EXTENDED REPORT

Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany

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Ann Rheum Dis 2006;**65**:1175–1183. doi: 10.1136/ard.2005.046367

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Accepted 5 March 2006
Published Online First
15 March 2006

Objective: To estimate and compare the direct and indirect costs of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE), and to evaluate the effect of sex, disease duration and functional status on the various cost domains.

Methods: Data of outpatients, aged 18–65, with rheumatoid arthritis (n=4351), ankylosing spondylitis (n=827), PsA (n=908) or SLE (n=844), who were enrolled in the national database of the German collaborative arthritis centres in 2002, were analysed. Data on healthcare consumption, out-of-pocket expenses and productivity losses were derived from doctors and patients. For the calculation of indirect costs, the human capital approach (HCA) and the friction cost approach (FCA) were applied.

Results: Mean direct costs amounted to €4737 a year in rheumatoid arthritis, €3676 in ankylosing spondylitis, €3156 in PsA and €3191 in SLE. By using the HCA, total costs were calculated at €15 637 in rheumatoid arthritis, €13 513 in ankylosing spondylitis, €11 075 in PsA and €14 411 in SLE, whereas with the FCA the numbers were €7899, €7204, €5570 and €6518, respectively. Costs increased with disease duration and were strongly dependent on functional status. In patients with the highest disability (<50% of full function), the total costs on applying the HCA were €34 915 in rheumatoid arthritis, €29 647 in ankylosing spondylitis, €37 440 in PsA and €32 296 in SLE.

Conclusion: The costs of illness are high in all four diseases, with a strong effect of functional status on total costs. Indirect costs differ by the factor 3, based on whether the HCA or the FCA is used.

The enormous socioeconomic effect of rheumatic diseases has been increasingly recognised in the past decades. Important cost-of-illness studies were carried out more than 20 years ago in the USA,^{1–4} followed, in the 1990s, by studies in the Netherlands,^{5–7} Sweden,⁸ Canada,^{9–10} the USA^{11–12} and Germany.^{13–14}

For rheumatoid arthritis, the heterogeneous results were compared and evaluated in systematic reviews. According to Cooper¹⁵ and Merkesdal *et al.*,¹⁶ mean direct costs of rheumatoid arthritis cover a range of about €1600 to about €11 000 in various studies. The mean of these studies was reported as €5000¹⁶ and US\$5720.¹⁵ Differences in reported costs can be attributed to (i) the cost domains included; (ii) the study populations; and (iii) the general differences in the healthcare systems. To enhance comparability, the Outcome Measures in Arthritis Clinical Trials group has been working on a cost matrix for future studies.¹⁷

In a recent study in Germany, clinical data and patient reports on healthcare consumption were linked with health insurance data to estimate the validity of cost data derived from patients.¹⁸ A high validity of reports from patients was confirmed for hospitalisation and drug consumption, as well as for productivity losses because of sick leave and work disability related to rheumatoid arthritis.

Few data are available for inflammatory rheumatic diseases other than rheumatoid arthritis, and it is rarer that more than one disease can be investigated in one study. Additionally, there is little information on the variability of costs according to disease duration, activity, severity and demographic data of the patient. We took advantage of a large national rheumatology database, which includes data on all requisite components of direct and indirect costs.

In the present investigation, we aim at answering two questions:

1. What are the direct and indirect costs of rheumatoid arthritis, ankylosing spondylitis, systemic lupus erythematosus (SLE) and psoriatic arthritis (PsA) in a large cohort of German patients treated for rheumatology?
2. What is the variance of these costs in each disease group according to demographic markers, functional status, disease duration and self-assessed health status?

PATIENTS AND METHODS

We used data from the National Database of the German Collaborative Arthritis Centres (Nucleic Acid Database Project) previously described in detail.^{19–20} In brief, rheumatologists in 24 arthritis centres have recorded the clinical data of all outpatients with inflammatory rheumatic diseases once a year since 1993, and patients have answered a comprehensive questionnaire. The rheumatologists are supposed to register each outpatient with an inflammatory rheumatic disease, except those who refuse to participate.

The database comprises newly referred and prevalent cases. Patients seen on a regular basis are registered once a year. The following analysis is based on data for 2002 of all outpatients with confirmed diagnoses of rheumatoid arthritis, ankylosing spondylitis, PsA or SLE, who had been in rheumatological care for at least 1 month. For better

Abbreviations: FCA, friction cost approach; FFbH, Hannover Functional Status Questionnaire; HAQ, Health Assessment Questionnaire; HCA, human capital approach; PsA, psoriatic arthritis; SLE, systemic lupus erythematosus

comparability of the four disease groups with distinctly different age structure, we restricted the analysis to patients of working age (<65 years).

