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Trends in economic consequences of rheumatoid arthritis over two subsequent years

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Objective. To examine changes in direct costs and in working status over 2 yrs in patients with rheumatoid arthritis (RA).
Patients and methods. In both 1999 and 2000, RA patients ($n = 461$) filled out a questionnaire retrospectively regarding utilization of health care, other RA-related direct costs and working status. Patients were categorized into four disease duration groups: 0–2 yrs, 2–6 yrs, 6–10 yrs and >10 yrs. At the same time points, disease activity was assessed. Logistic regression analyses were performed to identify a possible association between disease activity (high >66th percentile) measured at start of the second year and high direct costs (high >66th percentile) in the second year.
Results. Compared with the first year, a significant decrease in the costs for contacts with health care workers and for costs for laboratory tests was observed in the second year for the <2 yrs group. In the 2–6 yrs group and the >10 yrs group, we found a significant decrease in costs for devices and adaptations, but medication costs increased in the <2 yrs and the >10 yrs group in the second year. In the >10 yrs group, this was mainly due to an increasing number of patients who started to use biological agents during the second year. In all four disease duration groups, worse Visual Analogue Scale (VAS) disease activity and VAS general well-being were significantly associated with high direct costs. Of 97 patients working without disability at time of the first assessment, 12 (12%) patients became (partial) work disabled during follow-up.
Conclusion. In particular, costs for devices/adaptations and for medication changed during follow-up. The latter was probably due to an increase in the use of biological agents. Hopefully a decrease in direct costs and a reduced percentage of patients getting work disabled by better disease control will outweigh the high costs of biological drugs in the future.

KEY WORDS: Rheumatoid arthritis, Direct costs, Working status, 2 yr follow-up.

Introduction

Rheumatoid arthritis (RA) influences quality of life and working status and has considerable economic consequences for the individual patient as well as for his or her social environment and the society. These economic consequences are evaluated in cost-of-illness studies which provide data on direct and indirect costs. For direct costs, actual payments are made such as costs for medication, for hospitalization, contacts with health care workers and special aids. Indirect costs are costs for which resources are lost, but no direct payment is actually made. They can be classified into two groups: morbidity costs which are mainly productivity losses borne by the individual, their family, society and employer due to illness (i.e. loss of paid productivity and loss of household productivity) and mortality costs which are the present value of lost production due to premature death caused by illness [1].

We previously estimated in a study among Dutch RA patients that mean annual direct and indirect costs were, respectively, 5058 Euro [2] and 2322 Euro [3]. The estimated direct costs resemble those found in other cross-sectional studies on direct costs as reported in reviews [4, 5]. In our former study, total direct costs mainly consisted of costs for admissions to the hospital and/or rehabilitation centre, especially in the first 2 yrs and after >10 yrs after diagnosis. From 2 yrs disease duration on, patients also mentioned an increase in costs for the purchase of devices and adaptations in and around the house. Costs for medication contributed only for a minor part to total direct costs (~10%). In the past years, more patients started to use biological drugs [6–9]. Since these biological agents are rather expensive compared with conventional disease modifying drugs (DMARDs), it is to be expected that the contribution of the costs for medication will rise in the future [10, 11].

In general, most studies on direct cost have been performed cross-sectionally. It is, however, interesting to assess whether specific costs change during follow-up and whether the group of patients with high costs or with high disease activity changes over time. One study documented the long-term costs of RA during a 10-yr follow-up period (1986–96) [12]. In that study, average cumulative direct costs were $57 201, in line with the direct costs we found. Both functional disability at baseline and change in functional disability were associated with total direct costs.

Next to direct costs, work disability is often increased among patients with RA. Several disease-related factors and work-related factors have been identified as predictors for work disability [13]. In this report, we will evaluate whether the working status has changed during follow-up. In the Netherlands, patients who are on sick leave for 1 yr may apply for a work disability pension if certain criteria are met. In the 1999 study, thirteen patients were on prolonged (>2 weeks) sick leave because of RA. In this study, we will also evaluate whether these patients did become work disabled indeed during the next year.

Patients and methods

RA patients visiting the out-patient clinic of one of the seven rheumatology departments of the Utrecht Rheumatoid Arthritis Cohort study group (SRU) who participated in our first cross-sectional study on economic consequences were asked to participate in this follow-up study on economic consequences of RA [2, 14].

