EXTENDED REPORT

Large differences in cost of illness and wellbeing between patients with fibromyalgia, chronic low back pain, or ankylosing spondylitis

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Objective: To compare the cost of illness of three musculoskeletal conditions in relation to general wellbeing.
Methods: Patients with fibromyalgia, chronic low back pain (CLBP), and ankylosing spondylitis who were referred to a specialist and participated in three randomised trials completed a cost diary for the duration of the study, comprising direct medical and non-medical resource utilisation and inability to perform paid and unpaid work. Patients rated perceived wellbeing (0–100) at baseline. Univariate differences in costs between the groups were estimated by bootstrapping. Regression analyses assessed which variables, in addition to the condition, contributed to costs and wellbeing.
Results: 70 patients with fibromyalgia, 110 with chronic low back pain, and 111 with ankylosing spondylitis provided data for the cost analyses. Average annual disease related total societal costs per patient were €7813 for fibromyalgia, €8533 for CLBP, and €3205 for ankylosing spondylitis. Total costs were higher for fibromyalgia and CLBP than for ankylosing spondylitis, mainly because of cost of formal and informal care, aids and adaptations, and work days lost. Wellbeing was lower in fibromyalgia (mean, 48) and low back pain (mean, 42) than in ankylosing spondylitis (mean, 67). No variables other than diagnostic group contributed to differences in costs or wellbeing.
Conclusions: In patients under the care of a specialist, there were marked differences in costs and wellbeing between those with fibromyalgia or CLBP and those with ankylosing spondylitis. In particular, direct non-medical costs and productivity costs were higher in fibromyalgia and CLBP.

Fibromyalgia, chronic low back pain (CLBP), and ankylosing spondylitis are three chronic musculoskeletal disorders with differences in epidemiology, aetiopathogenesis, and clinical signs and symptoms. Fibromyalgia and CLBP are considered to be a somatoform pain disorder following the DSM IV classification,[1] while ankylosing spondylitis is considered to be an autoimmune inflammatory disease. The estimated prevalence of the three conditions in adult Western populations varies between 4% and 14% for fibromyalgia,[2] between 20% and 50% for CLBP,[2] and between 0.1% and 1.1% for ankylosing spondylitis.[3] In fibromyalgia and CLBP there are typically no detectable inflammatory changes in laboratory assessments and there are no structural changes in the joints or spine. On the other hand, about 50% of patients with ankylosing spondylitis have an increase in erythrocyte sedimentation rate (ESR) or C reactive protein,[4] and by definition all patients have radiographic sacroiliitis. Despite the absence of inflammatory and structural abnormalities, fibromyalgia and CLBP are associated with substantial reductions in physical function and general wellbeing.[5]

Although the costs per patient have been reported in three studies of fibromyalgia,[6–8] one of CLBP,[9] and two of ankylosing spondylitis,[10–12] no study has yet been undertaken to compare the costs of these disorders. Indirect comparisons of cost of illness (COI) studies cannot be done reliably, mainly because of differences in the methods employed to assess resource use and to establish its cost in monetary terms. Nevertheless, comparisons can identify diseases that incur high costs and can identify the variables involved. This helps in setting priorities for future studies on the effectiveness of health interventions and health care services.

Our aim in this study was to determine whether patients with an unexplained pain syndrome (such as fibromyalgia or CLBP) have a different pattern of health care consumption and productivity loss from those with a specific inflammatory rheumatic disorder such as ankylosing spondylitis, independent of the differences in perceived wellbeing.

METHODS

Patients

Patients included in this comparison had participated in three different piggyback cost–utility studies which have been published previously.[13–15] The patients with fibromyalgia and CLBP participated between 1993 and 1995 in a randomised clinical trial comparing the cost-effectiveness of a six week (for fibromyalgia) or eight week (for CLBP) cognitive-behavioural rehabilitation programme, with appropriate control groups. Patients with fibromyalgia could be referred by the rheumatologist or the rehabilitation physician if they were older than 18 years, fulfilled the American College of Rheumatology (ACR) classification criteria for fibromyalgia, were hindered from fulfilling desired activities, and were prepared to participate in the six week intervention study.[14] Patients with CLBP could be referred by the general practitioner, the rheumatologist, or the rehabilitation physician if they were older than 18 years, had had low back pain for more than six months without evidence of a specific

