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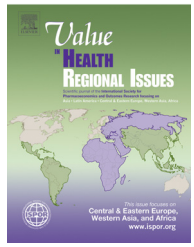

Medical and Productivity Costs of Rheumatoid Arthritis in The Czech Republic: Cost-of-Illness Study Based on Disease Severity

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ABSTRACT

Objective: International pharmacoeconomic studies suggest that functional impairment can be a significant predictor for the evaluation of direct and productivity costs for rheumatoid arthritis (RA). We calculated the direct and productivity costs for five Health Assessment Questionnaire (HAQ) groups of patients (HAQ scores <0.6, $0.6 \geq 1.1$, $1.1 \geq 1.6$, $1.6 \geq 2.1$, and ≥ 2.1) in the Czech Republic. **Methods:** This was a retrospective cross-sectional study. We included 261 patients with RA, aged 18 to 84 years. We applied a bottom-up method by retrospectively reviewing individual patient medical records. Patients' demographic characteristics, patient-reported outcome, and clinical parameters were gathered at the time of data collection. For the calculation of productivity costs, we used the friction cost approach, based on patient absenteeism with a friction period of 130 workdays, with average monthly income used as the denominator. Costs were expressed as a mean value per patient with RA in each HAQ group. **Results:** Mean patient age was 56.4 years. average time from diagnosis was 14.5 years, the mean HAQ score was 1.15, and the Disease Activity Score in 28 joints was 3.45. A total of 47.5% patients were treated with biologics. Mean annual direct medical costs for each HAQ group were €5315, €7357, €7697, €7716, and €8968, respectively. The mean annual indirect costs associated with productivity loss were €1414, €1459, €1610, €1876, and €2307, respectively. **Conclusions:** Direct costs and productivity costs for patients with RA are closely related to the value of the HAQ score. The annual mean total (direct plus productivity) costs per patient 1) treated with biologics, 2) without biologic treatment, and 3) from the overall cohort were €14,763, €3,559, and €8,882, respectively.

Keywords: cost-of-illness, health economics, quality of life, rheumatoid arthritis.

Introduction

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease associated with gradual destruction of bone and articular structures and loss of function and sometimes requires joint replacements, all of which can result in significantly reduced quality of life and premature death. RA affects 0.7% to 1.0% of the adult population [1–3], and it represents a substantial cost to both public health insurance and societal resources, making it a significant economic issue [4–6].

The results of international pharmacoeconomic studies suggest that functional impairment measured by the Health Assessment Questionnaire (HAQ) is an important predictor of direct costs (health care–related or medical) as well as indirect costs (related to loss of work productivity) [7–9].

The HAQ is a specific questionnaire or instrument used to measure the quality of life of patients with RA that is straightforward and easy to complete. Therefore, the HAQ is one of the most widely used questionnaires for patients with RA [10]. For the purpose of this study, we used the Czech version of the HAQ, which was validated in 2010 [11].

In contrast to Western European countries, there have been few published studies in central and eastern European countries describing costs (direct and productivity) in relation to patient functional impairment and disease status (severity) for the diagnosis of RA [12,13]. These cost studies are crucial for understanding the burden of the disease, which should be of particular importance to policymakers, and simultaneously offer the presteps for cost-effectiveness modeling of RA, which are usually based on health states relative to disease severity/functional impairment (i.e., HAQ states).

Methods

We performed a bottom-up cross-sectional cost-of-illness study [14] retrospectively reviewing individual medical records of

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Conflict of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

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2212-1099$36.00 – see front matter

http://dx.doi.org/10.1016/j.vhri.2014.07.004

patients undergoing treatment for RA at the center for treatment of rheumatic diseases in the Czech Republic (Institute of Rheumatology, Prague, which is the biggest and the most specialized center for the treatment of RA in the Czech Republic). Patients consecutively coming for regularly scheduled outpatient visits in turn of the year 2012 and 2013 were evaluated. According to the study protocol, 50 patients (±10) in each of five HAQ categories were intended to be included, summing up to approximately 250 patients in the whole study.

Demographic data (including the date when RA was first diagnosed, employment status, and work disability) and clinical and patient-reported outcomes were reported by participating physicians. Functional impairment (HAQ scores) data were obtained from patients after completing the HAQ, representing time 0 month of the study. These data were gathered at time 0 month (i.e., time of data collection) together with data for all resources used during the previous 6 or 12 months (the 12-month period refers to biologic treatment only). All resources used and cost data were annualized. Hence, the value of patients' HAQ score was attributed to health and productivity resources and costs of the previous year. Patients were divided into five categories on the basis of HAQ scores measured at time 0 month: 1) <0.6, 2) $0.6 \geq 1.1$, 3) $1.1 \geq 1.6$, 4) $1.6 \geq 2.1$, and 5) ≥ 2.1.

