

EXTENDED REPORT

Burden and cost of illness in patients with juvenile idiopathic arthritis

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Objective: To estimate the cost of illness in an incidence based cohort of patients with juvenile idiopathic arthritis.

Methods: Direct costs (healthcare and non-healthcare costs) and indirect costs (productivity loss due to sick leave and work disability) were measured in 215 JIA patients, assessed on an average of 17 years after disease onset. Assessment included a clinical evaluation, a structured interview, and two self completion questionnaires. Annual direct costs were estimated based on the reported use of healthcare services and resources, using average unit prices. Indirect costs were estimated from the number of work days missed—that is, using the human capital approach.

Results: The mean total cost of late JIA was estimated to be €3500 per patient and year, of which the direct cost contributed more than half. Patients with still active disease (55%) incurred the major share (90%) of the cost. They had a mean total cost of €5700 per patient year, with those under rheumatological care incurring a cost of €9300. Having a certain JIA subgroup, functional disability, or receipt of specialised care independently contributed to the total cost in active JIA. Highest mean total costs were found in active seropositive polyarthritis (€17 000) and extended oligoarthritis (€11 000), while the lowest were found in active enthesitis related arthritis (€1500) and persistent oligoarthritis (€2700).

Conclusions: Estimated 12 month costs in late JIA are considerable, differing among the various JIA subgroups. Treatment strategies in JIA should be analysed for their cost effectiveness in the long term.

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Limited resources and rapid increments in healthcare expenditure in all countries have led to an increased interest in the economic impact of various diseases. Musculoskeletal disorders have gained special attention, with numerous studies showing their tremendous economic burden.^{1–6} Although literature on the cost of illness in rheumatic diseases has burgeoned in recent years, there has been very little research into cost of juvenile idiopathic arthritis (JIA).^{7–8}

JIA represents a heterogeneous group of chronic inflammatory arthritides in children, and is very variable in its presentation and course. While many patients experience remission, as many as 50% enter adulthood with active disease and functional limitation.^{9–10} Recent studies have shown that adult JIA patients have to cope with impairments of body functions and structures, limitations to their activity, and restricted participation in society.^{9–14} This may result in a considerable impact on the individual, their family and friends, and society.

This study aimed to assess the socioeconomic impact of JIA, and to provide information about the magnitude of JIA associated costs relating to the different JIA subgroups, disease activity, functional limitation, and types of healthcare provision.

METHODS

Study design

This was an incidence based, retrospective study conducted from a societal and patient's perspective, estimating 12 month costs associated with late JIA.

Study population

The data for the present cost analysis were derived from a 17 year follow up study.⁹ The whole cohort comprised 215 JIA patients, (83% of the original cohort), who were assessed at the 2nd Children's Hospital between 1998 and 2000. All

patients met the modified International League of Associations for Rheumatology criteria for JIA¹⁵ at disease onset and had been referred to the Children's Hospital at Berlin-Buch between 1978 and 1988 (for greater detail, see Minden *et al*⁹).

Outcome definition

Assessment included a clinical examination and a global physician's assessment of functional status (numeric rating scale from 0 to 10 on the Numeric Rating Scale-11 (NRS-11), and Steinbrocker functional status¹⁶) and disease activity (NRS-11, remission according to defined criteria¹⁷). For this study, a patient was considered to be in remission if he/she had had no active uveitis or inflammatory back pain for at least 2 months and fulfilled five or more of the following criteria: morning stiffness not exceeding 15 minutes, no fatigue, no joint pain, no joint tenderness, no swelling in joints or tendon sheaths, and/or an erythrocyte sedimentation rate (ESR) <20 mm/hour. In addition, patients rated their pain, functional status, general health, and disease activity on NRS-11. Self completion questionnaires containing standardised instruments, such as German versions of the Health Assessment Questionnaire (HAQ¹⁸), the Rheumatoid Arthritis Quality of Life Questionnaire (RAQol¹⁹), and the Center for Epidemiologic Studies Depression Scale (CES-D²⁰), were additionally employed. The patients also assessed their burden of illness concerning their physical, psychological, professional, financial, and family situation on a 4 point

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; DMARDs, disease modifying anti-rheumatic drugs; FC, friction cost; HAQ, Health Assessment Questionnaire; JIA, juvenile idiopathic arthritis; NRS-11, Numeric Rating Scale-11; NSAIDs, non-steroidal anti-rheumatic drugs; RA, rheumatoid arthritis; RAQol, the Rheumatoid Arthritis Quality of Life Questionnaire

Likert scale ranging from “not at all” to “very much” and reported on their need for help with daily routines.