Abbreviations: CLBP, chronic low back pain; CPI, consumer price index; DSM IV, *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition

spinal disease, and were prepared to participate in the study.[13] Follow up of both studies was 52 weeks. Patients with ankylosing spondylitis participated in 1999 in a randomised controlled trial comparing the cost–utility of a three week spa exercise treatment course in Austria or a three week local spa exercise course in the Netherlands along with their usual care. They were recruited through the Ankylosing Spondylitis Patients' Society. They were included if they were older than 18 years, fulfilled the modified New York criteria, had pain, stiffness, and functional limitation in the three months before the start of the study, and were available to participate. The study follow up was 40 weeks.[15]

Data sources

At the start of the study all patients completed a questionnaire on sociodemographic variables. Clinical evaluations were study specific. During the entire follow up period, patients in all three studies completed cost diaries.

Demographics

Each study assessed sex, age, cohabitation status, highest achieved education, engagement in paid work and hours of paid work per week, presence of work disability, and, if applicable, whether work disability was full or partial. For the statistical analyses the educational level was dichotomised into low and high, distinguishing patients who had achieved a university or higher non-university degree from the remainder.

Clinical outcomes

Only two clinical variables were comparable among the three studies. In all studies, patients were asked to report disease duration since the onset of symptoms. In addition, a global wellbeing assessment on a 0–100 rating scale (visualised as a thermometer, higher values indicating greater wellbeing) was included in all three studies—as a separate instrument in the fibromyalgia and CLBP study[16 17] and as part of the EuroQol in the ankylosing spondylitis study.[18]

Resource utilisation

We aimed to evaluate resource utilisation from a societal perspective, with assessment of direct health care and non-health care resource use and productivity losses. In all three studies cost diaries were used (developed and partially validated by Goossens *et al*.[19]). Patients were instructed to report only the disease related resource utilisation, including the disease related comorbidity, but not to report utilisation related to the study protocol. In the ankylosing spondylitis study the resources were recorded for a period of 40 weeks, so the results were extrapolated to 52 weeks to make them comparable with the other conditions. In case of missing cost diaries, mean values over the available time were extrapolated to one year, for all three conditions.

Sources of costs estimate

Resources recorded in the diaries were valued for this analysis by cost estimates for the year 2002. True cost estimates are available in the Dutch guidelines for pharmacoeconomic studies.[20] The costs per unit were adjusted to 2002 costs by applying the health care consumer price indices (CPI) to all medical resources and by applying the CPIs based on the gross national product (GNP) for the unit costs of formal and informal care and for the loss of paid productivity.[21] Costs for alternative medicine, informal care, over the counter drugs, and aids and appliances were reported directly (including the patient contribution) by the patients in their diaries and were adjusted for differential timing using the appropriate CPI.[22] The costs of prescribed and over the counter drugs were calculated using the wholesale prices. For prescription drugs, an additional pharmacist's fee of €4.64 per prescribed item (with a maximum prescription period of three months) was added, as this was practice in the Netherlands. When valuing the costs of personal inactivity reported by the patients, the hours of formal and informal help received were subtracted from the hours of inactivity reported by the patient in order to avoid double counting. The sources and values of cost estimates for each resource are given in table 1.

The productivity costs resulting from loss of paid labour were calculated by applying the friction costs method, which limits the period of production loss to the time during which the work of the sick person is not replaced.[23] In 2002, the length of the friction period was set at 22 weeks (110 working days). Paid production was valued by the average national gross wage per hour, broken down by sex and five

Table 1 Units of the resources reported in the cost diary, source of the estimate of the cost per unit of each resource, and the cost per unit if applicable

Item	Unit of resource collected	Source of the cost per unit	Cost per unit (€)
Direct medical resource use			
General practitioner	Number of visits	Dutch guidelines on pharmacoeconomic evaluation	17.69/visit
Specialist physician	Number of visits	Dutch guidelines on pharmacoeconomic evaluation	77.56/visit
Physiotherapy	Number of visits	Dutch guidelines on pharmacoeconomic evaluation	17.35/visit
Psychologist	Number of visits	Dutch guidelines on pharmacoeconomic evaluation	108.36/visit
Complementary medicine	Total cost	Patient reported cost in diary	
Admission hospital	Days admitted	Dutch guidelines on pharmacoeconomic evaluation	353.68/day
Admission rehabilitation centre	Days admitted	Dutch guidelines on pharmacoeconomic evaluation	301.12/day
Prescription drugs	Kind and number of prescriptions	Official Dutch price list of prescription drugs (TAXE)	
OTC drugs	Kind and total cost of drug	Official Dutch price list of non-prescription drugs (TAXE-OTC)	
Direct non-medical resource use			
Aids/appliances/adaptations	Total costs	Patient reported cost in diary	
Formal household care	Hours of help	Dutch guidelines on pharmacoeconomic evaluation	25.22/hour
Private (paid) household help	Hours and total costs	Dutch guidelines on pharmacoeconomic evaluation	8.83/hour
Unpaid household help	Hours and total costs	Dutch guidelines on pharmacoeconomic evaluation	8.83/hour
Personal inactivity	Hours of inactivity	Dutch guidelines on pharmacoeconomic evaluation	8.83/hour
Paid productivity loss			
Absence at paid work	Number of days (including half days)	Gross wage per hour by sex and five age categories (Dutch Bureau of Statistics)	9.23 to 18.04/hour