For the data recording, we used an online electronic case report form to ensure availability of all data required.

Resource Utilization and Use

The direct cost analysis was based on records of all resources drawn upon from the public health insurance fund for a particular patient. Only resources directly related to RA were recorded; for example, only medicines and outpatient and inpatient visits directly related to the diagnosis of RA were considered to be relevant for our study. The decision of which resources to include/exclude related to RA was taken by the attending physicians, that is, staff rheumatologists at the clinic.

We also recorded resources use (health care utilization) of treatment. Detailed data for each of several drug groups (anti–tumor necrosis factors, other biologics, disease-modifying antirheumatic drugs, corticosteroids, nonsteroidal anti-inflammatory drugs, etc.), including dosing, treatment pattern, and duration of therapy, were registered; the data also included all changes in treatment. The recall period for all medicines was 12 months to prevent a possible bias that can happen with shorter recall periods, which cannot capture medication changes or discontinuation or changes in dosing schemes.

Apart from medicines, other recorded resources were outpatient visits related to RA (such as the number of office visits), physical therapy, imaging techniques (X-ray, magnetic resonance imaging, sonography, etc.), surgery and inpatient hospital stays related to RA, and spa procedures. Except for spa procedures, all mentioned health care data were obtained with a recall period of 6 months; spa procedures had a recall period of 12 months. Items that were recorded for the previous 6 months were multiplied by 2 (annualized).

Cost Valuation

Costs were calculated for a full year in Czech crowns (CZK) and then adjusted for inflation using the Eurostat's Harmonised Index of Consumer Prices to obtain costs in 2013 CZK. Costs were then converted to the euro using the mean exchange rate for 2013 (€1 = 25.74 CZK; source: Czech National Bank). For 2013, we used the average Harmonised Index of Consumer Prices and the exchange rate valid for the first 10 months in 2013.

According to resource use, monetary values were subsequently assigned. For medicines, we used the official list of reimbursed medicines established by the State Institute of Drug Control (effective November 2013). With regard to health care procedures including inpatient and outpatient visits, the prices were assigned on the basis of "Public Note of the Czech Ministry of Health no. 134/1998, Coll. of Acts," health care procedure list (amended by later regulations), and "Public Note of the Czech Ministry of Health no. 396/2010, Coll. of Acts" for the determination of point values.

Only resources and costs reimbursed from public insurance were relevant; patient co-payments and out-of-pocket expenses were not included in the study.

Productivity Costs

With regard to the indirect costs of RA, we focused on productivity costs (i.e., costs associated with lost productivity). We used the friction cost approach [15], which is recommended by the Czech Pharmacoeconomic Association [16]. This method assumes that patients—both with disabilities and prematurely deceased—will be replaced in their job positions. Work productivity loss is then calculated as the maximum time necessary to recover full work productivity for a given job position. This time is referred to as the *friction period*, and costs to society are assumed to be equal to zero after this period ends. The friction period also includes the time necessary for training or initiating a new worker [16–18].

The duration of the friction period varies widely in the published literature. The duration often fails to reflect the local characteristics of health care and social systems and rarely takes the unemployment rate into consideration [15–17,19]. In particular, frictional unemployment should be of great interest.

We used a friction period of 6 months, that is, 130 workdays, which was based on recommendations of the Czech Pharmacoeconomic Association [16]. The costs related to work productivity loss were accordingly calculated using this period as the maximum time. We used the mean gross salary in the Czech Republic for 2013 as the denominator in our calculations [20], which we converted to euros (€45.4 per workday).

The calculation of productivity costs included patients of productive or potentially productive age (18–64 years). Unemployed patients, retired pensioners, and students were not included. We included days spent on sick leave (up to a maximum equal to the friction period) and the period of time spent on full disability pension or partial disability pension (again, up to a maximum equal to the friction period). The information about the productivity impairment was obtained by physicians on the basis of their inquiry with patients at time 0 month, simultaneously with the HAQ score determination. Patients were questioned in terms of work/employment status, disability, and number of days on sick leave in the previous 6 months.