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In 1999 (first assessment) and in 2000 (second assessment), patients were asked to fill out a questionnaire retrospectively comprising questions regarding utilization of health care, other RA-related direct costs and working status. In 1999, patients were categorized into four disease duration groups: 0–2 yrs, 2–6 yrs, 6–10 yrs and >10 yrs. In this follow-up study, patients were designated to the same groups for both assessments.

Disease activity

The following clinical data were assessed for all patients at the time of filling out the questionnaire: ESR (mm/hr^{1st}), morning stiffness (0–180 min), Visual Analogue Scale (VAS) for pain (0–100 mm = worst pain), VAS general well-being (0–100 mm = worst score), VAS disease activity (0–100 mm = worst score), Thompson joint score (a weighted score of swelling and tenderness of joints (0–534), [15] and functional disability (HAQ, Dutch version (0–3 = worst score)) [16]. The EuroQol-5D (EQ-5D) was used to calculate health status [17]. The EQ instrument comprises five items each addressing a different attribute (domain) of health status (EQ-5 Dimension), covering mobility, self-care, daily activities, pain and mood. Each of the five items can be scored on a three-point categorical scale. The final utility transformation results in an equation that provides utility values, ranging from −0.594 to 1.00 = best health status (i.e. better utility).

Direct costs

Costs were estimated for the following six cost categories: (i) admissions to the hospital (including surgical interventions) and/or rehabilitation centre; (ii) contacts with health care workers (e.g. rheumatologist, physiotherapist); (iii) medication for RA; (iv) purchase of devices and/or adaptations in and around the house; (v) laboratory tests including X-rays and (vi) extra costs (e.g. transportation costs, extra energy, alternative medicines). All costs were calculated from a societal point of view and expressed in 2003 Euros. The year 2003 was chosen because the latest update on prices for health care utilization in the Netherlands was 2003.

Patients were asked to report the number of admitted days to the hospital or to the rehabilitation centre in the past year. Number of days admitted were multiplied by standardized 2003 prices for one day's admissions provided in the Dutch guidelines for cost-of-illness studies [18]. For hospitalization costs, distinct cost estimates were used for patients admitted in a general hospital *vs* patients admitted in a university hospital. For surgical interventions, 2003 CTG (College Tarieven voor Gezondheidszorg) tariffs were used [19]. Utilization rates per 3 months of contacts with health care workers (e.g. rheumatologist, general practitioner, home help, physiotherapist) were multiplied by prices provided in the Dutch guideline for cost-of-illness studies. Costs were then extrapolated to annual costs. Prices provided in the Dutch pharmaceutical formulary (year 2003) were used to obtain costs for medication. Prices were increased by a 6% tax rate and a handling fee for the pharmacist. Patients were also asked to report costs of the purchases of devices and/or adaptations in and around their house in the previous year. These aids and adaptations were categorized into: (a) large aids and adaptations (e.g. electric wheelchair, adapted kitchen or car); (b) orthopaedic aids (e.g. orthopaedic shoes); (c) aids for mobility (e.g. crutches, rollator); (d) adapted bicycle; (e) aids and adaptations in and around the house (e.g. adapted taps); (f) domestic aids (e.g. adapted kitchen tools). Next to these predefined categories for aids and adaptations, free text space was available to also report other aids and adaptations. The reported costs in Dutch guilders were converted to 2003 Euros applying the consumer price index for health care (CPI). Costs for laboratory tests included costs for monitoring for adverse effects of different DMARDs according to schedules used in the University Medical Centre Utrecht and costs for routine RA-related laboratory tests multiplied by number of visits to the rheumatologist. Costs of one X-ray of the hands and feet per year were included in total laboratory costs when patients had at least one visit to the rheumatologist. Patients were also asked to report whether they had made any additional costs in the previous three months because of RA (e.g. alternative medicine, clothing and energy costs). Reported costs were multiplied by four and converted to 2003 costs applying CPI. These extra costs also included travel expenses which were estimated by multiplying the number of contacts with health care workers by the average distance to the health care worker and costs per kilometre (Dutch guideline). If patients mentioned the utilization of one of the cost categories above, but did not report rates or costs, mean rates or costs as reported by other patients pertaining to that specific item were imputed.