OTC, over the counter.

Table 2 Sociodemographic and disease characteristics of patients

Variable	FM (n = 69)	CLBP (n = 110)	AS (n = 111)	p Value*
Male (%)	13	40	71	<0.0001
Age (years) (mean (SD))	44.9 (9.4)	40.9 (8.7)	47.8 (10.1)	<0.0001
Disease duration (years) (mean (SD))	12.4 (14.9)	10.4 (8.7)	17.8 (9.2)	<0.0001
Married or living together (%)	87	95	94	0.148
High educational level† (%)	4.5	0.9	9.2	0.011
Paid work‡ (%)	25	11	56	<0.0001
Work disability‡ (%)	31	71	34	<0.0001
Full work disability (%)	74	82	62	
Global wellbeing score§ (mean (SD))	48.2 (14.9)	42.2 (15.2)	67.0 (20.0)	<0.0001

*p Value assessed by χ^2 test for dichotomous variables and by analysis if variance for continuous variables.
†Distinguishes patients who achieved a higher non-university or university degree.
‡After adjusting for age and sex by indirect standardisation with the general Dutch population.
§Range 0 to 100, higher values indicating increased wellbeing.
AS, ankylosing spondylitis; CLBP, chronic low back pain; FM, fibromyalgia.

different age categories.[22] It was considered that one working day comprises on average eight working hours.

Statistical analysis

Labour force participation and work disability rates were adjusted to the Dutch general population by indirect standardisation for five age categories.[22] Univariate differences in costs among groups were assessed by 95th centile bootstrapped confidence intervals of the difference after 1000 replications.

Several multivariate regression analyses were computed with direct (health care and non-health care), indirect, or total cost as outcome. In all analyses diagnostic group and assigned intervention were forced into a first block to assess the possible effect of the intervention on the costs; in a second block, additional sociodemographic variables (age, sex, educational level, and marital status) and disease related variables (disease duration and general wellbeing) were added, applying a backward elimination procedure. Interactions between the diagnostic group and each of the other independent variables were tested. As the data on costs were skewed, linear regression on the log transformed costs, Cox proportional hazard analyses, and logistic regressions (distinguishing the 25% of patients with the highest costs) were compared. Because the results of these three procedures were similar, we decided to present the Cox proportional regression analyses in this paper because they allow one to visualise differences between groups in terms of figures, and the regression coefficients are easy to interpret.

Separate Cox proportional regression analyses were carried out to examine the influence of diagnosis (first block), and sex, age, disease duration, and educational level (second block) on wellbeing. Interactions between the diagnostic group and each of the other independent variables were tested.

Sensitivity analyses

Within the open ended answering category ''visits to other health care providers,'' only patients with CLBP specifically mentioned such visits as a separate resource. Thus we could not exclude the possibility that patients with fibromyalgia and ankylosing spondylitis may not have included such visits in their cost diaries. Therefore, in the first sensitivity analyses, the direct medical, total direct, and direct plus productivity costs were recalculated after excluding the costs of psychotherapy reported by patients with CLBP. In a second sensitivity analysis we considered the friction period to be 14 weeks (70 working days) instead of 22 weeks (110 working days). In 2002, the employment situation in the Netherlands was more favourable than in the years of each of the original studies, resulting in a longer friction period.