The definition of "patient disability pension" was derived from Czech law (Amendment of the Act no. 306/2008, Coll. of Acts, on pension insurance). *Full disability pension* was defined as work productivity reduced by 70% and *partial disability pension* as work productivity reduced by 52%.

Statistical Analysis

Descriptive statistics are presented as means ± standard deviations, and medians. The differences between groups were tested by using the nonparametric Mann-Whitney test (two groups' nominal data), the chi-square test (proportions of patients in groups), and the Kruskal-Wallis test (more than two groups' nominal data comparison). Test results were considered statistically significant at $P \leq 0.05$. Potential predictors of both direct and overall costs were assessed by linear regression analyses on log-transformed costs. The logarithmic transformation for costs was

Table 1 – Demographic characteristics and clinical parameters of the sample.

Demographic characteristic	All patients (N = 261, 100%)		Without biologics (n = 137, 52.5%)		With biologics (n = 124, 47.5%)		P
Age (y)*	56.38 ± 13.8	60	58.85 ± 12.9	61	53.64 ± 14.2	56	0.005†
Patients younger than 64 y	173 (66.3)		82 (59.9)		91 (73.4)		0.021‡
Women	220 (84.3)		137 (82.5)		124 (86.3)		0.398
Full-time work	78 (29.9)		44 (56.4)		34 (43.6)		0.408
Students	4 (1.5)		0 (0.0)		4 (100.0)		0.034‡
Old-age pensioners	87 (33.3)		48 (55.2)		39 (44.8)		0.54
Fully disabled patients§	58 (22.2)		9 (15.3)		17 (29.8)		0.005†
Partially disabled patients§	57 (21.8)		10 (18.2)		15 (25.8)		0.14
Information on disease							
RA duration (y)*	14.5 ± 10.2	14.0	13.6 ± 11.6	11.0	15.5 ± 8.4	15.0	0.002†
HAQ score*	1.15 ± 0.81	1.12	1.12 ± 1.00	0.88	1.18 ± 1.17	0.74	0.314
DAS28 score*	3.45 ± 1.52	3.53	3.35 ± 1.56	3.06	3.56 ± 1.48	3.43	0.099‖

DAS28, Disease Activity Score in 28 joints; HAQ, Health Assessment Questionnaire; RA, rheumatoid arthritis.
* Data are presented in the following format: mean ± SD, median, or number (%).
† Statistical significance at the 0.01 level.
‡ Statistical significance at the 0.05 level.
§ Only for patients younger than 64 y.
‖ Statistical significance at the 0.10 level.

selected because of skewed cost data; moreover, age revealed nonlinear shape (reverse U-shape) and that is why we also included squared age (age^2), which allows more precise assessment of costs in relation to age. Statistical analyses were performed using the STATA 11.2 package (StataCorp, College Station, TX).

Results

Demography, Employment Status, and Clinical Parameters

Data were collected from consecutive patients coming for regular outpatient visits to generate approximately the same size of groups (~50 patients) according to their HAQ score. Altogether, 261 patients were included in the analysis. Table 1 presents the demographic characteristics of a sample for the whole cohort of patients, for the subgroup of patients treated with biologics, and for the subgroup without biologics (plus the comparison between the two groups). Mean patient age was 56.4 years. Most patients had a long history of the disease—the mean RA duration was 14.5 years. The cohort had 84% women. The mean value of the HAQ score and the RA Disease Activity Score in 28 joints, for the studied population, was 1.15 and 3.45, respectively.

A total of 29.9% of the patients were fully employed and 33.3% were already receiving old-age pensions (some of these patients were disabled before retirement). A total of 22.2% of the patients younger than 64 years were already receiving a full disability pension and 21.8% were receiving a partial disability pension.

Overall, 52.5% of the patients were treated with biologic agents. Patients treated with biological drugs were younger ($P = 0.005$) and, at the same time, more disabled in terms of full disability ($P = 0.005$). Moreover, they had slightly longer disease durations ($P = 0.065$) and a higher proportion were students ($P = 0.034$).

Table 2 presents all the characteristics of the sample grouped by the HAQ score: 1) <0.6, 2) 0.6 ≥ 1.1, 3) 1.1 ≥ 1.6, 4) 1.6 ≥ 2.1, and 5) ≥2.1. Each group of patients had a significantly higher mean Disease Activity Score in 28 joints (ranging from 2.64 to 4.41) and longer times since diagnosis (ranging from 15.1 to 22.9 years), with $P < 0.001$ for both; age was not statistically different among groups and neither was the proportion of women. Fewer

Table 2 – Characteristics of the cohort by HAQ scores.