Labour force participation

In both 1999 and 2000, patients were asked to state their working status. If patients were work disabled, they had to fill out whether this was due to RA or any other reason and the year they became work disabled. Only work disability associated with RA was taken into account. Patients with a paid job and of working age (<65 yrs) during the first assessment were further asked to report whether they had been on sick leave during the last 2 weeks because of RA and to mark how many (partial) days they were on sick leave. If patients were on sick leave for the entire two weeks, they had to indicate the start of the sick leave period.

In this study, we investigated a possible change in working status during follow-up. In addition, we investigated the change in working status, especially with respect to work disability of those patients who were on prolonged sick leave in 1999.

Household activities

Patients reported the number of hours that they received paid (e.g. home help) and/or unpaid (e.g. family) household help during the last two weeks because of inability to perform housekeeping tasks due to RA.

Statistical analyses

Costs are expressed as mean and the 95% CI. The 95% CI was obtained after bootstrapping (1000 replications). Mean change between the first and the second assessment were calculated and the 95% CI was obtained after bootstrapping. Both for the first and for the second assessment, patients were divided into two groups, i.e. high *vs* low costs and high *vs* low disease activity (ESR, VAS disease activity, VAS pain, VAS general well-being, Thompson joint score and functional disability). Per assessment, a cut-off point at the 66th percentile was chosen to subdivide patients with high costs and disease activity from those with low costs and disease activity. For both total direct costs and for the disease activity variables, we present the percentage distribution of patients who remained in the low or in high group during follow-up.

For each disease duration group, univariate logistic regression analyses were applied to see if demographic and clinical variables assessed at the start of the second year were associated with high costs during the second year, including high costs (>66th percentile of total direct costs) as dependent variable and demographic and individual clinical variables as independent variables. Clinical variables were categorized into two groups based on the 66th percentile of total direct costs. Age was entered as continuous variable in the regression analyses. In multivariate logistic regression analyses, a forward selection procedure was applied in order of highest significance level obtained in the univariate regression analyses. In addition, logistic regression analyses were applied to see if variables assessed at the start of the

second follow-up year (independent variables) could predict the need for (un)paid household help (dependent variable) in 2000.

Results

Of the 576 RA patients filling out the questionnaire in 1999 on direct costs and work disability, a total of 461 also filled out the questionnaire in 2000. Of these 461 patients, demographic characteristics and disease activity, measured in 1999 and in 2000, for the four disease duration groups are shown in Table 1. At time of the first assessment, mean disease duration of the total study population ($n = 461$) was $6.4 \pm$ S.D. 6 yrs, mean age was $59 \pm$ S.D. 13 yrs; and 72% were females. Except for morning stiffness and VAS disease activity, all clinical variables improved during this follow-up study in the <2 yrs disease duration group. For all other three disease duration groups, minimal changes with respect to disease activity were observed.

Patients who did not fill out the questionnaire the second time had, compared with patients who did, a longer mean disease duration at time of the first measurement (9.5 *vs* 6.5, $P < 0.0001$), worse functional disability score (1.3 *vs* 1.1, $P = 0.046$), a worse score on VAS general well-being (39 *vs* 33, $P = 0.035$), and a higher Thompson joint score (62 *vs* 43, $P = 0.029$). The other patient characteristics did not differ statistically significantly.

Direct costs

For the total study population, mean $\pm$ S.D. [median ($IQ_{0.25–0.75}$)] total direct costs in Euros were 5187 ± 8771 [2596 (1377–5450)] during the first assessment and 4218 ± 6402 [2040 (1134–4512)] at the second assessment. Mean (95%CI) difference in total direct costs for the four distinguished disease duration groups are shown in Table 1. Mean (95% CI costs) costs during the first and second assessment for health care workers, devices and adaptations, medication, admissions to the hospital and rehabilitation centre, extra costs and laboratory tests are shown in Fig. 1A–D for each disease duration group. In the <2 yrs disease duration group, costs for contacts with health care workers and laboratory tests decreased significantly, but increased significantly for medication use. In the 2–6 yrs group, a significant decrease in costs for devices and adaptations was observed, and a significant increase in medication and extra costs. In the 6–10 yrs group, no statistically significant changes were observed. In the >10 yrs group, costs for devices/adaptations decreased significantly but increased significantly for medication use.

