VALUE IN HEALTH 14 (2011) 192–200

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Using HAQ-DI to estimate HUI-3 and EQ-5D utility values for patients with rheumatoid arthritis in Spain

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Keywords:
Rheumatoid arthritis
Quality of life
Health status
Utility assessment

ABSTRACT

Background/Objective: Utility values are not usually assessed in clinical trials and do not allow cost-utility analysis to be performed with the data collected. The aim of this study was to derive relation functions so that Health Assessment Questionnaire – Disability Index (HAQ-DI) scores could be used to estimate Health Utilities Index - 3 (HUI-3) and EQ-5D utility values for patients with rheumatoid arthritis (RA).

Methods: An observational, cross-sectional, naturalistic, multicentre study was conducted. A total of 244 patients aged 18 years or older, with RA according to American College of Rheumatology diagnostic criteria, were recruited. Sociodemographic and clinical variables were recorded and patients completed three generic HRQoL questionnaires: the HAQ-DI, the HUI-3, and the EQ-5D. Two linear regression models were used to predict HUI-3 and EQ-5D utility values as functions of HAQ-DI scores, age, and gender.

Results: Patient mean age was 57.8 years old (standard deviation [SD], 13.3 years); 75.8% of the patients were women and 95.9% were white. Mean disease duration was 10.8 years (SD, 9 years). Patient distribution according to HAQ-DI severity was as follows: HAQ-DI $<$ 0.5, 29%; 0.5 $\leqq$ HAQ-DI $<$ 1.1, 28%; 1.1 $\leqq$ HAQ-DI $<$ 1.6, 16%,1.6 $\leqq$ HAQ-DI $<$ 2.1, 15%; and HAQ-DI $\geqq$ 2.1, 12%. HAQ-DI and EQ-5D mean scores were 1.02 (SD, 0.78) and 63.1 (SD, 20.3), respectively. Mean utility values for HUI-3 and time trade-off (TTO) were 0.75 (SD, 0.21) and 0.65 (SD, 0.3), respectively. The equations converting HAQ-DI scores to utilities were HUI-3 = 0.9527 – (0.2018 $\times$ HAQ-DI) $+\varepsilon$ (R^2=0.56), and TTO = 0.9567 – (0.309 $\times$ HAQ-DI) + ε (R^2=0.54). Error distribution was non-normal. Age and gender were found to have no bearing on the utility functions.

Conclusions: HAQ-DI scores can be used to estimate HUI-3 and EQ-5D utility values for patients with RA in data obtained from studies where utility values have not been collected.

Funding: This research was sponsored by Roche Pharma. However, the analysis was performed independently by the authors.

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1098-3015/$36.00 – see front matter

doi:10.1016/j.jval.2010.11.001

Introduction

Musculoskeletal diseases are the most frequent cause of incapacity in the world. The long-term care required by patients with these diseases is included among the most costly diseases to treat [1]. The cost of care correlates directly to increasing functional incapacity [2,3]. Rheumatoid arthritis (RA) is a chronic progressive disease characterized by inflammation and joint destruction; it limits patient mobility, causes functional deterioration, affects health-related quality of life (HRQoL), and increases morbidity and mortality [4]. Prevalence varies geographically, ranging from 0.45% in the south of Europe to 0.65% in the north and center of Europe and the United States [5].

Some treatments aim to slow down disease progression but a majority of therapies claim to alleviate symptoms such inflammation, pain, stiffness, swollen joints, and fatigue [5]. HRQoL measures reflect a subjective evaluation of the following key dimensions: the physical dimension (pain and deterioration of physical functioning), the psychological dimension (anxiety and depression), the intellectual or cognitive dimension (attention and memory), and the social dimension (self-esteem and interpersonal relationships) [6].

The economic impact of RA and corresponding treatments, due to limited health-care resources and increased pressure to use these resources efficiently, is of growing concern. The cost effectiveness of new treatments must be compared to already available alternatives. In order to assess treatment effectiveness, the use of quality-adjusted lifeyears (QALYs) incorporates measures of both quantity and quality of life, and obtains a utility value associated with each health state. Utility values correspond to perfect or full health state (corresponding to a value of (1) and death (0) as well as collecting values of health states worse than death. A utility value indicates the weight that general population or patients with a specific disease gives to a specific health state. In chronic and progressive diseases with negative impact on HRQoL, such as RA, the use of cost-utility analysis in economical evaluations facilitates the global assessment of disease progression and the associated impact on HRQoL.