RESULTS

Patients

Altogether, 131 patients with fibromyalgia, 135 patients with CLBP, and 120 patients with ankylosing spondylitis had been randomised in the initial cost–utility studies. As the waiting list control group of patients with fibromyalgia (n = 43) did not take part in the economic analyses because they continued with their usual care after the six week assessment, only 70 patients with fibromyalgia could be included in the study, as opposed to 110 with CLBP and 111 with ankylosing spondylitis. Patients included in the cost analysis were not significantly different in sociodemographic and disease characteristics from the ones who were not included except in the CLBP group, where the included patients were older (41 *v* 37 years; p = 0.01). Table 2 compares sociodemographic and clinical characteristics of the final study cohorts. Patients with ankylosing spondylitis had a longer disease duration, a higher educational level, and a lower work disability rate. In cases of work disability, they were more likely to continue to work part time.

General wellbeing and its determinants

General wellbeing was strikingly reduced in patients with fibromyalgia and chronic CLBP compared with ankylosing spondylitis (table 2). In univariate analyses patients with fibromyalgia had a threefold increased risk of lower general wellbeing (95% confidence interval (CI), 2.1 to 4.1) compared with the patients with ankylosing spondylitis, while those with CLBP had a 3.9-fold increased risk (2.9 to 5.3). No other sociodemographic or disease related variables contributed to differences in wellbeing among the three disorders.

Costs

The average annual resource utilisation and costs per patient for each of the three conditions are provided in tables 3 and 4. Total direct costs were higher in patients with fibromyalgia or CLBP than in ankylosing spondylitis because of higher direct non-medical costs. Within the direct medical costs, cost drivers were visits to health care providers for patients with fibromyalgia (29% of the costs) and CLBP (29% of the costs) compared with visits to physiotherapy (43% of the costs) for patients with ankylosing spondylitis. Notwithstanding the lower proportion of patients with fibromyalgia and CLBP who had a paid job, and their somewhat lower average income (fibromyalgia, €16.3/hour; CLBP, €17.0/hour; ankylosing spondylitis, €19.0/hour), the friction costs were higher. In those with a paid job, 63%, 47%, and 39% of patients with fibromyalgia, CLBP, and ankylosing spondylitis, respectively, reported an episode of sick leave. Mean length of sick leave was 34, 79, and 12 days per working patient-year for fibromyalgia, CLBP, and ankylosing spondylitis.

Table 3 Resource utilisation and costs for the different categories of health care resource for the three chronic musculoskeletal conditions

	Annual health resource use per patient			Annual costs (€/patient)		
	FM (n = 69)	CLBP (n = 110)	AS (n = 111)	FM (n = 69)	CLBP(n = 110)	AS (n = 111)
General practitioner (visits)	4.6 (2.0) [73%]	4.8 (3.0) [73%]	2.1 (1.3) [57%]	81 (35) [1.5%]	85 (53) [1.5%]	37 (23) [1.5%]
Specialist physician (visits)	3.8 (2.0) [79%]	3.1 (1.0) [56%]	2.8 (2.6) [56%]	296 (155) [5.6%]	243 (78) [4.3%]	215 (202) [9.1%]
Physiotherapist (visits)	15.3 (0.0) [46%]	9.5 (0.0) [40%]	23.2 (11.7) [60%]	297 (0) [5.7%]	185 (0) [3.3%]	449 (226) [18.9%]
Complementary medicine (visits)	2.4 (0.0) [100%]	0.9 (0.0) [13%]	0.6 (0.0) [9%]	180 (0) [3.4%]	97 (0) [1.7%]	41 (0) [1.7%]
Psychotherapist (visits)	No separate data	1.2 (0.0) [15%]	No separate data	–	124 (0) [2.2%]	–
Hospital admissions (days)	0.6 (0.0) [7%]	0.47 (0.0) [7%]	0.14 (0.0) [3%]	226 (0.0) [4.3%]	167 (0) [3.0%]	48 (0) [2.0%]
Prescription drugs (No of prescriptions)	3.8 (3.0) [85%]	1.8 (1.0) [66%]	5.9 (3.9) [87%]	183 (87) [3.5%]	186 (41) [3.3%]	249 (148) [10.5%]
Non-prescription drugs*	[32%]	[20%]	[12%]	50 (133) [0.9%]	24 (0) [0.4%]	4 (0) [0.2%]
Direct medical costs				1311 (673) [25%]	1104 (594) [20%]	1043 (691) [44%]
Unpaid household help (hours)	93.9 (10.5) [57%]	88.6 (0.0) [46%]	29.5 (0.0) [20%]	829 (93) [15.8%]	782.5 (0) [14.0%]	261 (0) [11.0%]
Paid household help (hours)	59.7 (0.0) [47%]	55.9 (0.0) [35%]	17.9 (0.0) [15%]	1505 (0) [28.7%]	1410 (0) [25.2%]	454 (0) [19.1%]
Paid and unpaid help (hours)	153.6 (58.0) [70%]	144.5 (55.0) [61%]	47.5 (0.0) [26%]	2334 (964) [44.5%]	2193 (840) [39.2%]	715 (0) [30.0%]
Inactivity (hours)	33.1 (14.5) [54%]	41.1 (8.0) [48%]	11.7 (0.0) [25%]	1454 (336) [27.7%]	1925 (0) [34.4%]	584 (0) [24.6%]
Aids/appliances/adaptations*	[30%]	[35%]	[5%]	142 (0) [2.7%]	372 (0) [6.6%]	31 (0) [1.3%]
Direct non-medical costs				3930 (2362) [75%]	4491 (2502) [80%]	1330 (0) [56%]
Total direct costs				5241 (3166) [100%]	5594 (3770) [100%]	2373 (1305) [100%]