In the total study population, the percentage contribution of each cost category at the first and second assessment was, respectively: for contacts with health care workers (23% *vs* 27%), for purchase of devices and adaptations (32% *vs* 20%), for medication (12% *vs* 24%), for admissions to the hospital and/or rehabilitation centre (19% *vs* 12%), for extra costs (9% *vs* 12%) and for laboratory tests (5% *vs* 5%). The increased fraction for drug expenses was largely determined by a growing number of patients receiving biological drugs; i.e. from one patient during the first assessment to 15 patients during the second assessment. For the four disease duration groups, the percentages of patients receiving conventional DMARDs or biological drugs either with or without a conventional DMARD were, respectively, at the first and second assessment: <2 yrs (DMARDs, 95 *vs* 92; biological agents, 0 *vs* 1); 2–6 yrs (DMARDs, 87 *vs* 80; biological agents, 0 *vs* 2); 6–10 yrs (DMARDs, 75 *vs* 76; biological agents, 0 *vs* 3); >10 yrs (DMARDs, 90 *vs* 82; biological agents, 2 *vs* 12). Costs for biological agents comprised 5% of total drug costs in 1999 and 40% of total drug costs in 2000.

Percentage of patients in high and low cost or disease activity group

For all four disease duration groups, approximately 50% of the patients were part of the low cost group at the first assessment as well as at the second assessment. About 20% of the patients were part of the high costs group for both assessments. The remaining patients changed from the low cost group to the high cost group or *vice versa*. The percentages of patients with high disease activity at both assessments were; for the <2, 2–6, 6–10, >10 yrs groups, respectively: ESR (22, 25, 26, 21), morning stiffness (22, 12, 19, 11), VAS disease activity (17, 16, 18, 15), VAS pain (26, 24, 24, 24), VAS general well-being (21, 21, 23, 16), Thompson joint score (20, 21, 24, 18), QoL (18, 20, 31, 46), and for functional disability (20, 23, 24, 22).

Factors associated with direct costs

Table 2 gives an overview of the variables obtained at the start of the second assessment which were statistically significantly associated with high cost in the second year. In all four disease duration groups, patients in the high disease activity group (>66th percentile) for VAS disease activity and VAS general well-being had significantly more chance to have high direct costs (>66th percentile) in the next year than patients with a low disease activity. In the <2 yrs disease duration group, no other associations were found. In the other three disease duration groups, high Thompson joints score, worse QoL and worse functional disability were all significantly associated with high costs. High ESR was associated with high costs in the 6–10 yrs and the >10 yrs disease duration group. Demographic characteristics were not associated with high costs in any disease duration group.

In multivariate regression analyses, VAS general well-being predicted high direct costs (OR 4.0, 95% CI 1.3–12.2) in the <2 yrs disease duration group. In the 2–6 yrs disease duration group, high direct costs were predicted by worse QoL (OR 3.8, 95% CI 1.7–8.3), worse functional disability (OR 4.9, 95% CI 2.2–10.7) and younger age (OR 0.97, 95% CI 0.94–0.99). In the 6–10 yrs disease duration group, the final model included: high ESR (OR 5.9, 95% CI 1.96–17.8), worse functional disability (OR 8.8, 95% CI 2.8–27.7) and worse general well-being (OR 3.4, 95% CI 1.1–10.2). In the group of patients with the longest disease duration, the final model included: high Thompson joint score (OR 13.0, 95% CI 2.7–61.8). Also female gender was associated with high costs, but with a wide 95% CI, indicating unreliability of the odds ratio (OR).

Labour force participation

At time of the first assessment, 294 patients were of working age (<65 yrs). The change of working status during follow-up is shown in Table 3. Of the 97 patients working at time of the first assessment without work disability, 12 (12%) patients became (partially) work disabled during follow-up. Twenty-three patients were partially work disabled and were (part-time) working in 1999. In this group of patients, two patients (9%) became fully work disabled in the second year and one patient was working again without a disability pension. Nine patients who were employed and four patients who were working part-time and were partially work disabled were on prolonged sick leave (>2 weeks) at the first assessment. Of these patients, six became (fully) work disabled during follow-up. Five of these six patients had a disease duration of <2 yrs at time of the first assessment.