Parameter	Patient groups by HAQ scores					P
	<0.6	0.6–<1.1	1.1–<1.6	1.6–<2.1	≥2.1	
No. of patients	69	54	58	38	42	
Mean HAQ score	0.15	0.81	1.27	1.84	2.42	0.000*
Mean DAS28 value	2.43	3.21	3.56	4.20	4.60	0.000*
Mean age (y)	52.9	54.6	57.3	60.0	59.8	0.065†
Proportion of women, n (%)	55 (79.7)	42 (77.8)	51 (87.93)	34 (89.5)	38 (90.4)	0.250
Time from diagnosis	11.0	12.5	14.9	16.7	20.0	0.000*
Full employment, n (%)						
Yes	38 (55.1)	18 (33.3)	16 (27.5)	6 (15.8)	0 (0.0)	0.000*
Student	2 (2.89)	2 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)	0.321
Old-age pensioner	16 (23.2)	19 (35.2)	25 (43.1)	15 (39.5)	12 (33.3)	0.144

DAS28, Disease Activity Score in 28 joints; HAQ, Health Assessment Questionnaire.
* Statistical significance at the 0.01 level.
† Statistical significance at the 0.10 level.

Table 3 – Resource use and mean direct and productivity annual costs (€) per patient by HAQ score.

Utilization	Resource by HAQ score										Annual costs per patient by HAQ score (€)					P
	<0.6		0.6–<1.1		1.1–<1.6		1.6–<2.1		≥2.1		<0.6	0.6–<1.1	1.1–<1.6	1.6–<2.1	≥2.1	
DMARDs*	93%		87%		79%		79%		83%		474	437	396	373	522	0.519
Corticoids*	39%		56%		62%		74%		83%		11	20	24	29	47	0.000†
Biologic agents*	38%		52%		57%		50%		43%		4071	6080	6278	6243	4418	0.086‡
NSAIDs*	62%		44%		78%		68%		64%		29	18	32	21	26	0.037§
Total for drugs											4585	6554	6729	6666	5013	0.383
RA-associated hospital stays‖	1%	1/15	2%	1/1	5%	3/7.7	8%	3/7.3	40%	17/33.2	36	31	65	176	2330	0.000†
Rheumatologist, no. of visits	100%	2.5	100%	2.6	100%	2.3	100%	2.4	98%	2.5	211	221	200	209	202	0.695
Other specialists, no. of visits	65%	2.6	76%	2.8	79%	2.6	89%	2.5	83%	3.7	186	228	205	247	350	0.083‡
Physiotherapy, no. of procedures	4%	2.7	11%	4.5	16%	1.8	13%	4.2	12%	20.3	5	11	20	13	16	0.335
Spa therapy, no. of weeks	3%	4.0	4%	3.8	7%	3.2	8%	3.8	10%	3.5	51	65	98	138	146	0.574
X-ray	78%	2.0	81%	2.0	86%	2.0	82%	2.2	86%	4.4	98	110	112	124	246	0.012§
MRI	4%	1.0	0%	–	9%	1.0	8%	1.0	12%	2.0	40	0	80	73	221	0.122
Ultrasound	38%	1.8	26%	1.8	24%	1.3	26%	1.6	33%	1.7	67	46	31	42	57	0.324
Other¶	12%	–	11%	–	16%		13%	–	33%	–	7	7	9	12	49	0.015§
Surgery including inpatient stay	6%	–	6%	–	9%	–	3%	–	14%	–	29	84	148	15	338	0.265
Total direct costs											5315	7357	7697	7716	8968	0.014§
Sick leave, mean no. of days#	12%	15	9%	21	10%	17	16%	35	0%	–	78	89	68	250	0	0.181
Full disability pension#	4%	–	17%	–	21%	–	32%	–	52%	–	179	688	854	1303	2161	0.000†
Partial disability pension#	38%	–	22%	–	22%	–	11%	–	5%	–	1157	682	688	323	146	0.000†
Total productivity costs											1414	1459	1610	1876	2307	0.000†
Total costs											6730	8816	9307	9591	11274	0.014§

Resource use: First column in the respective HAQ group refers to the proportion of patients who consume the resource. Second column refers to the average number of units for patients who consume the particular resource. *P* is related to costs and tests whether the mean value is equal among all five groups.

CT, computed tomography; DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; RA, rheumatoid arthritis.