Resource use data

Resource use data were obtained from the study participants by use of self completion questionnaires and a structured interview. Data on the patient’s functional capacity, quality of life, depressive symptoms, income, vocational status, and out of pocket expenses were obtained by questionnaire, while information on the current state of signs and symptoms, current treatment, number and type of comorbidities, and use of healthcare services and resources over the preceding 3 months was collected by interview. Subsequently, a full review of the patient’s clinical notes was performed to verify the interview/questionnaire data, including the medical records from the Children’s Hospital, which were available for all patients, and those available for approximately half the patients still receiving medical care. No relevant differences between the information obtained from the patients and that given in the records were noted.

Table 1 summarises the estimates of unit prices used in this article. The average price of a rheumatologist visit estimated by Merkesdal *et al.*²¹ was used as the unit price for rheumatology service use. This tariff had been estimated by those authors by means of a survey amongst rheumatologists, providing an average physician charge inclusive of routine laboratory tests and imaging. Unit prices for non-rheumatologist visits were valued according to data from the Federal Association of Panel Doctors, based on the German Act for Physician Charges.²² Standardised reimbursement rates by the health insurance companies for specific services were used as the unit prices for non-physician service use (such as physiotherapy and occupational therapy).²³ The Red List²⁴ was the source for unit prices of specific drugs, from which the annual cost was estimated for the reported or a standard drug dose. An average price was used when only the substance was known. To estimate the cost of inpatient care for JIA, the daily generic hospital cost in Germany according to the federal statistical state office²⁶ was applied. A standardised unit price based on the average expenditure by pension insurance companies for a medical service in 1999²⁸ was applied for the use of non-acute hospital facilities. For all analyses, 1999 unit prices were used.

Non-healthcare costs expended by the patients covered 3 months and included disease related expenditures such as

transportation, alterations to the home, cash adjustments to prescribed therapy, non-prescribed and alternative therapy, use of private and community services, and special equipment. All costs were converted into euros, applying 1.95583 German marks to 1 euro.

Cost estimation

To estimate the total annual outpatient cost of JIA, the number of each service type used because of JIA within the preceding 3 months was multiplied by 4, as was by the unit price for that service, and the two subsequently added together. For the estimation of hospitalisation cost, all acute hospital admissions with and without surgery related to JIA were considered. The cumulative number of days in hospital within the preceding 12 months was multiplied by the daily generic hospital cost. Additional charges for specific surgery, such as joint replacement, were taken into account. To calculate the rehabilitation cost, the average price per measure was applied, then inpatient and outpatient costs were added to calculate the total cost of direct medical care. Patient expenditures reported for the preceding 3 months were multiplied by 4 to compute the annual non-healthcare cost. Both healthcare and non-healthcare costs were then added to calculate the direct JIA cost.

The indirect costs of JIA were evaluated for the whole JIA group and for the active population ($n = 105$), which refers to those aged 16 years or over who were working or willing to work. Consequently, younger patients, students, and housewives were excluded from this group. The productivity costs were calculated by means of the human capital approach, taking into account all costs to society that arose from lost productivity caused by sick leave and work disability (complete cessation of employment and entitlement to a social security pension). The cumulative number of work days lost over the preceding 12 months was calculated for each patient individually. Population data of the year 1999²⁹ were used for the valuation of the loss of productivity. An estimate of the loss of productivity was obtained by multiplying the number of work days lost per year by the gross annual income of all gainfully employed workers (€1.053 billion), divided by the total number of labour force participants (32.497 million) and by 365 days. Thus, the cost of lost productivity amounted to approximately €89/person/day.