The use of QALYs to evaluate benefits, in terms of health, is widely used and is recommended by agencies for the assessment of health technologies such as the National Institute for Health and Clinical Excellence (NICE) [7]. Utility values can be assessed using direct methods (e.g., time trade-off [TTO] or standard gamble [SG]) or indirect methods based on preference or utility values assigned to health states defined by generic HRQoL questionnaires (the EQ-5D and Health Utilities Index – 3 [HUI-3]). The use of direct methods is the best way to obtain utility values in any population, including RA patients [8]. Nevertheless, due to resource restrictions, patients' burden and complexity of these methods, direct methods are not usually included in clinical trials. The Health Assessment Questionnaire Disability Index (HAQ-DI), developed to assess difficulty performing day-to-day activities, is widely used in clinical research and in conditions of standard clinical practice by patients with RA [9]. Linking HAQ-DI scores to utility values enables the prediction of health state utility values for cost per QALY analysis in cases where no preference-based measure has been included in the study. This will aid cost-utility analysis (one possible method of economic evaluation) using data obtained from clinical trials and other clinical studies.

Studies have been performed in other countries to relate HAQ-DI scores to utility that is measured by RA patient-completed HRQoL questionnaires [10,11]. Utility values measured by generic questionnaires should be obtained at the country level due to social and cultural variability. In a preference study performed to compare EQ-5D utility values based on TTO method between the United Kingdom and Spain, it was shown that UK raters ascribed greater importance to dimensions of pain/discomfort and anxiety/depression, whereas Spanish raters placed more importance on functional dimensions of mobility and self-care [12]. A recent study examined the effects of differences in national EQ-5D value sets on absolute and marginal utilities of health states [13]. It was reported that differences between the EQ-5D value sets were too great to be ignored. It was further reported that some differences could reflect cultural dissimilarities between countries and that transferring utility values from one country to another without any adjustment was not advisable. Differences between utility functions between countries should also be reflected in the corresponding relation function with other HRQoL questionnaires.

The aim of this study was to obtain a relation function between HAQ-DI scores and HUI-3 and EQ-5D questionnaire utility values in a sample of Spanish patients, and compare the obtained function with those obtained in previous studies performed in other countries.

Methods

Study design

An observational, cross-sectional, naturalistic, multicenter national study was conducted. The investigators who participated in the study were rheumatology specialists working in outpatient clinics in hospitals in Spain. A total of 14 specialists (based in outpatient clinics) recruited patients over a 2-month period. Patients were included consecutively. Because the study was cross-sectional, patients made a single visit to provide the necessary information. Physicians recorded sociodemographic and clinical data, and administered the questionnaires included in the case report form to the patients. In order to obtain the minimum acceptable number of patients for each level of RA severity, each physician was required to include at least one patient per level: $0 \leq$ HAQ-DI < 0.5 (level 1); $0.5 \leq$ HAQ-DI < 1.1 (level 2); $1.1 \leq$ HAQ-DI < 1.6 (level 3); $1.6 \leq$ HAQ-DI < 2.1 (level 4); $2.1 \leq$ HAQ-DI < 2.6 (level 5); and HAQ-DI ≥ 2.6 (level 6). The study was approved by the ethical committee of the hospital Virgen de la Macarena (Seville) and all the included patients were informed of the study characteristics, their right not to participate in the study, and their right to withdraw from the study at any time. All patients signed an informed consent to indicate their willingness to participate in the study.

Table 1 – Values for the multi-attribute utility function of the Spanish version of the HUI-3 simplified best PH-PITS scales.

Vision		Hearing		Speech		Ambulation		Dexterity		Emotion		Cognition		Pain	
A_1	b_1	A_2	b_2	A_3	b_3	A_4	b_4	A_5	b_5	A_6	b_6	A_7	b_7	A_8	b_8
1	1.00	1	1.00	1	1.00	1	1.00	1	1.00	1	1.00	1	1.00	1	1.00
2	0.99	2	0.95	2	0.96	2	0.94	2	0.95	2	0.99	2	0.91	2	0.95
3	0.92	3	0.87	3	0.89	3	0.86	3	0.86	3	0.74	3	0.95	3	0.89
4	0.85	4	0.80	4	0.78	4	0.73	4	0.74	4	0.56	4	0.80	4	0.77
5	0.74	5	0.72	5	0.62	5	0.62	5	0.62	5	0.35	5	0.69	5	0.64
6	0.62	6	0.59			6	0.52	6	0.49			6	0.62		

Source: Ruiz M et al.[16]
Utility function: $U_{HUI3} = (1.0078 \times b_1 \times b_2 \times b_3 \times b_4 \times b_5 \times b_6 \times b_7 \times b_8) - 0.0078$.
HUI-3, Health Utilities Index - 3; PH-PITS, possible-worst possible health.