* Percentage of patients who used a certain drug.

† Statistical significance at the 0.01 level.

‡ Statistical significance at the 0.10 level.

§ Statistical significance at the 0.05 level.

‖ Average no. of hospital stays in the previous 12 mo/average no. of days in the previous 12 mo.

¶ Other means densitometry, CT, arthrography of the knee.

Only for patients younger than 64 y.

Table 4 – Unit costs in 2013 €.

Health care	Unit	Cost
Hospitalization	1 d	167
Rheumatologist	1 visit	85
Other specialist	1 visit	100
Rehabilitation	1 visit	8
Spa	1 wk	438
X-ray	1 examination	70
MRI	1 examination	928
Sonography	1 examination	100

MRI, magnetic resonance imaging.

people were employed among those with higher HAQ scores ($P < 0.001$). This was driven by two factors: 1) by increasing severity of disease and its disabling nature and 2) by increasing age, as patients drew closer to the natural retirement age.

Health Resource Use and Direct Medical Costs

Table 3 presents a detailed description of use of all health resources (resource consumption) for each of the HAQ groups, representing annualized data (12 months). In addition, we provide unit costs for some of the most frequently items used in the calculations (apart from drugs) (see Table 4).

With increasing disease severity (defined by increasing HAQ scores), there was clearly a higher probability of RA-associated hospital stays; for example, 40% of the patients with HAQ scores of 2.1 or more were hospitalized, on average, 2.44 times with an average stay of 33.8 days. Patients visited the rheumatologist, on average, about 2.5 times per year. Outpatient visits to other specialists (apart from rheumatologists, e.g., cardiologist, ophthalmologist, etc.) were seen in greatest numbers (on average 3.7 times per year) for patients with HAQ scores of 2.1 or more. Also, X-rays were most often associated with patients with HAQ scores of 2.1 or more.

Annual costs per patient for particular HAQ groups are also presented in Table 3. From the total sum of direct costs, expenditures for drugs represent the greatest amount, except for the HAQ group of the most severe patients for whom the greatest driver of costs was RA-associated hospital stays (representing 26% of all direct costs). Overall, drug expenditures did not differ significantly among HAQ score groups ($P = 0.383$).

The costs associated with biological therapy (biologic agents) represented 88% to 94% of the total mean costs for drugs per patient per year; in terms of the total direct costs, biological therapy represented 49% to 83%. Yet, the cost of biological therapy does not differ among groups ($P = 0.086$). However, we can see that the costs of corticoids, nonsteroidal anti-inflammatory drugs, RA-associated hospital stays, X-rays, full disability pensions, and partial disability pensions were statistically different among HAQ groups.

We also provided an analysis of a subgroup of patients without consumption of biologic agents. Table 5 presents a direct cost analysis of these patients. Total direct costs for these patients were substantially lower than for the whole patient cohort mainly because of the extremely low costs for drugs, which represented 50%, 40%, 34%, 37%, and 15% of total direct costs, respectively, for each HAQ group: 1) <0.6, 2) 0.6 ≥ 1.1, 3) 1.1 ≥ 1.6, 4) 1.6 ≥ 2.1, 5) ≥2.1. There was no difference in the average cost for pharmacotherapy associated with increasing HAQ scores ($P = 0.63$); however, there was a rapid increase in costs for hospital stays associated with RA ($P = 0.000$) and X-rays ($P = 0.004$). For patients with HAQ scores of 2.1 or more, RA-associated hospital stays represented almost 26% of the total direct cost of the group. There was a mild increase in total direct costs with increasing HAQ score, with an extreme jump in these costs for patients with HAQ scores of 2.1 or more (nonetheless, the groups' costs still differed significantly; $P = 0.001$).

Productivity Impairment and Productivity Costs

Table 3 presents productivity impairment and productivity costs for each HAQ group. The number of days on sick leave (short-term

Table 5 – Mean annual costs (€) per patient by HAQ score in the Czech Republic: Patients without consumption of biologic agents.

