of the national healthcare organisations, with high out of pocket payments in Belgium, patients with AS in that country have substantially more healthcare contributions. Also in France, out of pocket payments are part of the healthcare system. However, in France the system includes exemption from financial contributions for patients with a (severe) chronic disease (such as severe AS), reducing substantially the overall healthcare contributions. In our study, 87% of French patients had this special status. Interestingly, the higher patient contributions in Belgium did not result in lower healthcare use. Strong belief in the effectiveness of medical care and supplier induced demand may help to explain this phenomenon.

Although Belgian patients had the highest healthcare expenditure, they had the lowest non-healthcare expenditure

and the lowest income loss, resulting in the lowest total patient costs. In contrast, Dutch patients had high expenditure for aids and adaptations, formal and informal help, and financial contributions to societies or exercise groups. They also had a greater loss of income. These high patient costs were seen despite higher reimbursement rates for aids and adaptations and for formal care and by the relatively more favourable sick leave and work disability benefits in Belgium compared with both other countries. Apparently, the more favourable reimbursement and benefit schedules may be an incentive for resource use, prolonged sick leave, and work disability. Also, different health beliefs and cultural attitudes towards paid employment despite disease may explain some of the differences. In this part of the study, health beliefs, coping with disease, or willingness to pay for health have not been assessed and their possible contribution to differences in healthcare use and sick leave or withdrawal from work cannot be explored.

Country was not the only predictor of the total patient costs. Older age and worse physical function were also associated with higher patient costs. In addition, non-healthcare costs were higher in female patients and this could be attributed to the expenditure for private household help. We found a recent publication on disease related healthcare and non-healthcare out of pocket expenditure in RA among Australian patients with a mean disease duration of 15.6 years.<sup>14</sup> Converted to 1998 values by consumer price indices and expressed in euros, the annual out of pocket costs were €968 (SD 1700) per patient, which is considerably higher than in our patients with AS. Similar, however, was that female gender and longer disease duration were associated with higher out of pocket expenditure. Whereas we showed significant differences in patients' costs among countries, the Australian study showed differences in patients' costs among groups with different insurance schemes (pensioners paying less and privately insured patients more), reflecting the important influence of organisational aspects on a patient's costs.

Perceived QoL, as a substitute for the intangible costs, was significantly better in Dutch patients and in those with higher education, no peripheral joint disease, better physical function, and lower disease activity. Although Dutch patients more often had lower education and had somewhat worse physical function, they experienced a better QoL than patients in both other countries. Unknown factors or variables not measured such as health beliefs and coping with disease may be important contributors to QoL. Interestingly, while income was not associated with reduced QoL, income loss due to work disability resulted in a worse QoL.

During the study, none of the patients were treated with one of the new biological drugs. Because worse physical function is a predictor of patient's out of pocket costs, income loss, time consumption, and QoL and because the new biological treatments have a proven effect on physical function, it seems likely that these drugs can substantially improve economic outcome for the patients.

The limitations of the study have been discussed in the article on the direct costs from a societal point of view (see p 732). It should be noted that the differences in patient's expenditure among the countries should be interpreted in the light of differences in social contributions and insurance premiums. The higher social contributions and insurance premiums in the Dutch population together with the low patient copayment imply a higher social solidarity in this country. Finally, it was impossible to correct a patient's costs for additional private insurance (to cover expenditure not included in the insurance package). We suggested that the premium for the additional insurance would balance out the copayments but could not ascertain that this hypothesis was correct.

In conclusion, for patients with AS, the disease is time consuming and associated with substantial out of pocket costs, income loss, and reduction in quality of life. There are striking differences in patient's costs and the QoL experienced among

countries. In all countries, patients with worse physical function lose more time, have the highest total costs, and experience a worse QoL.

### ACKNOWLEDGEMENTS

We thank Willy Peeters for providing information on the Belgian healthcare system, Maryse Meziere for providing additional information on the French patients, Christel Grimbergen, Sandra Boesen, and Erik de Klerk for developing the database.

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Two appendices can be found on the website at <http://www.annrheumdis.com/supplemental>

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## **Appendix 1**

Description of the health insurance system and social security system in view of patients' contributions and patients' loss of income.

All three countries have an obligatory health insurance system. People with a lower income in the Netherlands (public insured) and all subjects in both other countries contribute a proportion of their gross wage for healthcare insurance. In the Netherlands this is 17.25% (5.85% paid by employer), in France 19.6% (12.8% paid by the employer but this figure includes contribution for sick leave and work disability) and in Belgium 7.35% (3.55% paid by the employer). In The Netherlands, people with a higher income, have an (obligatory) private insurance for the basic insurance packet, which was approximately € 1,036 per subject per year in 1998. Two-thirds of the Dutch population is public insured and one third (obligatory) private. In addition to the above mentioned income related contribution, all Belgians have a small personal yearly contribution (about € 4 per year) to their health insurance company. In contrast to the situation in The Netherlands, patient contributions in France and Belgium are substantial. In The Netherlands, there are no patient contributions for provisions included in the basic coverage package. The basic coverage package covers most health care provisions. In France, patients with severe AS can become officially exempted from personal contributions. In all countries, there is a possibility for reinsurance for personal contributions. In The Netherlands, there is a strong primary care acting as a gatekeeper towards access to secondary or tertiary care but most patients with a chronic rheumatic disease are referred to the rheumatologist. In both other countries, access to primary, secondary and tertiary care is unrestricted. General practitioners and specialists in The Netherlands are paid on a capitation basis for care provided to public insured patients but on a fee for service system for privately insured patients. In France and Belgium, most healthcare providers are paid on a fee per service system. In all countries, healthcare providers working in



academic hospitals are salaried and ambulatory working physiotherapists are paid on a fee per service basis. In the Netherlands, but not in both other countries, hospitals are strictly budgeted.