Values are mean (median) [% of patients].
*For these categories only the costs and not the number of resources used were recorded. Thus the ''health resource use'' columns present only the proportion of patients who incurred costs for this category.
AS, ankylosing spondylitis; CLBP, chronic low back pain; FM, fibromyalgia.

Table 4 Annual direct, indirect, and total costs per patient for the three chronic musculoskeletal conditions

	FM (€/pt/year)	CLBP (€/pt/year)	AS (€/pt/year)	Difference FM−CLBP (€/pt/year)*	Difference FM−AS (€/pt/year)*	Difference CLBP−AS (€/pt/year)*
Direct medical costs	1311 (673) [17%]	1104 (594) [13%]	1043 (691) [32%]	207 (−226 to 645)	268 (−132 to 663)	61 (−273 to 412)
Direct non-medical costs	3930 (2362) [50%]	4491 (2502) [53%]	1330 (1330) [41%]	−561 (−2086 to 898)	2600 (1476 to 3758)	3161 (2943 to 4931)
Total direct costs	5241 (3166) [67%]	5594 (3770) [66%]	2373 (2373) [74%]	−353 (−2010 to 1277)	2869 (1555 to 4237)	3221 (1961 to 4640)
Productivity (friction) costs	2573 (0) [33%]	2939 (0) [34%]	834 (0) [26%]	−366 (−1802 to 1207)	1739 (356 to 3039)	2105 (843 to 3293)
Total costs	7814 (5145) [100%]	8533 (5068) [100%]	3205 (1793) [100%]	−719 (−3353 to 1624)	4609 (2467 to 6662)	5328 (3618 to 7253)

Values are mean (median) [% of patients] or mean (95% confidence interval (CI)).
*95% CI if the mean difference was assessed by bootstrap.
AS, ankylosing spondylitis; CLBP, chronic low back pain; FM, fibromyalgia; pt, patient.

Table 5 Determinants of the direct medical, direct non-medical, productivity, and total costs assessed by Cox proportional hazards analysis with costs as outcome

	Direct medical costs	Direct non-medical costs	Friction costs*	Total costs
FM *v* AS	0.93 (0.45 to 1.88) p=0.8	1.61 (1.36 to 2.27) p=0.007	1.64 (1.20 to 2.33) p=0.007	2.17 (1.59 to 2.94) p<0.0001
CLBP *v* AS	1.12 (0.58 to 2.13) p=0.7	1.92 (1.43 to 2.56) p<0.0001	1.49 (1.23 to 2.00) p=0.01	2.27 (1.69 to 3.03) p<0.0001
Intervention	1.30 (0.74 to 2.33) p=0.4	0.84 (0.66 to 1.08) p=0.2	1.03 (0.80 to 1.31) p=0.8	0.88 (0.71 to 1.15) p=0.3
Female sex		1.52 (1.15 to 1.96) p=0.003	0.69 (0.53 to 0.92) p=0.009	

Values are exp(B) (95% confidence interval).
*Cost of production losses during the time when the work of the sick person was not replaced.
AS, ankylosing spondylitis; CLBP, chronic low back pain; FM, fibromyalgia.