During the first assessment, 31 patients of working age reported that they wanted to change their working conditions because of RA. One of these 31 patients who was partially working and partial work disabled in the first year became fully work disabled in the second year and one patient who was on prolonged sick leave in the first year became also (partial) work disabled in the second year. One patient stopped working to take care of her children. No changes in working status were observed among the other 28 patients wanting to change their working conditions at the first assessment. Of the 31 patients, 11 patients (34%) had actually changed their working conditions in the second year of evaluation. However, these changes were only partially in the

TABLE 1. Patient characteristics measured in 1999 and in 2000 for four groups of patients with increasing disease duration

	<2 yrs $n=73$			2–6 yrs $n=214$			6–10 yrs $n=114$			>10 yrs $n=60$		
	m1	m2	*P*	m1	m2	*P*	m1	m2	*P*	m1	m2	*P*
Patient characteristics												
Age, yrs	54 ± 14			58 ± 13			61 ± 13			60 ± 11		
Gender, % female	77			73			62			78		
Disease duration, yrs	0.9 ± 0.6			4.0 ± 1.2			7.7 ± 1.1			19 ± 8.0		
ESR, mm/hr[1st]	28 ± 23	21 ± 18	0.002	17 ± 13	19 ± 22	0.131	22 ± 18	20 ± 17	0.239	28 ± 18	31 ± 22	0.284
Thompson joint score	67 ± 109	28 ± 54	<0.01	35 ± 63	32 ± 61	0.616	41 ± 68	34 ± 56	0.186	54 ± 78	41 ± 52	0.212
VAS disease activity, mm	33 ± 24	31 ± 23	0.202	38 ± 25	40 ± 24	0.126	40 ± 26	42 ± 25	0.731	49 ± 22	50 ± 20	0.903
VAS pain, mm	24 ± 27	19 ± 23	0.037	21 ± 24	22 ± 24	0.274	25 ± 26	22 ± 25	0.044	38 ± 28	31 ± 26	0.111
VAS general well being, mm	34 ± 30	24 ± 24	0	30 ± 25	31 ± 23	0.976	33 ± 25	31 ± 24	0.227	43 ± 26	38 ± 26	0.378
Morning stiffness, min	32 ± 48	24 ± 41	0.111	26 ± 41	30 ± 48	0.164	36 ± 55	33 ± 55	0.288	53 ± 50	47 ± 49	0.448
Functional disability, HAQ	1.1 ± 0.7	0.9 ± 0.7	0.021	1.0 ± 0.7	1.1 ± 0.7	0.009	1.2 ± 0.8	1.1 ± 0.8	0.731	1.5 ± 0.7	1.6 ± 0.7	0.1
QoL, EuroQoL	0.62 ± 0.3	0.72 ± 0.2	0.001	0,66 ± 0.2	0.66 ± 0.2	0.88	0.67 ± 0.2	0.65 ± 0.3	0.22	0.52 ± 0.3	0.60 ± 0.2	0.042
Mean (median) costs per category												
Admissions to the hospital/rehabilitation center	1240 (0)	353 (0)		891 (0)	371 (0)		579 (0)	615 (0)		1858 (0)	898 (0)	
Contacts with health care workers	1704 (1364)	1199 (910)		1035 (520)	1117 (577)		1085 (512)	962 (481)		1365 (791)	1337 (548)	
Medication	460 (336)	870 (259)		569 (447)	758 (371)		651 (362)	978 (381)		999 (573)	2143 (561)	
Purchase of devices and/or adaptations	1102 (186)	1649 (0)		1292 (124)	621 (0)		1373 (194)	965 (0)		4140 (597)	366 (0)	
Laboratory tests	344 (316)	291 (242)		255 (242)	240 (242)		252 (242)	248 (242)		285 (275)	271 (246)	
Extra costs	540 (65)	495 (82)		345 (27)	494 (37)		497 (25)	376 (27)		559 (157)	765 (132)	
Total direct costs			**Change 95% CI**			**Change 95% CI**			**Change 95% CI**			**Change 95% CI**
Mean	5392	4857	−535	4389	3601	−787	4439	4144	−295	9204	5781	−3424
SD	10662	6759	−3017; 1473	7515	4859	−1853; 174	5139	8306	−1730; 1349	13667	6491	−6722; −468
Median	3195	2694		2264	1984		2316	1586		4279	2870	

Scores for patient characteristics are mean values ± SD or number of patients (%).
P = *P*-value to test for statistically significantly difference between clinical variables assessed in the first year (m1) and the second year (m2) of measurement.
VAS disease activity, pain and general well-being [0–100 mm = worst score].
HAQ, functional disability score [0–3 = worst score].
Quality of life, EuroQol [−0.594–1.0 = worst health status].
Total direct costs are shown as mean ± SD and median costs.
95% CI = 95% confidence interval of mean change in direct costs over 2 yrs. 95% CI was obtained after bootstrapping.