Assessments

Standard forms were used for data recording. The doctors recorded the date of onset of disease and of previous and current treatments. Diagnoses were made according to the Austrian Cooperative Research criteria for rheumatoid arthritis and SLE, and the New York criteria for ankylosing spondylitis. Diagnosis of PsA was made by the treating doctor. No further criteria were applied.

Disability was recorded by the patient by using an 18-item scale of activities of daily living, the Hannover Functional Status Questionnaire (FFbH). The FFbH is similar to the Health Assessment Questionnaire (HAQ), but is more widely used in Germany. The two scales are highly correlated ($r = 0.87$). FFbH values can be transformed into HAQ values by using the formula $HAQ = 3.16 - 0.028 \times FFbH$.²¹ We used this transformation in table 1.

Cost calculation

Costs were calculated for each patient for the 12 months preceding the day of documentation. Items that were recorded for the previous 3 months (visits to doctors and out-of-pocket expenditures) were multiplied by four. If resource utilisation was recorded but the incidental data were missing (eg, duration of stay in hospital), the missing data were replaced by the respective group median. We used the median instead of the arithmetic mean to avoid an overestimation of costs due to a small number of extremely high values. For calculation of total costs on an individual basis, missing data for one cost item were replaced by the mean costs of the group as surrogate for that item.

For drug treatment, we only had the information that the patient was treated with that drug at some time during the past 12 months. We assumed an average treatment duration of 9 months. This estimate was taken from a long-term observational study,²² which showed an average treatment duration of 9 months in the real world over all disease-modifying anti-rheumatic drugs. We performed a sensitivity analysis to estimate the differences in costs, assuming shorter or longer average treatment.

Cost assessment is performed by applying the societal perspective. The following resource utilisations are captured (direct cost components): fees for visits to doctors, drug and non-drug treatments, surgery, imaging techniques and inpatient stays in acute care hospitals and rehabilitation clinics. Direct cost components also comprise the patients' additional payments for prescribed treatments, and those disease-related expenses that patients pay fully out of pocket. Visits to doctors comprise visits to the general practitioner or another non-rheumatologist, as well as those to the rheumatologist. For drug and non-drug treatments, it was not feasible to ascertain exact quantities because we only had the information that a certain treatment was applied during the past 12 months. For drug treatments, the average annual drug costs, including those of monitoring, were calculated.¹⁶ For additional drug treatment, only Cox II selective and non-selective non-steroidal anti-inflammatory drugs, glucocorticoids and drugs for the prevention or treatment of osteoporosis (calcium or vitamin D, bisphosphonates, fluorides) were included. Antibiotics and analgesics that have low prescription rates were not included in the costs.

If non-drug treatments were prescribed, we assumed that at least one prescription with 10 single treatments was issued. We used a price list that integrates the mean prices of the major German healthcare payers.²³

Imaging techniques were recorded by the doctor as radiographs of hands or feet or spine, or others such as magnetic resonance image, computed tomogram, joint ultrasound or measurement of bone density. Prices were calculated according to the standard schedule of fees for outpatient contract doctors, which are different in the 16 federal states of Germany.²⁴ We calculated the mean of prices for those federal states where the highest numbers of patients with the respective cost component lived.^{25–28}

Daily costs for stays in acute-care hospitals or rehabilitation clinics were calculated according to the respective statistics.^{29–30} Co-payments for prescribed treatments or full out-of-pocket expenditures were listed by the patients in the questionnaire.

Indirect costs comprise productivity losses owing to sick leave and early retirement. Productivity losses were assessed by both the human capital approach (HCA) and the friction cost approach (FCA). The FCA was used in addition to the internationally more common HCA to generate transparent and easily comparable indirect costing data in accordance with the German guidelines for socioeconomic evaluation.³¹

The use of a friction period takes into account that no economy achieves full employment. Productivity losses are therefore counted in the period only until the productivity of the patient is replaced by that of a previously unemployed person.³² The friction period of 58 days is the mean time before a vacancy reported to the employment office is filled.³³ The friction period was applied only to patients on permanent retirement for health reasons, not to those on sick leave.