Determinants of costs

Determinants of costs are shown in table 5. Diagnostic group was the most important variable associated with direct non-medical, productivity, and total costs. The treatment assignment did not explain differences in costs for any of the cost categories but there was an interaction between intervention and CLBP ($p = 0.04$) for the direct non-medical costs. This can be explained by a small increase in the need for unpaid help among patients with CLBP in the intervention group, a phenomenon already described in the original publication.[13] Female patients had more direct non-medical costs but male patients had more productivity costs. There were no interactions between the diagnostic group and any of the other determinants. Figure 1 shows the differences in costs between the diagnostic groups. Only 7.5% of patients with ankylosing spondylitis incurred more than €10 000 total annual costs, compared with more than 30% of patients with fibromyalgia and 37% of patients with CLBP. In the linear regression analysis on the log transformed total costs, lower general wellbeing had a slightly greater association with the total costs ($B = -0.03$ (95% CI, −0.001 to −0.02); $p = 0.04$). Within each of the diseases separately, no specific variables were associated with higher total costs in fibromyalgia and CLBP, while in ankylosing spondylitis lower educational level was associated with higher total costs ($B = 2.9$ (95% CI, 1.4 to 6.3)).

Sensitivity analyses

Excluding the costs for psychotherapists from the direct medical costs of patients with CLBP the mean annual costs per patient decreased slightly from €1104 to €984 and total direct cost from €5594 to €470. Reducing the friction period to 14 weeks decreased the cost to €2333, €2750, and €798 per patient per year for fibromyalgia, CLBP, and ankylosing spondylitis, respectively. Neither sensitivity analysis influenced the conclusions on the differences in costs.

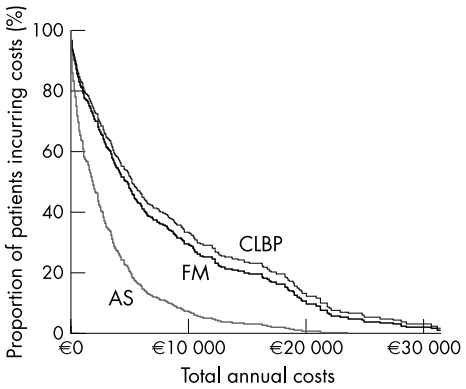

Figure 1 Cox probability curve illustrating the proportion of patients incurring more than a specific amount of costs in €/patient per year for each of the three chronic back conditions. AS, ankylosing spondylitis; CLBP, chronic low back pain; FM, fibromyalgia.

DISCUSSION

Patients with fibromyalgia and CLBP referred to a specialist express lower general wellbeing and are economically more costly than patients with ankylosing spondylitis. Although the poor general wellbeing experienced by patients with unexplained pain has been recognised before,[5] this is the first study to show that these patients behave in a different way economically. The direct *non-medical* and productivity costs were, in particular, markedly higher in fibromyalgia and CLBP. This points to the important impact of these two pain syndromes on function, both in private and in professional life. Also, within the *medical* costs some remarkable differences were noted between fibromyalgia and CLBP on the one hand and ankylosing spondylitis on the other. Costs for disease related hospital admissions, alternative medicine, and over the counter drugs tended to be higher in fibromyalgia and CLBP, but costs for physiotherapy and prescription drugs were higher in ankylosing spondylitis.

Explaining such differences is complex, as medical resource utilisation does not simply reflect the patient's behaviour but is equally influenced by the behaviour of the physician, who has scientific convictions but has to work within the constraints of the health care system. For example, the higher costs for physiotherapy and prescription drugs in ankylosing spondylitis may show that health care providers recognise the failure of physiotherapy and drug treatment to have any sustained effect in fibromyalgia and CLBP while they are effective treatment for ankylosing spondylitis. On the other hand, the maximised number of physiotherapy sessions reimbursed by the Dutch health insurance for non-inflammatory musculoskeletal disorders is likely to be an additional explanation. Costs for alternative medicine and non-prescription drugs were higher in fibromyalgia and CLBP, probably reflecting the continued quest by these patients to find relief from their complaints. In multivariate analyses the diagnostic group was the only variable explaining the total costs.

Although this study was not primarily designed to compare costs and wellbeing but was a secondary analysis of three distinct studies, its main strength is that resource utilisation was assessed in each study by the same cost diary, and that the same cost estimates (2002) were attributed to the resource use. However, we recognise that the analysis has several limitations.