Table 1 Sources of unit costs and resource use (cumulative number of used resources per year, proportion of patients having used that resource)

Expenditure costs assessed	Resource use			Utilisation reference
	Annual number	Number of patients (%)	Applied unit prices in € (superscripts are references)	
Direct costs				
Healthcare costs				
Outpatient costs				
JIA-related rheumatology service use	517	82 (38)	49 ²¹	Interview, records
Other JIA-related physician service use	885	97 (45)	30 ²²	Interview
Non-physician service use	1500	42 (19)	Standardised rates/unit ²³	Interview
Surgery	1	1 (0.5)	Average charge ²²	Interview
Medication	NA	83 (39)	Average medication price ²⁴	Interview, records
Devices and aids	NA	67 (31)	Average price ²⁵	Interview, questionnaire
Inpatient costs				
Acute hospital facilities	606 days	24 (11)	300/day ²⁶	Interview, records
Surgery	2	2 (1)	Case based lump sum ²⁷	Interview, records
Non-acute hospital facilities (rehabilitation)	NA	6 (3)	4511/stay ²⁸	Interview
Non-healthcare costs				
Patient expenditures (3 months)	NA	71 (33)		Questionnaire
Indirect costs				
Loss of productivity	913 days	23 (11)	89/day ²⁹	Questionnaire, interview

NA, not applicable.

Statistical analysis

Statistical analyses were performed using an SPSS database (version 10.0). The main descriptive statistics presented are the arithmetic mean, standard deviation (SD), median, and interquartile range (IQR). Bootstrap estimates were used to calculate the 95% confidence intervals (CI) by means of Gauss Mathematical and Statistical System software.³⁰ Kruskal-Wallis test and Mann-Whitney U test were used for statistical comparisons. Spearman's rank correlation was applied to study the correlation between direct and indirect cost. To evaluate the contribution of various disease variables to the costs in the whole cohort and in active JIA, respectively, two analyses were performed: a logistic regression analysis with backward elimination and cumulative logit models for ordinal responses in which the JIA groups were summed up to two groups with clearly different costs. The latter analysis contrasting four groups with different costs (€0, €1–500, €501–5000, and >€5000) considered the following variables: JIA subgroup (persistent oligoarthritis or enthesitis related arthritis; systemic arthritis, extended oligoarthritis, or seropositive polyarthritis), HAQ score (0, 0.13–0.74, and ≥ 0.75), CES-D score (0–10, 11–15, and ≥ 16), and utilisation of specialised care (no or yes). A p value <0.05 was considered statistically significant.

Sensitivity analysis

Due to the wide range in reimbursement rates for outpatient visits and inpatient stays across Germany, applied generic unit costs for outpatient visits and inpatient stays were uncertain parameters. In 1999, rates for outpatient visits varied by 35% depending on federal state, health insurance, and specialist,²² while cost for inpatient care varied by 55% among the different hospitals and federal states.²⁶ In order to investigate the sensitivity of the cost estimated, the applied prices for the respective parameters were thus varied by the aforementioned percentages. In addition, as evaluation of the indirect costs according to the human capital approach leads to an overestimation of productivity costs in economic systems with underemployment, the friction cost method (FC) was also used to calculate productivity costs. This method limits the time of productivity loss to that period until replacement of the worker has taken place, assumed to equal to an average vacation period.³¹ Therefore, in this analysis, costs due to productivity loss by the patients having been retired or on sick leave for more than 6 weeks were not taken into account to calculate indirect FC.

RESULTS

Out of 260 JIA patients referred to the 2nd Children's Hospital at Berlin-Buch between 1978 and 1988, 215 (83%) could be assessed. From table 2, it can be observed that more than half were female, mean age was 23 years, and mean disease duration was 17 years.

Outcome

At follow up, 45% of the JIA patients were in remission according to the defined criteria, although slightly more of the patients (48%) considered their disease as being inactive (NRS-11 = 0). As regards general health, 69% felt somewhat limited (NRS-11 >0), with 25% stating moderate to severe restrictions (NRS-11 ≥ 4). This was predominantly due to their rheumatic illness, as comorbidities were infrequent; they included atopic disorders in 20%, nephrolithiasis in 5%, osteoporosis in 3%, and psychiatric disorders in 3% of the patients. Overall, impairments in functioning (HAQ score >0) and quality of life (RAQol score >0) were reported by 39% and 60%, respectively. As assessed by the HAQ, 9% of patients needed assistance with activities of daily living, and when asked in general, 24% stated the need for help in order