Cost (in 2013 €)	Patient groups by HAQ scores					P
	<0.6	0.6–<1.1	1.1–<1.6	1.6–<2.1	≥2.1	
DMARDs	766	579	603	582	643	0.576
Corticoids	14	26	34	38	58	0.001*
NSAIDs	26	9	13	17	20	0.088†
Total for drugs	806	615	651	637	720	0.630
RA-associated hospital stays	76	62	144	159	2156	0.000*
Rheumatologist	207	211	203	231	214	0.982
Other specialist(s)	173	178	131	186	367	0.068†
Physiotherapy	10	22	45	23	23	0.183
Spa treatment	106	130	219	250	204	0.742
X-ray	134	145	157	127	299	0.004*
MRI	28	0	107	88	278	0.237
Ultrasound	18	26	15	29	40	0.436
Other‡	10	10	13	11	57	0.282
Surgery + hospital stays	53	149	203	0	387	0.199
Total	1621	1547	1889	1740	4747	0.001

CT, computed tomography; DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; RA, rheumatoid arthritis.

* Statistical significance at the 0.01 level.

† Statistical significance at the 0.10 level.

‡ Other means densitometry, CT, arthrography of the knee.

Table 6 – Overall annual costs per patient (in 2013 €).

Cost	All patients		Patients without biological treatment		Patients with biological treatment		P
Direct costs	7,204 ± 6,068	5,811	2,255 ± 2,536	1,447	12,673 ± 3,645	12,926	0.0000*
Productivity costs	1,678 ± 1,895	0	1,304 ± 1,830	0	2,090 ± 1,888	3,070	0.0004*
Total costs	8,882 ± 6,710	8,162	3,559 ± 3,347	3,004	14,763 ± 4,044	14,433	0.0000*

Note. Data are presented in the following format: mean ± SD, median.
* Statistical significance at the 0.01 level.

absenteeism due to hospital stays, relapses, other problems leading to absence from paid work) was relatively small and trended downward with higher HAQ scores. This phenomenon can be accounted for by the difference in working status associated with higher HAQ scores; that is, patients with HAQ scores of more than 2.1 had zero days of sick leave because none was fully employed. The proportion of those receiving a disability pension increased with higher HAQ scores.

Overall, there were 58 (22.2%) patients on a full disability pension (aged 64 years or younger) and 57 patients (21.8%) were on a partial disability pension (aged 64 years or younger); more details are presented in Tables 1, 2, and 3. At the same time, it was possible to show that patients from our study groups were more than five times more likely to be disabled (5.4 times) compared with the general population (aged 20–64 years) in the Czech Republic [21]. Total mean productivity costs per patient increased with increasing HAQ scores ($P < 0.001$).

Overall Costs

The last row of Table 3 provides the total costs by HAQ group; the costs, as expected, increased with the HAQ score and were statistically different ($P = 0.014$). Table 6 presents the total mean annual cost per patient with RA that had to be covered by health care payers (i.e., direct costs) and the cost related to work productivity loss (i.e., productivity costs). In addition, we compared the cost of patients with and without biological treatment; as expected, direct, productivity, and total costs were significantly higher ($P < 0.001$) in patients with biological treatment of RA. Figure 1 shows the overall and breakdown mean annual costs per patient according to functional impairment.

Cost Predictors

To determine cost predictors (only direct and total costs because productivity costs were equal to zero in 135 of 261 cases), we performed a linear regression analysis using log-transformed costs as the dependent variable. HAQ, time from diagnosis, age and age^2, sex, and an indicator of biologic treatment were used as independent variables. The results in Table 7 present that the HAQ score ($P < 0.001$), age^2 ($P = 0.013$), biological treatment ($P < 0.001$), and years since diagnosis ($P = 0.001$) were significant predictors of overall costs. Interestingly, costs increased with age but from the age of 67.8 years costs started to decrease; that is, costs exhibited a reverse U shape and for this reason we included age^2 as a potential predictor. When analyzing direct costs, HAQ scores and biological treatment were statistically significant ($P < 0.001$ for both) as well as years since diagnosis ($P = 0.002$). To conclude, a patient on biological treatment had 4.28 times the total costs and 6.44 times the direct costs of a patient without this treatment while controlling for other variables (age, sex, time since diagnosis, etc.). Moreover, an increase in the HAQ score by 1 increased direct costs by 29% and total costs by 32%; each additional year of disease duration led to a mean increase of 13% in both direct and total costs.

Discussion

This article provides a description of the care and resource consumption for patients with RA grouped according to their HAQ scores (functional impairment) in the Czech Republic. The costs were divided into health care costs and costs attributed to productivity loss. Possible limitations of this cost-of-illness study were that out-of-pocket expenditures and productivity lost by families and/or friends (informal caregivers) relative to other societal costs of RA were not included.