Evaluation criteria

Patients were included if they fulfilled all the inclusion criteria: adult diagnosed with RA as per the diagnostic criteria of the American College of Rheumatology [14] and signed the informed consent form. Patients were excluded if they met any exclusion criteria: a diagnosis of other rheumatic or degenerative diseases, participation in a clinical trial, or the inability to read and understand the questionnaires.

Study variables

The information collected in the study was grouped into two categories:

- Sociodemographic variables (age, gender, ethnic origins, level of education, and occupational status) and clinical variables (date of diagnosis, number of surgical interventions, number of joints affected, family history of the disease, concomitant diseases, and previous and current treatments received for RA).
- HRQoL and health state variables: HRQoL data and health state preference information were compiled in order to assess the status of patients with RA.
  - HAQ-DI: The HAQ-DI is a self-completed questionnaire to assess the extent of the RA patient's functional ability that assesses outcomes in patients with a wide variety of rheumatic diseases, including RA. The HAQ-DI contains 20 items distributed across eight dimensions (dress and groom, arise, eat, walk, reach, grip, maintain hygiene, and maintain daily activity). Each item is scored on a scale from 0 to 3 (reflecting no difficulty to disability). Some additional points are added to the sum of the corresponding items to calculate the dimension scores. For example, if the patient needs assistance from another person or uses adapted tools, this is regarded as reflecting a higher disability level [9]. For each dimension a disability score from 0 to 3 is obtained. HAQ-DI scores were categorized in order to reflect the disease activity level: HAQ-DI < 0.5 (level 1); $0.5 \leq$ HAQ-DI < 1.1 (level 2); $1.1 \leq$ HAQ-DI < 1.6 (level 3); $1.6 \leq$ HAQ-DI < 2.1 (level 4); $2.1 \leq$ HAQ-DI < 2.6 (level 5); and HAQ-DI ≥ 2.6 (level 6).
  - HUI-3: The HUI-3 questionnaire is composed of eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain). Each attribute has either five or six response levels, reflecting normality to severe deterioration. The attributes and levels combined describe 972,000 health states that can be transformed into a measure of preference or utility for the population [15]. Utility measurement instruments reflect patient preferences for each health state by means of a single score that summarizes, on a scale from 0 to 1, the subject's health state and the population's preference for this state. Scoring of the HUI-3 Spanish version questionnaire was based on the utility function and values depicted in Table 1 [16].
  - The EQ-5D questionnaire is a standardized, generic instrument for describing and valuing health [17]. The EQ-5D questionnaire consists of a five-dimensional descriptive system and a visual analogue scale (EQ VAS). The descriptive system defines health in terms of five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension is divided into three levels, indicating no problem (coded as 1), some or moderate problems (coded as 2), or extreme problems (coded as 3). Combinations of these levels define a total of 243 health states. A health state defined by the descriptive EQ-5D system can be described by a five-digit number, each digit indicating the score of the corresponding dimension. The EQ VAS asks respondents to rate their perception of their overall health on a vertical visual analogue scale with "best imaginable health state" set at 100 and "worst imaginable health state" set at 0. Utility values corresponding to each EQ-5D health state were obtained in different countries using TTO method based on general population valuations [18]. Scoring in the Spanish version of the EQ-5D questionnaire was based on the utility function and values depicted in Table 2 [19].

Statistical analysis

SAS version 9.1 for Windows (Chicago, IL, USA) was used to analyze the data. A statistical significance of 0.05 was applied to all the tests performed. Results were categorized according to RA disease activity level that was measured by the HAQ-DI.

Table 2 – Coefficients and function for calculating the TTO index for the EQ-5D.

EQ-5D variables		EQ-5D utility values
Constant	—	−0.0399
Mobility (MOB)	2 (some problems)	−0.0957
	3 (many problems)	−0.4230
Self-care (SCR)	2 (some problems)	−0.1341
	3 (many problems)	−0.3114
Daily activities (ACT)	2 (some problems)	−0.0775
	3 (many problems)	−0.2017
Pain/discomfort (PND)	2 (some problems)	−0.0830
	3 (many problems)	−0.2560
Anxiety/depression (AND)	2 (some problems)	−0.0506
	3 (many problems)	−0.1358
Presence of 3 in state (ST3)	—	−0.2855

Source: Badia X, et al.[19]
EQ-5D (utility function) = $1 - 0.0399 + MOB_{TTO} + SCR_{TTO} + ACT_{TTO} + PND_{TTO} + AND_{TTO} + ST3_{TTO}$.
TTO, time trade-off.