Table 2 Characteristics of study participants

Patients' characteristics	
Number of patients	215
Female (%)	54
JIA subgroups, n (%)	
Systemic arthritis	30 (14)
Oligoarthritis	85 (40)
Seronegative polyarthritis	27 (13)
Seropositive polyarthritis	3 (1)
Psoriatic arthritis	3 (1)
Enthesitis related arthritis	33 (15)
Other arthritis	34 (16)
Mean age, years (SD)	23 (5.3)
Mean disease duration, years (SD)	17 (4.0)
Steinbrocker functional class, n (%)	
I	118 (55)
II	75 (35)
III	21 (10)
IV	1 (0)
Patient status, n (%)	
Students/trainees	94 (44)
Employees	85 (40)
On maternity leave	13 (6)
Retired	8 (4)

to be able to engage in their daily routines at all. That help was provided by a paid social worker in only 2% of the cases.

Of those not having attained remission, 90% and 80% of patients respectively reported impairments of global health (NRS-11 >0) and quality of life (RAQol >0). Functional limitations were stated by 63% (HAQ score >0) and 51% (NRS-11 >0), respectively. Joint pain within the previous week was reported by 78%, and restrictions in motion of at least one joint were observed in 80%. Almost 90% of the patients with active disease considered themselves to be physically burdened and 56% felt emotionally burdened by their illness. Moreover, 64% claimed to be somewhat burdened by the illness in terms of their professional goals or at the workplace. However, only 50% of them had been seen by a rheumatologist at least once within the preceding 12 months. Of the patients not in remission, 40% were receiving disease modifying anti-rheumatic drugs (DMARDs) and 37% non-steroidal anti-rheumatic drugs (NSAIDs) at follow up. Physiotherapy had been prescribed to only 28%. Overall, one third of the patients with an active disease were rated as being insufficiently provided with specialised care by the assessing physician, taking into account complaints stated by the patients, and results of the laboratory and clinical assessments. Patients under rheumatological care were the more severe cases; more than half (56%) had systemic arthritis, extended oligoarthritis, or polyarthritis, whereas these subgroups amounted to less than one third in those cases treated only by general practitioners. Furthermore, these patients had a significantly higher mean disease activity (3.9 v 2.3 on NRS-11, p = 0.001) and functional limitation (1.9 v 1.0 on NRS-11, p = 0.023) than those treated by general practitioners.

Total cost of illness

The number of resources used by the JIA patients and the proportion of patients having used these resources over the preceding 12 months form the basis of the cost estimation given in table 1. The resultant total mean cost was estimated to be €3471 per JIA patient and year (95% CI €2257 to €4685). Of the total cost, 55% was incurred by the healthcare service in the form of visits to health professionals, inpatient stays, and medications, and by the patient in the form of non-healthcare cost. The remaining 45% of the total cost was indirect cost due to loss of productivity. Only a small

proportion of the patients incurred high cost; 12% (n = 26) were responsible for 80% of all costs, while 30% caused no cost at all.

When the various JIA subgroups were compared, it was seen that mean total cost diverged significantly among them ($p < 0.001$). Patients with seropositive polyarthritis and extended oligoarthritis incurred the highest total mean cost, while patients with persistent oligoarthritis incurred the lowest mean cost. The mean healthcare, non-healthcare, and indirect costs related to subgroup are summarised in table 3.

As would be expected, persistent disease activity, functional disability, and restricted quality of life were associated with significantly higher cost ($p < 0.001$), as shown in table 4. Furthermore, patients with an active disease who received specialised care incurred a higher cost than those not receiving such care (mean €9292 v €2069), which was due not only to a higher direct cost (€4994 v €1269), but also to a higher indirect mean cost (€4298 v €800).