In terms of direct (medical) costs, we found HAQ scores and treatment with biologics to be significant predictors. Although these costs are poorly predicted by age, they can be reliably

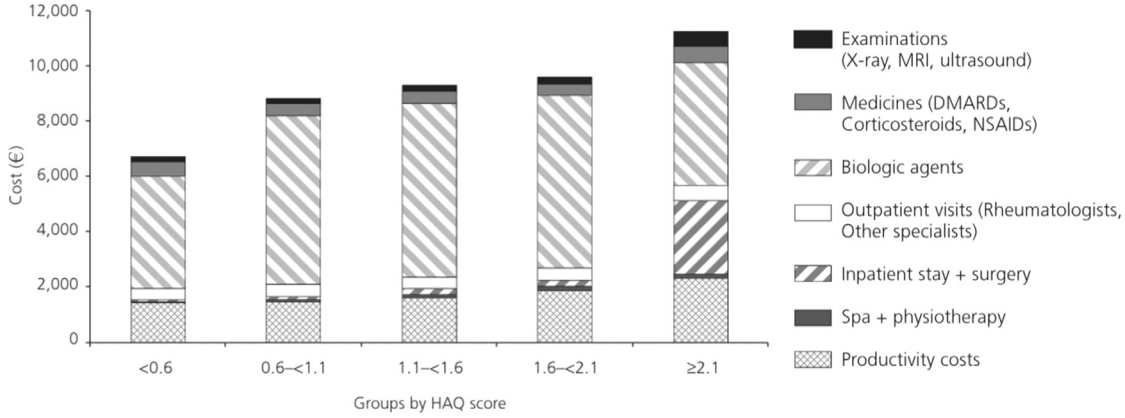

Fig. 1 – Overall and breakdown mean annual costs per patient according to functional impairment (HAQ category). DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 7 – Cost predictors, results of the linear regression models.

Parameter	ln direct costs		ln total costs	
	Coefficient	SE	Coefficient	SE
HAQ score	0.256*	0.057	0.279*	0.054
Female	−1.214	0.103	0.026	0.116
Age	−0.005	0.003	0.0346†	0.020
Age^2			−0.0005*	0.000
Biologics	2.008*	0.070	1.665*	0.075
Years from diagnosis	0.126*	0.004	0.136*	0.004
Constant	10.502*	0.190	10.192*	0.528
R^2	0.781		0.713	
Robust errors	Yes		Yes	
N	261		261	

HAQ, Health Assessment Questionnaire; ln, natural log; SE, standard error.
* Statistical significance at the 0.01 level.
† Statistical significance at the 0.10 level.

predicted by the amount of time since diagnoses. In terms of overall costs, we found that HAQ scores, treatment with biologics, age, and age^2 (all led to increasing cost) should be taken into account when predicting the extent of these costs.

Moreover, we found that productivity costs were significantly higher for patients with higher HAQ scores (Table 3). Within our study, productivity costs represented 18.9% of the total costs (whole cohort study group), with 36.6% in patients without biologic treatment and 14.2% in patients on biological agents (Table 6). These percentages are lower compared with findings in some articles that describe the percentage of productivity costs to be up to 75% of total costs [5,6]. This difference was mainly linked to the methodology we used, because we calculated productivity costs according to the friction cost approach, which produces different results than does the human capital approach. From the societal perspective, we find the friction cost approach to be a more suitable approach for describing productivity loss from a macroeconomic point of view compared with the human capital approach, which tends to focus on the microeconomic perspective [16].

One limitation of our productivity costs calculation was that only absenteeism was studied (short- and long-term absenteeism and early retirement expressed as a full or partial disability pension); no presenteeism was assessed. There is still, however, a lot of debate on how to describe productivity loss in monetary values [22].

Next, an issue that should be stressed in our study is that costs directly related to RA were included, with the exception of osteoarthritis. It was almost impossible to distinguish whether resources consumed should be attributed only to RA or to its directly related comorbidity, osteoarthritis. Even though there are other comorbidities that are prevalent in those with RA, for example, metabolic syndrome [23,24], costs associated with the treatment of cardiovascular diseases and other comorbidities were not included.

In conclusion, the results from our study provided useful inputs into health-economic modeling of cost-effectiveness within the diagnosis of RA, particularly in the Czech Republic.

Source of financial support: This work was supported by Ministry of Health of Czech Republic (grant no. 000 000 23728) and the Charles University, Prague, Czech Republic (grant no. SVV 260 066).