The sick leave days are the cumulated numbers of absence days due to the respective disease. These physical units (productivity losses) are then appraised by assuming that a day of lost productivity costs society as much as the average daily German wage estimated by population data. To calculate the average daily wage in Germany, the gross income from dependent work was divided by the number of people employed in dependent jobs for 2002 divided by 365 days, resulting in €95 a day.³⁴ Periods of income loss were calculated for 7 days per week.

Statistical analyses

Data analysis was performed with the statistical package SPSS.³⁵ Table 2 gives the mean with standard deviation and bootstrap confidence interval (1000 drawings) and the median for each of the cost domains. Differences in costs were compared by Kruskal–Wallis test and differences in proportions by χ^2 test; all differences in the following are significant at a level of $p < 0.001$. Major cost drivers were analysed by multivariate linear regression analysis.

RESULTS

Sample

Even though we restricted our analysis to patients aged <65, in accordance with the different ages at onset, there was a significant difference between the groups for mean age (42–53 years; table 2). Patients with rheumatoid arthritis had considerably lower employment rates for men and women than those with other diseases (table 3). The percentages of patients on disability pension and of those with a stay in hospital were the highest in patients with rheumatoid arthritis and SLE, and the percentage of patients without sickness during the past year was the highest in ankylosing spondylitis.

Total costs

Table 2 shows the annual costs of all direct and indirect domains included for rheumatoid arthritis, ankylosing spondylitis, PsA and SLE. Median and mean total direct costs were the highest in rheumatoid arthritis with median

Table 1 Mean annual costs (in euros) by disease and functional status (Hannover Functional Status Questionnaire or Health Assessment Questionnaire)

FFbH/HAQ	RA			AS			PsA			SLE		
	>70	50-70	<50	>70	50-70	<50	>70	50-70	<50	>70	50-70	<50
	<1.2	1.2-1.7	>1.7	<1.2	1.2-1.7	>1.7	<1.2	1.2-1.7	>1.7	<1.2	1.2-1.7	>1.7
n	2469	970	795	458	216	130	596	189	101	643	114	63
Mean age	51	54	55	44	47	49	48	51	54	41	48	49
Disability	14	37	54	10	28	52	7	32	67	17	61	57
pension (%)												
Direct costs												
Visits to doctor	243	334	434	163	239	408	197	320	373	189	308	406
Drugs	1448	2176	2709	1644	1488	1389	961	1222	1702	825	947	992
Non-drug treatments*	254	538	765	251	390	496	182	502	743	120	408	435
Inpatient treatment	901	1907	3531	845	1278	1556	650	1921	2113	1295	2116	2755
Patient "out-of-pocket" expenditure	378	705	964	496	469	742	341	496	790	386	394	878
Σ	3225	5661	8403	3399	3865	4590	2331	4461	5721	2814	4174	5467
Indirect costs (loss of productivity)												
Sick leave	856	3212	7619	1444	4045	6925	904	3051	8391	1486	5947	6941
Permanent work disability (HCA)	4731	12707	18894	3397	9882	18132	2364	11201	23329	6011	21073	19887
Permanent work disability (FCA)	752	2019	3002	540	1570	2881	376	1780	3707	955	3349	3160
Total costs (HCA)	8811	21580	34915	8241	17791	29647	5599	18712	37440	10311	31193	32296
Total costs (FCA)	4832	10892	19024	5384	9480	14396	3610	9292	17819	5255	13469	15569

AS, ankylosing spondylitis; FCA, friction cost approach; FFbH, Hannover Functional Status Questionnaire; HAQ, Health Assessment Questionnaire; HCA, human capital approach; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

*Including imaging and endoprosthesis.

Table 2 Annual costs (in euros) for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus

	RA	AS	PsA	SLE
No of cases	4351	827	908	844
Age (mean)	53	46	49	42
Employed (%)	45	67	63	55
Disability pension (%)	26	22	19	27
Sick leave (%)	33	38	27	30
Mean duration of sick leave	53.6	65.2	52.5	64.8
Hospitalisation (%)	21	11	14	20
Mean days in hospital (all patients)	19.8	20.8	18.5	21.1
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
	Median (95% CI ₉₅)	Median (95% CI ₉₅)	Median (95% CI ₉₅)	Median (95% CI ₉₅)
<i>Direct costs</i>				
Visits to doctor	298 (291)	220 (223)	240 (233)	218 (222)
Drugs	1843 (356.5)	1531 (337.9)	1104 (196.8)	850 (923)
DMARDs	1517 (355.6)	1200 (346.4)	825 (197.0)	635 (86.9)
Other	327 (262)	331 (216)	279 (231)	215 (224)
Physical treatment	135 (178)	189 (176)	138 (200)	119 (199)
Imaging	47 (48)	52 (67)	44 (49)	32 (68)
Endoprosthetic surgery	229 (130.6)	86 (81.0)	137 (101.7)	33 (49.9)
Inpatient treatment	1624 (393.5)	1080 (307.5)	1080 (283.4)	1516 (427.1)
In acute-care hospitals	1314 (366.4)	725 (278.9)	820 (258.4)	1310 (390.0)
In rehabilitation clinics	310 (95.6)	354 (84.1)	260 (76.7)	206 (85.2)
Patient "out-of-pocket" expenditures	559 (1390)	517 (928)	412 (875)	424 (866)
Additional payment	224 (800)	199 (340)	187 (640)	160 (361)
Own purchase	336 (1204)	318 (930)	225 (613)	263 (825)
Σ	4737 (6306)	3676 (5083)	3156 (4118)	3191 (4847)
	Median (95% CI ₉₅)	Median (95% CI ₉₅)	Median (95% CI ₉₅)	Median (95% CI ₉₅)
<i>Indirect costs (loss of productivity)</i>				
Sick leave	1700 (501.7)	2336 (639.7)	1374 (444.7)	1835 (542.1)
Permanent work disability (HCA)	9201 (1526.1)	7501 (1427.9)	6545 (1359.6)	9385 (1544.9)
Permanent work disability (FCA)	1462 (242.5)	1192 (226.9)	1040 (216.0)	1491 (245.5)
Total costs (HCA)	15637 (17242)	13513 (15728)	11075 (14789)	14411 (16595)
Total costs (FCA)	7899 (801.0)	7204 (796.9)	5570 (622.2)	6518 (71.68)

AS, ankylosing spondylitis; DMARDs, disease-modifying anti-rheumatic drugs; FCA, friction cost approach; HCA, human capital approach; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Table 3 Mean annual costs (in euros) by disease and sex

	RA		AS		PsA		SLE	
	Women	Men	Women	Men	Women	Men	Women	Men
n	3434	917	311	516	504	404	756	88
Mean age	52	54	47	45	50	48	42	42
Employed (%)	43	54	57	72	53	75	53	72
Disability pension (%)	26	29	21	22	23	14	27	24
<i>Direct costs</i>								
Visits to doctor	295	310	238	211	249	234	219	203
Drugs	1869	1749	1322	1658	1000	1231	837	968
Non-drug treatments*	433	330	338	321	411	206	192	118
Inpatient treatment	1670	1458	1123	1054	1253	866	1481	1812
Patient "out-of-pocket" expenditures	607	390	609	482	494	318	440	283
Σ	4874	4236	3630	3726	3406	2855	3168	3385
<i>Indirect costs (loss of productivity)</i>								
Sick leave	1619	1943	2014	2477	1600	1202	1804	2039
Permanent work disability (HCA)	8987	10008	7168	7701	7863	4932	9503	8370
Permanent work disability (FCA)	1428	1590	1139	1224	1250	784	1510	1330
Total costs (HCA)	15479	16187	12812	13904	12870	8989	14475	13793
Total costs (FCA)	7921	7769	6783	7426	6256	4841	6482	6753

AS, ankylosing spondylitis; FCA, friction cost approach; HCA, human capital approach; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

*Including imaging and endoprosthetics.

€2256 and mean €4737. This was mainly attributable to drug costs and inpatient treatments. Ankylosing spondylitis had a mean direct cost of €3676 (median €1705), which was significantly higher than those in PsA and SLE, with nearly equal costs around mean €3200 and median €1600. SLE had less than half the drug costs of rheumatoid arthritis. Patients with ankylosing spondylitis or PsA had lower costs of inpatient treatment in acute-care hospitals than those with rheumatoid arthritis and SLE. Out-of-pocket expenditures were highest in rheumatoid arthritis, at €559 a year. Patients with ankylosing spondylitis, however, had costs that were almost as high (€517) and those with PsA or SLE had costs of about €420.