In multivariate analysis contrasting patients with no v any cost, absence of remission ($p = 0.041$) and utilisation of specialised care ($p < 0.001$) were determinants of the total cost. Altogether, the patients without remission incurred 90% of all costs. In the multivariate cumulative logit analysis it was found that presence of functional limitation, JIA subgroup, and utilisation of rheumatological care significantly contributed to the total cost in active JIA. Having a HAQ score of 0.13–0.74 or a score of ≥ 0.75 significantly increased the risk of incurring higher cost (OR 4.0; 95% CI 1.4 to 11.6; $p = 0.005$ and OR 8.5; 95% CI 1.9 to 37.7; $p = 0.005$, respectively). Furthermore, patients with systemic arthritis, extended oligoarthritis, or seropositive polyarthritis had an increased risk of incurring higher cost (OR 3.5; 95% CI 1.3 to 9.5; $p = 0.014$), as had those under rheumatological care (OR 10.5; 95% CI 3.6 to 33.3; $p < 0.001$). Generally, direct and indirect costs were found to be positively associated (Spearman's rank correlation coefficient $r_s = 0.4$; $p < 0.001$).

Direct cost

Healthcare cost accounted for the major part of the direct cost (96%), while non-healthcare cost was almost negligible. Despite there being only 26 (12%) reported inpatient stays (acute and non-acute), these accounted for 53% of the direct and 55% of the total healthcare cost incurred by the entire cohort. Outpatient care took 43% of direct cost. Visits by health professionals accounted for 25% (5% rheumatology service use, 6% other JIA-related physician service use, 14% non-physician service use), devices and aids for 3%, and medications for 14% of direct care cost. Drugs cost was split as follows: 48% due to DMARDs, 17% to NSAIDs, 5% to osteoporosis treatment/prophylaxis, and 7% to gastroprotective agents. Only 26% of all patients were taking DMARDs

Table 4 Annual JIA costs (€) by selected parameters

	n	Mean (SD)	Median (IQR)
Remission			
Yes	97	782 (3809)	51 (0–254)
No	118	5681 (11243)	1170 (70–4916)
Disease activity*			
0	100	430 (1337)	13 (0–240)
1–3	68	3772 (7888)	738 (64–3280)
4–6	27	5428 (8486)	1173 (792–8085)
7–10	18	15101 (20495)	2714 (1227–32899)
HAQ score†			
0	130	917 (3273)	51 (0–303)
0.1–0.74	57	4558 (8435)	1370 (258–5007)
≥ 0.75	26	13034 (18076)	3653 (1150–23238)
RAQoL score‡			
0	84	424 (1987)	28 (0–128)
1–4	71	2568 (5447)	760 (26–2872)
5–14	48	8743 (15284)	1387 (234–9445)
≥ 15	5	11730 (13669)	6931 (2072–23789)
CES-D score§			
0–10	172	2785 (7344)	141 (0–1441)
11–15	20	8088 (17432)	939 (65–7932)
≥ 16	16	4670 (9138)	741 (42–5805)

*NRS 0–10; †range 0–3; ‡range 0–30; §range 0–45.
IQR, interquartile range.

and 21% NSAIDs at follow up. Patients with active disease incurred direct costs of approximately €3000 per year, whereas those with remission incurred only €400 (table 5). While the proportion of the non-healthcare cost was similar in both patient groups, other components contributed in different extents to the direct costs, as shown in fig 1.

The total annual mean non-healthcare cost incurred by the patients was rather low (€77), contributing to 4% of the direct cost. The largest proportion was due to cash adjustments to prescribed inpatient and outpatient treatments (€46), followed by expenditure for non-prescribed/alternative therapy (€20), and transportation (€11).

Indirect cost

While indirect cost amounted to 45% of the total cost in the whole cohort, it made up 68% of the total cost in the active population. Cost due to sick leave was 16% of the indirect costs in the active population. Within the preceding 12 months, 16% of the active population (28% of those with active disease) had been on sick leave, with a mean number of 34 days (range 2–120) of sick leave because of JIA per patient year. Patients with a part time job incurred significantly higher indirect and total costs than those employed full time (€1791 v €199 and €5057 v €898, respectively; $p = 0.001$). With regard to the active population, mean indirect costs were highest in patients with seropositive

Table 3 Estimated 12 month healthcare, non-healthcare, and indirect costs (€) per JIA subgroup