REFERENCES

[1] Pedersen JK, Svendsen AJ, Hørslev-Petersen K. Prevalence of rheumatoid arthritis in the southern part of Denmark. Open Rheumatol J 2011;5:91–7.
[2] Neovius M, Simard JF, Askling J. Nationwide prevalence of rheumatoid arthritis and penetration of disease-modifying drugs in Sweden. Ann Rheum Dis 2011;70:624–9.
[3] Capkin E, Cakirbay H, Karkucak, et al. Prevalence of rheumatoid arthritis in the eastern Black Sea region of Turkey. Int J Rheum Dis 2010;13:380–4.
[4] Bergman MJ. Social and economic impact of inflamantory arthritis. Postgrad Med Spec 2006:(Spec No: 5–11).
[5] Huscher D, Merkesdal S, Thiele K, et al. Cost of illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systematic lupus erythematosus in Germany. Ann Rheum Dis 2006;65:1175–83.
[6] Rat AC, Boissier MC. Rheumatoid arthritis: direct and indirect costs. Joint Bone Spine 2004;71:518–24.
[7] Kobelt G, Woronoff AS, Richard B, et al. Disease status, costs and quality of life of patients with rheumatoid arthritis in France: the ECO-PR Study 2008. Joint Bone Spine 2008;75:408–415.
[8] Kobelt G. Health economic issues in rheumatoid arthritis. Scand J Rheumatol 2006;35:415–25.
[9] Poulakka K, Kautiainen H, Möttönent T, et al. Use of the Standard Health Assessment Questionnaire in estimation of long-term productivity costs in patients with recent-onset rheumatoid arthritis. Scand J Rheumatol 2009;38:96–103.
[10] Russell AS. Quality-of-life assessment in rheumatoid arthritis. Pharmacoeconomics 2008;26:831–46.
[11] Šlégrová O, Dušek L, Olejárová M, et al. Assessment of functional ability in patients with rheumatoid arthritis: validation of the Czech version of the Stanford Health Assessment Questionnaire (HAQ) [in Czech]. Čes Revmatol 2010;18:73–83.
[12] Kaczor MP, Wójcik R. An economic analysis of TNF-α antagonists for rheumatoid arthritis in Polish settings. Reumatologia 2007;45:268–75.
[13] Péntek M, Poór G, Wiland P, et al. Biological therapy in inflammatory rheumatic diseases: issues in Central and Eastern European countries. Eur J Health Econ 2014;15(Suppl. 1):S35–43.
[14] Larg A, Moss JR. Cost-of-illness studies: a guide to critical evaluation. Pharmacoeconomics 2011;29:653–71.
[15] Brouwer WB, Koopmanschap MA. The friction-cost method: replacement for nothing and leisure for free? Pharmacoeconomics 2005;23:105–11.
[16] Czech Pharmacoeconomic Association. The Guideline of the Czech Pharmacoeconomic Association for pharmacoeconomic evaluation in the Czech Republic [in Czech]. Available from: http://www.farmakoe-konomika.cz/vyzkum_161.htm. 2008, updated 2011. [Accessed July 29, 2014].
[17] Verstappen SM, Boonen A, Verkleij H, et al. Productivity costs among patients with rheumatoid arthritis: the influence of methods and sources to value loss of productivity. Ann Rheum Dis 2005;64:1754–60.
[18] Van Asselt AD, Dirksen CD, Arntz A, Severens JL. Difficulties in calculating productivity costs: work disability associated with borderline personality disorder. Value Health 2008;11:637–44.
[19] Xie F. The need for standardization: a literature review of indirect costs of rheumatoid arthritis and osteoarthritis. Arthritis Rheum 2008;59:1027–33.
[20] Czech Statistical Office. Labour and Earnings; c2012. Available from: http://www.czso.cz/eng/redakce.nsf/i/labour_and_earnings_ekon. [Accessed July 29, 2014].
[21] Czech Social Security Administration. Annual report 2009. Available from: http://www.cssz.cz/en/information. [Accessed January 30, 2014].
[22] Loeppke R, Hymel PA, Lofland JH, et al. Health-related work place productivity measurement: general and migraine specific recommendations from the ACOEM expert panel. J Occup Environ Med 2003;45:349–59.
[23] Peters MJ, Symmons DP, Mccarey D, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 2010;69:325–31.
[24] Pham T, Gossec L, Constantin A, et al. Cardiovascular risk and rheumatoid arthritis: clinical practice guidelines based on published evidence and expert opinion. Joint Bone Spine 2006;73:379–87.