Sick leave benefits in The Netherlands are 100% of the subject's gross wage for the first year of disease while in both other countries there is an important decrease in income in case of sick leave (60% from the second month of sick leave onward). Disability benefits in The Netherlands and Belgium are (maximal) 60% of the former gross wage opposed to 50% in France. In The Netherlands and France, patients with partial work disability can continue in a paid job while this is very unusual in Belgium. Sick leave and disability benefits in The Netherlands are mainly financed through social contributions from the employer while in France and Belgium employer and employee pay part of these social contributions. For patients, reinsurance against loss of income due to sickness is possible in all three countries.

Appendix 1; Table 1: Financing of healthcare at macro-economic level.

|                                   | The Netherlands | France | Belgium |
|-----------------------------------|-----------------|--------|---------|
| Social contributions from taxes   | 4.80%           | 5.90%  | 34.80%  |
| Public health insurance premiums  | 73.80%          | 66.40% | 40.60%  |
| Private health insurance premiums | 14.10%          | 9.10%  | 5.80%   |
| Patient contribution              | 7.30%           | 17.00% | 17.90%  |
| Other sources                     | 0.00%           | 0.80%  | 1.00%   |

## Appendix 2: Country-specific regulations on patient's out-of-pocket payments.

|                                     | The Netherlands   | France  | Belgium   |
|-------------------------------------|---|---|---|
| <b>Category of patient's costs</b>  | All first 46.46 Euro per year   |   |   |
| Physicians visits                   | No contribution   | Contribution 25% of official tariff   | Contribution of 30% of the tariff for GP-visit and 40% of specialist physician visit.   |
| Social worker or rheumatology nurse | No contribution   | No contribution   | No contribution   |
| Physiotherapy                       | No contribution   | Contribution 25 to 40% of official tariff, depending on the treatment provided  | Contribution 25 to 40% of official tariff, depending on the treatment provided  |
| Alternative medicine                | No contribution if recognised physician   | Contribution 25% of official tariff physician if provided by recognised physician   | Contribution 30% of official tariff physician if provided by recognised general physician   |
| Drugs                               | No contribution (for drugs used by patients in this observational study)  | Contribution of 0%, 35% or 65% according to type of drug.   | Contribution of 0%, 25% or 30% according to the type of drug with maximum per prescription.   |
| Technical procedures                | No contribution   | Contribution 35% of official tariff   | From 10% up to 40% of official tariff   |
| Hospitalisation                     | 3.63 Euro per day   | 6.10 Euro per day for hotel costs and 20% of general treatment costs but maximised to the first 30 days.  | 27 Euro per hospitalisation + 11.50 Euro per day for hotel costs + 0.62 Euro per day for drug costs                                     |
| Emergency department                | No contribution   | See contribution of physician visit   | See contribution physician visit  |
| Rehabilitation clinic               | No contribution   | 6.10 € per day  | Not applicable in study   |
| Formal help                         | Patient contribution of 4.64 Euro/ hour with a maximum according to family income and family composition  | Patient contribution per hour according to family income and family composition.  | Patient contribution per hour variable according to family income and family composition.   |
| Aids and appliances                 | Variable but only small contribution  | Reimbursement to 70 or 100% after approval from health insurance  | Reimbursed at fixed amount if prescribed by specialist physician  |
| Adaptations at house                | After approval of community. Variable but usually no contribution.  | Reimbursed at variable amount after approval of community   | Reimbursed at variable amount by special fund for chronic diseased.   |
| Spa treatment                       | All costs exceeding 464.64 Euro per 2 year.   | All costs exceeding reimbursement which varies according to health insurance company.   | Not reimbursed  |
| <b>Non-medical patient costs</b>    |   |   |   |
| Private household help              | Hourly wage Eurostat handworkster (11.00 Euro)  | Hourly wage Eurostat handworkster (10.24 Euro)  | Hourly wage Eurostat handworkster (12.00 Euro)  |
| Transport                           | Price per km based on mean gasoline and fuel market price. Reimbursement from health insurance company possible for visits to health care provider. Cheap public transport possible after approval from community. Invalid parking cart after approval from community free but parking costs not free | Price per m based on mean gasoline and fuel price. Reimbursement from health insurance company possible at fixed amount but following variable requirements. Parking cart or "carte debout pénible" possible but no exemption from parking costs. | Mean gasoline and fuel price. No reimbursement for AS-patients. Parking cart possible after approval but no exemption of parking costs. |
| Contributions                       | Home-help organisation 22.50 Euro/year. Limited contribution to AS society 81.81 Euro/year  | 25 € per year   | 12.5 € per year   |
| Swim- & exercise-group              | Usually within the extended contribution to patient AS society (225 Euro/year)  | Swimming or exercising at patient reported cost (market price)  | Swimming or exercising at patient reported cost (market price)  |