JIA subgroup	Mean total cost (SD) (median)	Mean healthcare costs (SD) (median)	Mean non-healthcare costs (SD) (median)	Mean indirect costs (SD) (median)
Systemic arthritis	6758 (11682) (744)	3159 (6032) (271)	68 (140) (0)	3531 (9775) (0)
Oligoarthritis				
Persistent	971 (3174) (60)	534 (1393) (60)	35 (82) (0)	403 (2245) (0)
Extended	9048 (16774) (1361)	4571 (8286) (1061)	116 (208) (0)	4362 (11842) (0)
Polyarthritis				
RF+	17180 (23957) (6931)	4517 (5070) (3549)	221 (339) (51)	12442 (18698) (3382)
RF-	2711 (6820) (600)	1158 (2438) (440)	131 (259) (0)	1422 (6175) (0)
Psoriatic arthritis	2832 (4642) (307)	1137 (1710) (307)	34 (59) (0)	1661 (28780) (0)
ERA	1205 (2619) (51)	860 (1917) (51)	132 (264) (0)	213 (692) (0)
Other arthritis	2292 (5408) (100)	2053 (5178) (85)	32 (86) (0)	207 (849) (0)
All patients	3471 (9032) (240)	1821 (4593) (149)	78 (180) (0)	1571 (6554) (0)

RF+, rheumatic factor seropositive; RF-, rheumatic factor seronegative; ERA, enthesitis related arthritis

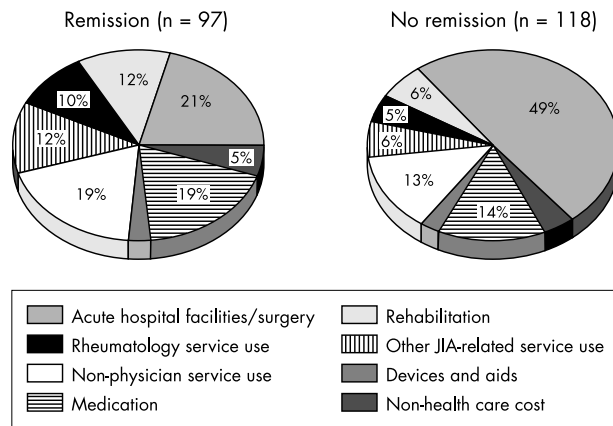


Figure 1 Direct costs incurred by patients not in remission v those having attained remission.

polyarthritis and extended oligoarthritis, where they contributed to 73% and 74% to the total cost. In contrast, the lowest indirect costs were estimated for patients with persistent oligoarthritis and enthesitis related arthritis (table 6).

Sensitivity analysis

The variation of the uncertain variables as reimbursement rates for outpatient (rheumatologist and non-rheumatologist) visits and inpatient stays by $\pm 35\%$ and $\pm 55\%$ resulted in a maximum change in healthcare cost of 30% and in total cost of 16%. In fact, the lower extreme for the mean healthcare cost (that is, reducing outpatient cost by 35% and inpatient cost by 55%) was €1278, and the upper extreme (that is increasing outpatient cost by 35% and inpatient cost by 55%) was €2365. Estimated lower and upper extremes for the mean total 12-month cost amounted to €2927 and €4014, respectively.

Applying the FC the indirect cost in the active population is €269, which is approximately one tenth of that estimated by means of the human capital method. The indirect FC accounts for 25% of the total cost—that is, €1087 or one third of that estimated by the human capital method.

DISCUSSION

Economic questions are now central to the practice of medicine in general and of rheumatology in particular. Recent data have shown the major economic impact of some musculoskeletal diseases on patients' daily life and on society.³²⁻³⁵ However, little information is available concerning the cost of JIA, the most common chronic inflammatory rheumatic disease in children.

To our knowledge, this is the first retrospective incidence based study providing descriptive data on the pattern of resource used by patients with late JIA. The study has shown that after a mean disease duration of 17 years, 55% of the JIA patients still had an active disease and 40% received specialised healthcare. Absence of remission and utilisation of rheumatological care were the main contributors to the total cost, up to approximately €3500 per patient year in this JIA cohort. This cost appears rather low, but it has to be borne in mind that: (a) this study was incidence based, and therefore included patients (45%) who had attained remission; (b) approximately one third of the patients with active disease were insufficiently provided with specialised care, and therefore incurred a lower healthcare cost; and (c) more than 40% were students for whom days absent from college or university due to JIA were not taken into account when calculating the productivity loss. However, patients with active disease incurred an annual cost of approximately €5700, with those under specialised care incurring €9000. This is similar to total costs estimated for patients with chronic arthritides acquired in adulthood, such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis.³²⁻³⁴