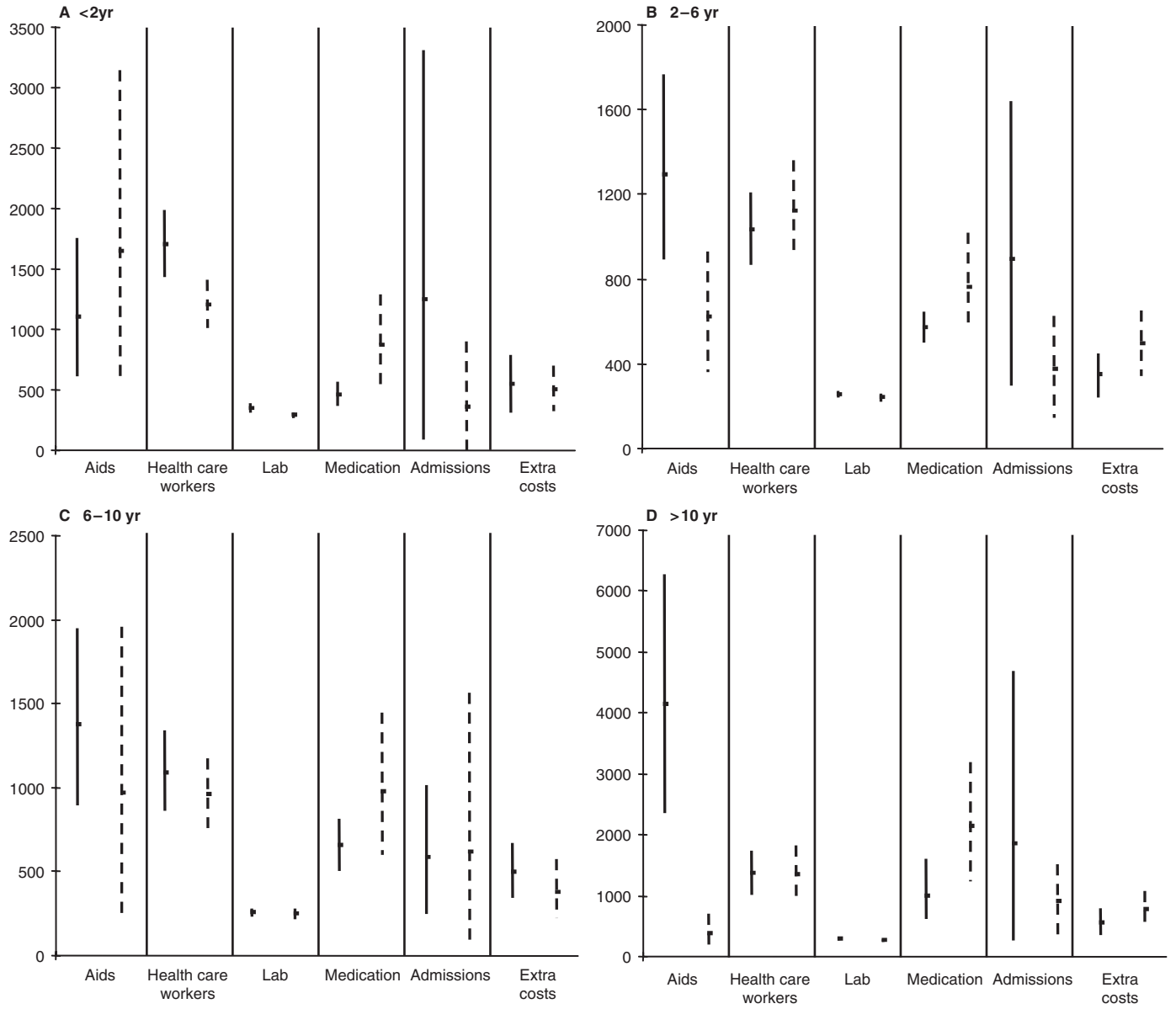

FIG. 1. (**A–D**) Mean (95% CI) costs in Euro's per cost category for each disease duration group estimated in the first year (solid line) and in the second year (dotted line) of the study. 95% confidence intervals were obtained after bootstrapping.