By using the HCA, mean indirect costs (due to sick leave and permanent work disability) were the highest in SLE (€11 220), followed by rheumatoid arthritis, at €10 901. Owing to the lower percentage of patients on disability pension, indirect costs in ankylosing spondylitis were €9837, even though they incurred the highest costs for sick leave. Patients with PsA had considerably lower indirect costs than the other groups, with an average of €7919. Total annual costs were the highest for rheumatoid arthritis (€15 637) and the lowest for PsA (€11 075).

Mean indirect costs with the FCA decline to about one third of that seen with the HCA. Median costs are similar between the two approaches and vary from €6045 for rheumatoid arthritis to €3214 for PsA with the HCA and from €4997 for RA to €3133 for PsA with the FCA.

Costs by sex

Table 3 shows the mean annual costs for men and women. Women with rheumatoid arthritis or PsA had considerably higher direct costs than men because of inpatient treatment and non-drug treatments, whereas drug costs were higher in men in all groups except the group with rheumatoid arthritis. Women in all disease groups had remarkably higher out-of-pocket costs, especially for own expenses. These were non-prescription drugs, unguents, measurement of bone density and costs for transportation and domestic help.

Indirect costs are directly related to the proportion of persons in gainful employment (cost of sick leave) and, using the HCA, the age of the patients (years of early retirement before the age of regular retirement). Men with ankylosing

spondylitis, rheumatoid arthritis and SLE had higher costs and those with PsA had lower costs owing to sick leave and early retirement than women with the same diagnosis. Again, the FCA results in much lower indirect costs.

Costs by disease duration

With the HCA, all disease groups show an increase in total costs with disease duration (table 4). This increase, however, is mainly attributable to costs of permanent work disability. Mean direct costs show little variation with disease duration. In all diseases except rheumatoid arthritis, mean costs for inpatient treatment decrease with duration of disease. With the FCA, patients with rheumatoid arthritis with long-standing disease incurred the highest costs, followed by patients with SLE with short disease duration.

Costs by functional status

Functional status is an even more important predictor of total costs (table 1). Patients with rheumatoid arthritis and PsA with a poor functional status of <50% of full function (corresponding with an HAQ of more than 1.7) had direct costs more than twice those of patients with good functional status (>70% of full function or an HAQ of <1.2). Costs for inpatient treatment, visits to the doctor, non-drug treatment and out-of-pocket expenses were directly related to functional status.

Indirect costs differed by a factor of 4–10 between good and poor functional status for both the HCA and the FCA, which is obviously a result of only a small proportion of patients with a functional status of <50% of normal (HAQ >1.7) being able to work and because those who still worked had frequent and long phases of sick leave.

Sensitivity analysis for drug costs

As drugs are the main cost domain in direct costs besides hospitalisation, and the mean duration of intake of 9 months was an assumption, we estimated the effect of different assumptions on total costs. Although drugs covered between 27% and 42% of the direct costs in the four diagnostic groups, an increase or decrease of 3 months in assumed duration of intake would have caused a maximum change of 6% of total costs with the HCA.

Table 4 Mean annual costs (in euros) by disease and disease duration (in years)

Disease (years)	RA			AS			PsA			SLE		
	<5	5-10	>10	<5	5-10	>10	<5	5-10	>10	<5	5-10	>10
N	1223	1237	1810	145	150	479	274	263	345	195	246	371
Age (mean)	51	52	54	41	41	48	46	48	52	38	41	45
Disability pension (%)	12	22	40	10	12	27	7	16	29	10	21	39
<i>Direct costs</i>												
Visits to doctor	320	278	302	190	246	224	236	221	251	239	217	211
Drugs	1322	1802	2243	1199	2076	1475	916	1166	1218	897	783	892
Non-drug treatments*	300	296	567	400	345	291	268	251	402	114	146	249
Inpatient treatment	1613	1300	1857	1840	992	885	1398	649	1127	2526	1129	1280
Patient "out-of-pocket" expenditure	582	488	595	536	613	510	437	315	456	427	390	440
Σ	4137	4163	5563	4165	4273	3385	3254	2602	3455	4202	2665	3074
<i>Indirect costs (loss of productivity)</i>												
Sick leave	1971	1450	1614	3103	2075	2131	2128	673	918	3787	860	1220
Permanent work disability (HCA)	4081	7504	14045	3444	4064	9530	2526	5692	10255	3360	7244	13401
Permanent work disability (FCA)	649	1192	2232	547	646	1514	401	905	1630	534	1151	2130
Total costs (HCA)	10190	13118	21222	10712	10412	15046	7908	8968	14628	11349	10769	17695
Total costs (FCA)	6757	6806	9409	7815	6994	7030	5783	4180	6003	8523	4676	6423

AS, ankylosing spondylitis; FCA, friction cost approach; HCA, human capital approach; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.
 *Including imaging and endoprosthesis.