Significant differences were observed among the incurred annual costs in the various JIA subgroups, underlining that JIA is a heterogeneous disease. Costs were highest in patients with seropositive polyarthritis, extended oligoarthritis, or systemic arthritis, while they were lowest in patients having persistent oligoarthritis or enthesitis related arthritis. This is unsurprising, bearing in mind the different long term outcomes of patients with different JIA subtypes⁹ and their different use of medical services. A comparison of the subgroup related costs is restricted owing to lack of data for other patients with juvenile arthritis. Moreover, as cost of illness studies in "adult" arthritis focus on active disease as a rule, with many of them performed at rheumatology disease

Table 5 Annual subgroup related 12 month cost (€) for patients in remission compared with those not in remission

JIA subgroup	Mean total cost (SD) (median)		Mean healthcare cost (SD) (median)		Mean non-healthcare cost (SD) (median)		Mean indirect costs (SD) (median)	
	Remission	No remission	Remission	No remission	Remission	No remission	Remission	No remission
Systemic arthritis	2971 (9024) (65)	11086 (13139) (4383)	930 (2392) (65)	5707 (7840) (2423)	36 (81) (0)	104 (183) (24)	2005 (8019) (0)	5275 (11525) (312)
Oligoarthritis								
Persistent	435 (1286) (51)	2695 (5929) (455)	312 (904) (51)	1248 (2275) (173)	13 (42) (0)	106 (131) (20)	111 (519) (0)	1341 (4509) (0)
Extended	532 (654) (149)	11075 (18143) (2253)	410 (589) (149)	5561 (8966) (1298)	123 (274) (0)	114 (198) (41)	0 (0) (0)	5400 (13016) (0)
Polyarthritis								
RF+	—	17180 (23957) (6931)	—	4517 (5070) (3549)	—	221 (339) (51)	—	12442 (18698) (3382)
RF-	373 (533) (130)	4319 (8583) (1223)	353 (531) (130)	1712 (3052) (599)	20 (60) (0)	208 (314) (84)	0 (0) (0)	2400 (7975) (0)
Psoriatic arthritis	0 (0)	4248 (5574) (4248)	0 (0) (0)	1704 (1977) (1705)	0 (0) (0)	51 (72) (51)	0 (0) (0)	2492 (3524) (2492)
ERA	165 (352) (0)	1485 (2892) (116)	165 (352) (0)	1047 (2122) (116)	0 (0) (0)	167 (288) (0)	0 (0) (0)	270 (773) (0)
Other arthritis	72 (143) (0)	3503 (6450) (850)	72 (143) (0)	3134 (6218) (719)	0 (0) (0)	49 (103) (0)	0 (0) (0)	320 (1047) (0)
All patients	782 (3810) (51)	5681 (11243) (1170)	380 (1180) (51)	3006 (5857) (761)	20 (78) (0)	126 (222) (3)	382 (3271) (0)	2549 (8226) (0)

RF+, rheumatic factor seropositive; RF-, rheumatic factor seronegative; ERA, Enthesitis-related arthritis.

Table 6 Total and indirect costs (€) for the active population (n = 105)

JIA subgroup	Mean total cost (SD) (median)		Mean indirect costs (SD) (median)	
	Whole group	Patients not in remission	Whole group	Patients not in remission
Systemic arthritis	10948 (15108) (1447)	13334 (15134) (7135)	8024 (13861) (0)	9031 (14449) (311)
Oligoarthritis				
Persistent	348 (887) (0)	669 (1277) (0)	403 (2245) (0)	267 (706) (0)
Extended	16557 (25367) (1300)	18627 (26293) (1777)	12185 (18842) (0)	13708 (18835) (623)
Polyarthritis				
RF+	25744 (26605) (25744)	25744 (26605) (25744)	18663 (21611) (18663)	18663 (21611) (18663)
RF-	3411 (9408) (328)	6458 (13126) (432)	2777 (9233) (0)	5553 (13002) (0)
Psoriatic arthritis	2832 (4642) (307)	4248 (5574) (4248)	1661 (2878) (0)	2492 (3524) (2492)
ERA	1470 (3132) (46)	2078 (3663) (133)	320 (833) (0)	469 (983) (0)
Other arthritis	944 (2928) (64)	1560 (3797) (72)	239 (999) (0)	413 (1311) (0)
All patients	4298 (11449) (124)	6906 (14066) (655)	2910 (9043) (0)	4593 (11075) (0)

RF+, rheumatic factor seropositive; RF-, rheumatic factor seronegative; ERA, enthesitis-related arthritis.

centres,^{32 34 35} a data comparison is further hampered. Taking this into account, the following relates to JIA patients with an active disease.