TABLE 2. Results of univariate logistic regression analyses to determine the prognostic value of demographic and disease activity variables at start of the second year for high costs *vs* low costs in the second year

	<2 yrs		2–6 yrs		6–10 yrs		>10 yrs	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.98 (0.95–1.02)	0.347	0.98 (0.96–1.00)	0.076	1.01 (0.98–1.04)	0.471	0.96 (0.91–1.01)	0.082
Gender	0.94 (0.30–2.94)	0.917	1.31 (0.68–2.51)	0.426	1.59 (0.70–3.60)	0.271	–	–
VAS disease activity	3.45 (1.22–9.72)	0.019	3.86 (2.09–7.15)	<0.01	5.41 (2.29–12.8)	<0.01	5.81 (1.78–19.0)	0.004
ESR	2.12 (0.77–5.83)	0.148	1.22 (0.66–2.23)	0.527	4.69 (2.02–10.9)	<0.01	4.43 (1.36–14.4)	0.013
Morning stiffness	1.37 (0.49–3.81)	0.552	2.33 (1.19–4.59)	0.014	1.58 (0.66–3.77)	0.307	1.29 (0.39–4.25)	0.680
VAS pain	1.47 (0.54–4.01)	0.456	2.49 (1.37–4.53)	0.003	4.10 (1.76–9.52)	0.001	2.16 (0.70–6.62)	0.179
VAS general well-being	3.51 (1.23–10.0)	0.019	2.07 (1.15–3.56)	0.016	3.52 (1.54–8.06)	0.003	3.44 (1.09–10.9)	0.035
Thompson joint score	1.87 (0.67–5.25)	0.236	2.16 (1.20–3.89)	0.011	3.98 (1.74–9.13)	0.001	8.76 (2.56–29.9)	0.001
QoL	2.43 (0.86–6.89)	0.095	5.60 (2.97–10.6)	<0.01	3.33 (1.45–7.65)	0.005	9.44 (1.91–46.7)	0.006
HAQ	2.16 (0.77–6.05)	0.142	6.13 (3.21–11.7)	<0.01	7.48 (2.94–19.1)	<0.01	8.22 (2.40–28.2)	0.001

OR = odds ratio.
95% CI = 95% confidence interval for odds ratio.
Results show the odds ratios = the ratio of probability that a person has high costs to the probability that a person has low costs. The cut-off point for high *vs* low costs was the 66th percentile within each disease duration group.
In the analyses, age was entered as a continuous variable and all disease activity variables were entered as dichotomized variables (high *vs* low disease activity, cut-off point was the 66th percentile within each disease duration group).

TABLE 3. Change in working status among 294 patients of working age in 1999 (<65 yrs) during two subsequent years

First year → Second year ↓	Working $n=97$	Working and disability $n=23$	Disability $n=74$	Other $n=100$
Working	77 (80%)	1 (4%)	0 (0%)	1 (1%)
Working and disability	4 (4%)	18 (78%)	0 (0%)	0 (0%)
Disability	8 (8%)	2 (9%)	72 (97%)	0 (0%)
Other	8 (8%)	2 (9%)	2 (3%)	99 (99%)

desired direction as reported the first time. In contrast, 15 patients did not report to desire a change in their working condition in the first year, but a change in working environment had nevertheless been made in the second year.

Household activities

There were no significant differences in mean (± SD) number of hours paid or unpaid help for household activities between the two assessments for any of the four disease duration groups, respectively: <2 yrs group (3.3 ± 5.9 *vs.* 3.6 ± 6.5), 2–6 yrs group (4.0 ± 6.7 *vs* 4.5 ± 7.2), 6–10 yrs group (4.3 ± 10.6 *vs* 4.6 ± 9.1), >10 yrs group (5.9 ± 8.0 *vs* 5.6 ± 7.3). The following variables measured at the beginning of the second year were associated with the need for (un)paid help for household activities: younger age (OR 0.97, 95% CI = 0.95–0.99), female gender (OR 4.26, 95% CI = 2.43–7.44), worse health status (OR 4.96, 95% CI = 1.11–220.1) and worse functional ability (OR 8.03, 95% CI 4.74–13.62).