First, patients with fibromyalgia and CLBP were referred by general practitioners or specialists, while patients with ankylosing spondylitis were recruited from the patients' society and might represent a sample with less severe disease. However, labour force participation (56% *v* 55%), general wellbeing (67 *v* 68), and the average total costs (€3205 *v* €3470) per patient with ankylosing spondylitis in this study are comparable to the average costs reported in Dutch ankylosing spondylitis patients under the care of a rheumatologist.[11 12] On the other hand, a recent study showed that in the Netherlands only about 20–30% of patients with chronic widespread pain and CLBP receive specialised care.[2] In this population sample, labour force participation was 57% among patients with CLBP, much better than observed in our study.[2] Therefore, data from this study are only generalisable to patients under treatment by a specialist.

Second, patients included in this analysis took part in a randomised controlled trial. In addition, it cannot be excluded that the longer duration of the intervention for patients with fibromyalgia or CLBP may have contributed to the selection of patients with no paid work in these diagnostic groups. In addition, the intervention might have changed health care utilisation in the treatment groups. Although a small reduction in resource utilisation was observed in the ankylosing spondylitis and fibromyalgia study, extensive statistical testing reliably excluded an influence of the intervention to explain the differences between the conditions.

Third, there was a period of six years between the studies in fibromyalgia and CLBP and the study in ankylosing spondylitis. By applying consumer price indices to the cost estimates, we could correct for differential timing and evolution of prices but there were no possibility of correcting for possible changes in health resource utilisation in the population over time. However, during the six year period no major changes in financing of health care or social security were introduced in the Netherlands and it is unlikely that patients or physicians changed their behaviour towards health care consumption.

Finally, the initial cost diary which was used in the fibromyalgia and CLBP study did not include technical examinations such as laboratory tests or *x* rays, which could not therefore be taken into account. However, costs of technical examinations are never a major cost driver in musculoskeletal disease and therefore it is unlikely that the exclusion of these costs would have altered the present conclusions.

The high costs for fibromyalgia and CLBP have been confirmed in other published reports. A top-down American study estimated the direct and productivity costs paid by insurance companies in fibromyalgia for the year 1998 at US$5945 (€7179 adjusted for differential timing and purchasing power parities (PPP)), which was 2.4 times higher than in controls.[7] A longitudinal American study in fibromyalgia patients under the care of a rheumatologist reported average annual medical costs in 1996 of US$2274 (€2847).[8] In a Canadian population based study, fibromyalgia incurred 2.2-fold higher costs in 1994 compared with non-pain controls for expenditure by health insurance on physician visits, laboratory tests, and radiology.[6] For CLBP, the total direct and productivity costs from the payer's perspective in a community sample were estimated at US$6807 in1990 (€10 148).[9] As mentioned, the annual costs observed for ankylosing spondylitis were comparable with another Dutch study, as well as with a study among American patients which reported direct costs of US$1775 (€2091).[10–12]

Apart from the costs per patient, the total national yearly cost per disease provide information on the societal economic impact of these diseases. In the Netherlands, the accepted prevalence of chronic widespread pain in the adult population is 5.3% (±0.7%), of CLBP, 21.2% (±1.7%),[2] and of ankylosing spondylitis, 0.1%.[3]. In addition, it is estimated that 20–30% of patients with fibromyalgia and 30–40% of patients with CLBP are under the care of a general practitioner or medical specialist.[2] For the adult Dutch population of 11.8 million, the above figures translate to 125 372 patients with fibromyalgia, 752 226 with CLBP, and 11 827 with ankylosing spondylitis, reflecting the profile of the patients studied in our analyses. This would result in average annual costs of €980 million, €6418 million, and €38 million for fibromyalgia, CLBP, and ankylosing spondylitis, respectively.

Conclusions

While for the patients and specialists physicians the impact of the unexplained pain syndromes on perceived general wellbeing is a major problem, for society the economic consequences are high, and even higher when compared to patients with a specific inflammatory disease such as ankylosing spondylitis.