In contrast to other musculoskeletal diseases,³⁶ the direct cost outweighs the indirect costs in late JIA. This is a result of the nature of the assessed patient cohort, which comprised adolescents and young adults still attending college or university and, therefore, not being available for work. In the active population, however, indirect cost accounted for approximately two thirds of the total cost. This is consistent with estimates in RA, where indirect cost made up 50–75% of the total cost.^{36–39} Admittedly, work disability and sick leave rates were much lower in late and active JIA, compared with late RA (5% v 39%⁴⁰ and 28% v 44%⁴¹, respectively).

Indirect costs were in turn highest in patients with seropositive polyarthritis and extended oligoarthritis. These were patients who experienced more frequent and more severe functional impairment, which is regarded as a relevant influencing factor on indirect costs.³⁵

There were difficulties in estimating indirect costs in this study. On the one hand, indirect costs were possibly underestimated because productivity loss referred only to the active population, and time lost from study by the patients or time lost from work by the patients' families and friends was not considered. Furthermore, a significantly higher proportion of patients were still completing their vocational training compared with the age matched population. It may be that some of these patients deferred their transition into the workforce or were even unable to work. This is supported by the fact that the part time employed incurred a significantly higher cost than the full time employed, which raises the suspicion of part time employment because of JIA. On the other hand, there may have been an overestimation of indirect cost as a result of using the human capital approach in a country with an unemployment rate of 12% among young adults.²⁹ By applying the friction cost method, the indirect cost would be only a tenth of that estimated by the human capital method, reducing the total cost to €1100 per patient in the active population.

The direct cost analysis revealed that in accordance with the majority of studies in RA^{34 37–39} inpatient care was the main source of expenditure in JIA. Even though only 12% of patients required inpatient care, it was responsible for more than half the direct costs. Patients with active disease under specialised care incurred significantly higher direct cost than those not receiving rheumatological care, as would be expected. However, these patients also incurred higher indirect costs because they were the more severe cases. In view of the long term morbidity and mortality in JIA,^{11–13 42} these data should not lead to the conclusion that specialised care simply increases cost of illness. The consequences of

absence of specialised care in late, still active JIA should be addressed in further follow up studies.

Self report questionnaires are an attractive, cost effective approach to assess the intangible cost for an individual patient.⁴³ Quality of life, functional status, and depression measures are particularly used to evaluate the "price" paid by the patient. In this study, approximately one in 10 patients showed substantial impairment of quality of life and functioning or felt considerably burdened by their illness. These were the patients who incurred the major share of the cost. Compared with other studies evaluating the impact of a chronic rheumatic disease, this is a rather low proportion.^{44 45} This could be explained by the fact that many patients, growing up with the disease, have adapted to their limitations, or that the chosen measures to assess the patients' health were not sensitive enough to disclose all the problems with which adolescents and young adults with JIA have to cope. The latter assumption is supported by the fact that twice as many patients stated the need of support in daily life when asked in general, compared with when asked using the HAQ.

As with any study, the results have to be interpreted in the light of the study's limitations. Cost estimation relied on self reported data where recall bias cannot be ruled out. This especially applies to the reported number of work days lost over the preceding 12 months, which is a very long recall period. "Standard" assigned cost per day, per visit, or per prescription based upon publicly available figures were used in this analysis, while the actual cost may vary from those considered. Further, the number of patients within some subgroups was relatively small. Otherwise, this study was incidence and population based and the obtained data can therefore be regarded as representative. An overestimation of cost due to patient selection can definitely be excluded.

This study gives an estimate of 12 month cost in late JIA, being only a fraction of the life long cost of illness. Further research should involve patients with recent onset of JIA and collect detailed cost data that can be used to assess the efficacy and cost effectiveness of different treatment strategies in JIA.

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