Discussion

In this follow-up study we focused on a possible change in direct costs over 2 yrs, working status and disease activity for four disease duration groups with increasing disease duration among patients with RA. Disease activity remained stable over the 2 yrs for those patients with a disease duration over 2 yrs, whereas most variables of disease activity decreased significantly in the <2 yrs disease duration group. The mean scores in the early disease duration group assessed during the second year were very similar to the disease activity as observed in the 2–6 yrs disease duration group. Although the total costs decreased in the <2 yrs group, which was also observed in another study among early RA patients [10], the costs observed in the second year of evaluation were still somewhat higher than those observed in the first year of the 2–6 yrs group. In the <2 yrs group, part of the patients had been treated according to a protocolized intensive treatment strategy comprising monthly visits with methotrexate as anchor drugs; thereafter rheumatologists could treat their patients according to their own expertise. In this group, the costs for contacts with health care workers decreased, and medication costs increased and became very similar to those calculated in the 2–6 yrs group. Whereas the purchase of devices and adaptations increased (albeit not statistically significant) in the <2 yrs group, these costs decreased in the other three disease duration groups. This decrease was mainly due to the decrease in number of patients acquiring small aids/adaptations (e.g. orthopaedic shoes, taps). In general, the number of patients with large adaptations (e.g. kitchen, car) was higher in the second year for the 6–10 yrs group but lower in the >10 yrs group when compared with the first year. A few patients mentioned a similar large adaptation in both 1999 and 2000. Since we think that it is very unlikely that the same large adaptation was obtained twice, the costs for an adaptation reported twice was only included in the calculation for costs during the first year. Large adaptations that were reported at both assessments a year apart were an electric wheelchair (one patient), a normal wheelchair (one patient) and an automatic car (one patient). In addition, less small aids were reported during the second year, which might be explained by a systematic error in the first year (e.g. patients tended to list all previously obtained items). These observations argue in general to be cautious when obtaining data on items like purchase of devices and extra costs retrospectively over a 1-yr period. Preferably, costs for aids and adaptations should be reported as soon as possible in diaries at time of purchase leading to less bias in data collection. We further found that the percentage contribution of medication became higher with follow-up time because more patients started to use biological agents as already observed in a previous follow-up study [20]. Long-term follow-up studies are necessary to see whether this increase of medication costs will further be accompanied by a reduction in other RA-related costs and in the risk of work disability.

We determined univariate associations between high disease activity at the beginning of the second year and high costs during the second year. The patient perspective of disease activity measured by the VAS for disease activity and for general well-being was associated with high costs in all four disease duration groups. Interestingly high ESR, an objective measurement of inflammation, was associated with high costs in only the 6–10 yrs and the >10 yrs disease duration group but not in the earlier disease duration groups. In the multivariate regression analyses, functional disability and general well-being were associated with high costs in two of the four disease duration groups. Although the results of the regression analyses must be interpreted with caution because of large 95% CIs, the results are similar to those found in a Canadian study [21]. In that study, global well-being, pain, functional disability and previous costs were the most important predictors of short term direct medical costs.

In 1-yr time, twelve patients (12%) who were working in 1999 became (partially) work disabled in the subsequent year. This again indicates that work disability is a serious economic outcome in RA and that the percentage work disability cumulates with increasing disease duration. Of these 12 patients, six were on prolonged sick leave in 1999 but six were not. In the Netherlands, persons who are on sick leave for 1 yr can apply for a work disability pension. This was, however, not always the case in our study although for four out of six patients who did not report a sick leave period, the period between the first and the second assessment was slightly more than 1 yr. In our study as well as in a German study [22], patients who reported high number of days on sick leave became work disabled during the first years of the disease.

This study has several drawbacks, first with respect to the retrospective data. Patients had to report whether they had purchased any aids or devices during the last year. For contacts with health care workers, we extrapolated the reported contacts during the last three months to annual values. For further cost-of-illness studies, we would recommend to use diaries which have to be filled out for example once every three months in a prospective way. Second, disease activity was measured at time of filling out the questionnaire; this might not have been a general representation of the disease activity during the past year during which the costs had been generated. Third, patients who did not fill out the economic questionnaire twice had significantly longer disease duration, worse functional disability and a higher Thompson joint score. Probably these patients might have had higher direct costs because of their severity of their disease compared with the population included in the present study. Thus, total direct costs may have been slightly underestimated in this study.

In conclusion, changes in costs were especially observed in the <2 yrs group and the >10 yrs group. In general, verification of costs, especially those for devices and adaptations and for extra expenditures, would improve the reliability of data obtained retrospectively by questionnaires. The percentage contribution of medication costs becomes higher because of the increased use of biological agents. If this is further accompanied by a reduction in other RA-related costs and of the risk of work disability in the

future has to be awaited. In addition, special attention is necessary for those patients who are vulnerable to become work disabled due to high disease activity in an early stage of their disease.

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