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REFERENCES

1 **Frances A**, Association WGotAP. *Diagnostic and statistical manual of mental disorders*, DSM-IV-TR, 4th ed. Washington, DC: American Psychiatric Association, 2000.
2 **Picavet HS**, Schouten JS. Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC(3)-study. *Pain* 2003;**102**:167–78.
3 **van der Linden SM**, Valkenburg HA, de Jongh BM, Cats A. The risk of developing ankylosing spondylitis in HLA-B27 positive individuals. A comparison of relatives of spondylitis patients with the general population. *Arthritis Rheum* 1984;**27**:241–9.
4 **Spoorenberg A**, van der Heijde D, de Klerk E, Dougados M, de Vlam K, Mielants H, *et al*. Relative value of erythrocyte sedimentation rate and C-reactive protein in assessment of disease activity in ankylosing spondylitis. *J Rheumatol* 1999;**26**:980–4.
5 **Hidding A**, van Santen M, De Klerk E, Gielen X, Boers M, Geenen R, *et al*. Comparison between self-report measures and clinical observations of functional disability in ankylosing spondylitis, rheumatoid arthritis and fibromyalgia. *J Rheumatol* 1994;**21**:818–23.
6 **White KP**, Speechley M, Harth M, Ostbye T. The London Fibromyalgia Epidemiology Study: direct health care costs of fibromyalgia syndrome in London, Canada. *J Rheumatol* 1999;**26**:885–9.
7 **Robinson RL**, Birnbaum HG, Morley MA, Sisitsky T, Greenberg PE, Claxton AJ. Economic cost and epidemiological characteristics of patients with fibromyalgia claims. *J Rheumatol* 2003;**30**:1318–25.
8 **Wolfe F**, Anderson J, Harkness D, Bennett RM, Caro XJ, Goldenberg DL, *et al*. A prospective, longitudinal, multicenter study of service utilization and costs in fibromyalgia. *Arthritis Rheum* 1997;**40**:1560–70.
9 **Webster BS**, Snook SH. The cost of compensable low back pain. *J Occup Med* 1990;**32**:13–15.
10 **Ward MM**. Functional disability predicts total costs in patients with ankylosing spondylitis. *Arthritis Rheum* 2002;**46**:223–31.
11 **Boonen A**, van der Heijde D, Landewe R, Guillemin F, Rutten-van Molken M, Dougados M, *et al*. Direct costs of ankylosing spondylitis and its determinants: an analysis among three European countries. *Ann Rheum Dis* 2003;**62**:732–40.
12 **Boonen A**, van der Heijde D, Landewe R, Spoorenberg A, Schouten H, Rutten van Molken M, *et al*. Work status and productivity costs due to ankylosing spondylitis: comparison of three European countries. *Ann Rheum Dis* 2002;**61**:429–37.
13 **Goossens ME**, Rutten Van Molken MP, Kole Snijders AM, Vlaeyen JW, Van Breukelen G, Leidl R. Health economic assessment of behavioural rehabilitation in chronic low back pain: a randomised clinical trial. *Health Econ* 1998;**7**:39–51.
14 **Goossens ME**, Rutten van Molken MP, Leidl RM, Bos SG, Vlaeyen JW, Teeken Gruben NJ. Cognitive-educational treatment of fibromyalgia: a randomized clinical trial. II. Economic evaluation. *J Rheumatol* 1996;**23**:1246–54.

15 **Van Tubergen A**, Boonen A, Landewe R, Rutten-Van Molken M, Van Der Heijde D, Hidding A, *et al*. Cost effectiveness of combined spa-exercise therapy in ankylosing spondylitis: a randomized controlled trial. *Arthritis Rheum* 2002;**47**:459–67.
16 **Bennett K**, Torrance G, Tugwell P. Methodologic challenges in the development of utility measures of health-related quality of life in rheumatoid arthritis. *Control Clin Trials* 1991;**12**(4 suppl): 118–28S.
17 **Bakker C**, Rutten M, van Doorslaer E, Bennett K, van der Linden S. Feasibility of utility assessment by rating scale and standard gamble in patients with ankylosing spondylitis or fibromyalgia. *J Rheumatol* 1994;**21**:269–74.
18 **The Euroqol Group**. Euroqol: a new facility for the measurement of health related quality of life. *Health Policy* 1990;**16**:199–208.
19 **Goossens ME**, Rutten-van Molken MP, Vlaeyen JW, van der Linden SM. The cost diary: a method to measure direct and indirect costs in cost-effectiveness research. *J Clin Epidemiol* 2000;**53**:688–95.
20 **Oostenbrink J**, Koopmanschap M, Rutten F. *Handleiding voor kostenonderzoek. Methoden en richtlijnprijzen voor economische evaluaties in de gezondheidszorg* [Guideline for cost evaluations. Methods and cost estimates for economic evaluations in healthcare]. Amstelveen: College voor Zorgverzekeraars, 2000.
21 **Organisation for Economic Cooperation,** Development (OECD). Health Data File 1999: www.oecd.org.IN.
22 www.cbs.nl, In.
23 **Koopmanschap MA**, Rutten FFH. The impact of indirect costs: the consequences of production loss or increased costs of production. *Med Care* 1996;**34**:DS59–68.