Table 5 Results from multivariate linear regression analyses of cost drivers

	RA		AS		PsA		SLE	
	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI
<i>Direct costs</i>								
Positive rheumatoid factor	825	377 to 1273	NI		NI		NI	
Steinbrocker's functional class (per unit)	1185	848 to 1522	NI		NI		NI	
Disease activity (per unit, 0–10)	336	214 to 458	207	10 to 403	387	211 to 563	506	291 to 721
Function (per unit of worsening; 100–0)	72	62 to 82	19	0.3 to 39	46	31 to 61	34	12 to 55
Disease duration (per year)							–65	–188 to –11
Years of education (per year)	234	82 to 387						
<i>Indirect costs (HCA)</i>								
Male sex	3014	1866 to 4163	2896	797 to 4994				
Positive rheumatoid factor	1328	320 to 2336	NI		NI		NI	
Steinbrocker's functional class (per unit)	2332	1600 to 3065			NI		NI	
Function (per unit of worsening; 100–0)	236	214 to 258	285	233 to 337	320	277 to 365	346	285 to 407
Disease duration (per year)	257	200 to 313	164	60 to 269	356	232 to 479	420	269 to 570
Age (per year)	111	61 to 160	249	149 to 349			118	15 to 222
Age at disease onset (per year)					130	42 to 218		
Years of education (per year)			–1384	–2235 to –533				
<i>Total costs (HCA)</i>								
Male sex	2995	1711 to 4279	2906	594 to 5218				
Positive rheumatoid factor	2295	1168 to 3422	NI		NI		NI	
Steinbrocker's functional class (per unit)	3844	3024 to 4663	NI		NI		NI	
Disease activity (per unit, 0–10)							902	244 to 1560
Function (per unit of worsening; 100–0)	314	289 to 338	317	259 to 375	379	331 to 426	370	300 to 441
Disease duration (per year)	253	189 to 317	366	245 to 486	322	187 to 458	353	184 to 522
Age (per year)	93	38 to 148	–137	–253 to –22			123	5 to 241
Age at disease onset (per year)			–1266	–2203 to –328	100	4 to 196		
Years of education (per year)								

AS, ankylosing spondylitis; Coeff, coefficient; FCA, friction cost approach; HCA, human capital approach; NI, not included; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

Multivariate analysis of major cost drivers

With multivariate linear regression analyses, we identified major cost drivers for direct, indirect and total costs in each of the disease groups. Table 5 gives the results. Major cost drivers for direct costs in rheumatoid arthritis were function (Steinbrocker's functional class and functional status reported by patients), positive rheumatoid factor and disease activity. The coefficients are the costs (in euros) for every unit of the respective parameter—for example, increase from Steinbrocker II to III results in an increase in costs of €1185. In addition to these, for indirect costs male sex and disease duration turned out to be cost drivers. Controlled for all other factors, men had €3014 higher indirect costs than women. In ankylosing spondylitis, only disease activity predicted direct costs; for indirect costs male sex, function, age and disease duration had a role. Education was negatively correlated with indirect costs. This is attributable to the risk of early retirement being closely correlated with the level of education in ankylosing spondylitis, as shown in a previous paper.³⁶ For PsA and SLE, sex did not have any influence on costs; major cost drivers were physical function and disease activity.

DISCUSSION

We reported a descriptive analysis of direct and indirect costs incurred by patients with the four most frequent inflammatory rheumatic diseases, and identified the most important cost drivers. Although several studies on cost of illness exist for rheumatoid arthritis, the data for ankylosing spondylitis are limited and are almost non-existent for SLE and PsA. The strength of this analysis is that it reflects the patient spectrum in daily rheumatological care, that we have the same body of information on all four diagnoses and that the high numbers of cases allow us to perform subgroup analyses.

The results are in line with those of other studies on cost of illness. Verstappen *et al*³⁷ compared direct costs incurred by patients with rheumatoid arthritis in four distinct disease duration groups (0–2, >2–6, >6–10 and >10 years). The total direct costs were €5235, €3930, €4664 and €8243. These data go well with our results, with the exception of patients with the highest disease duration. In the Dutch study, however, very high costs for devices and adaptations were included. If we subtract these, the directly comparable group of patients with >10 years disease duration had costs of €4984, which is comparable to our data (€5563).

Boonen *et al*⁷ compared patients with ankylosing spondylitis from the Netherlands, France and Belgium. The direct costs amounted to €2640 per year, which is lower than our data (mean 4.737). It has to be borne in mind that we restricted our analysis to patients of working age. If, however, we had included all patients, the total direct costs would have been quite similar (eg, €4505 for rheumatoid arthritis or €3507 for ankylosing spondylitis, data not shown).

For SLE, data from the UK are available.³⁸ Patients in a specific SLE clinic incurred direct costs of (converted) €3920 and indirect costs of €7950. Our direct costs are comparable with these data.

The decrease of direct costs with duration of disease seen in SLE might be a healthy-survivor effect. It is, however, mainly driven by hospitalisation, which occurs in nearly all of these patients during the first 5 years.

One of the limitations of our approach is the restriction to patients treated by rheumatologists. Therefore, conclusions cannot be drawn on all patients with the respective diseases in Germany. Patients in rheumatological care are more severely ill and receive more intense treatment than the average patient of the same diagnosis. This may explain why the total costs are rather similar across the four diseases.

As this was not a specific study on cost of illness, but the analysis of a routine database, some of the cost components are not as precisely documented as in a socioeconomic study (eg, the number of single applications of non-drug treatments). We used conservative estimates of components for which we did not have the exact quantities. Therefore, an underestimation of costs is more likely than an overestimation, and a potential bias would be effective in all disease groups. On the other hand, drug treatment for comorbid conditions is not included in the estimates.

The present data are derived from doctors or patients and may differ from administrative data. Even though the patients were advised to report only those utilisations or costs that were caused by the rheumatic disease, we cannot rule out that, for example, hospitalisation or sick leave for other reasons was reported as well. This can result in an overestimation of costs. The results of Ruof and Merkesdal,^{18, 39} comparing administrative costing data and costing data derived from patients show that patients report the main direct cost components and their productivity losses adequately.

The highest effect on the total costs comes from the principal decision to apply the HCA or the FCA.

The most relevant difference between the two approaches lies in the progressive increase of productivity costs over time by using the HCA. Productivity losses are counted until the date of usual retirement, although from a societal point of view the productivity of the person is substituted by another person who has been unemployed until then (in all economic systems with unemployment). Therefore, the cost gap between the estimates of the two approaches is strongly dependent on the age at early retirement. Therefore, the HCA overestimates the actual costs to society. It neglects, however, the burden on the person caused by permanent work disability. We therefore suggest reporting both kinds of data.

The difference of productivity losses would have been even larger if the friction period had been applied to long-term sick leave as well. But the periods of production loss due to sick leave were not cut off, assuming that as long as a person on sick leave is not replaced by a jobless person there will be a productivity loss to society.

Our multivariate analysis showed poor function as a major cost driver. This is in agreement with other economic analyses: Kobelt *et al*⁴⁰ found HAQ to be a significant predictor of resource consumption, and in an early Swedish study on rheumatoid arthritis, HAQ was the best predictor of high direct costs.⁴¹ Total costs according to the HCA increased by €314–379 across all four disease groups for each unit of the FFbH. Therefore, if a treatment is able to improve FFbH function in a patient from 50 to 70 (corresponding to an HAQ improvement from 1.7 to 1.2), this results in cost savings of €6280–7580, depending on diagnosis.

This study underlines the high economic burden of each of the four most frequent inflammatory rheumatic diseases. The data offer useful comparative figures when estimating the cost-effectiveness of new drugs.

ACKNOWLEDGEMENTS

This work was supported by grants from the German Federal Ministry of Health (1993–1999, FB2-433346-8/13) and the Federal Ministry of Education and Research in the programme “Competence Network Rheumatology” (since 1999, 91G19344/3). We thank those German rheumatologists who contributed to the database. The highest contributions came from U von Hinüber and W Demary (Hildesheim), S Wassenberg (Ratingen), E Gromnica-Ihle (Berlin), R Dreher (Bad Kreuznach) and G Hein (Jena). We thank Carolin Weber and Daniela Topsisch for a careful monitoring of the project.

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Competing interests: None declared.

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