A descriptive and comparative analysis of sociodemographic characteristics and HRQoL, assessed using the EQ-5D and the HUI-3 questionnaires, was performed according to the disability level assessed using the HAQ-DI. EQ-5D results were analyzed by taking into account the percentage of patients with problems (scores of 2 or 3) and the EQ VAS. The chi-square test was used for comparisons of categorical variables between groups that were homogenous in terms of degree of severity. Continuous variables were compared using the analysis of variance (ANOVA) test or using non-parametric techniques if normality criteria were not satisfied.

The relationships between HAQ-DI and utility values defined using the HUI-3 and EQ-5D questionnaires were obtained using two linear regression models, including utility values as dependent or explained variables and HAQ-DI scores, and age and gender as independent or explanatory variables. The Shapiro-Wilks test was used to test the normal distribution of residuals for both equations.

Results

Sociodemographic and clinical characteristics

The final study sample consisted of 247 patients with RA, three were considered ineligible for the analysis due to the failure to record HAQ-DI scores and 244 patients were considered to be evaluable. The mean age of patients was 57.8 years old (SD, 13.3), 75.8% were women, and 95.9% were white. In terms of education level, 46.7% had only primary education, 27.5% secondary, and 16.4% had completed a third level education. One-third of the patients were active, one-third were homemakers, and 20.9% were retired (Table 3).

Mean HAQ-DI score for the included patients was 1.02 points (SD, 0.78 points), which corresponds to a moderate degree of disability. In order to make category sizes more homogeneous, the two categories with the highest HAQ-DI scores were grouped together, resulting in a patient distribution according to HAQ-DI score as follows: 29% in Level 1, 28% in Level 2, 16% in Level 3, 15% in Level 4, and 12% in Levels 5-6.

The mean age at diagnosis of patients in the study was approximately 47 years, resulting in an average disease evolution of approximately 11 years. At the time of the patient's visit with the physician, the mean number of affected joints was 4 (SD, 4.7). A total of 14.8% of the patients had a family history of RA, 20.1% had been treated surgically for their disease (arthroplasty, 48%; synovectomy, 16%; and orthopedic surgery, 16%), and 52.9% had concomitant diseases (19.3%, endocrine or metabolic diseases). Only 25% of the patients had received treatment with anti-tumor necrosis factor (anti-TNF) agents prior to their current treatment (infliximab and etanercept, 57.4% and 41.0%, respectively). A total of 98.8% patients in the sample were receiving drugs or other therapy when they visited the rheumatologist (methotrexate, 56.4%; prednisone, 31.5%; leflunomide, 24.5%; deflazacort, 17.4%; etanercept, 17.0%; and infliximab, 6.6%).

HRQoL and health state

The mean EQ VAS score was 63.1 points (SD, 20.3 points) on a scale of 0 to 100, with statistically significant differences according to disability based on HAQ-DI ($P < 0.001$). Patients with lower HRQoL suffered from greater levels of disability. By dimension, 80.4% of the patients had pain or discomfort (maximum score in 12.3% of cases), 53.2% had difficulty performing daily activities, 44.2% had mobility problems, 39.6% experienced anxiety or depression, and 35.3% had problems with self-care. Figure 1 presents this information by degree of severity. The reported levels of problems for all EQ-5D dimensions increased according to the level of RA severity. Statistically significant differences were seen for all dimensions ($P < 0.01$). Major differences according to the level of RA severity were observed in all physical dimensions (mobility, self-care, and usual activities), and was collected by the HAQ-DI.

When the perceived health status for all five dimensions of the EQ-5D were combined and analyzed, only 14.5% of patients with RA in the study stated that they had no problems in any questionnaire dimension (health state 11111). No patient with an HAQ-DI score of 2.1 or more reported this health state.

The mean HUI-3 utility score was 0.75 points (SD, 0.21 points), with statistically significant differences between groups according to HAQ-DI ($P < 0.001$), with utility values decreasing as disability increased (Table 4). The mean utility values based on the EQ-5D questionnaire were 0.65 (SD, 0.3); utility values varied significantly in accordance with RA severity, which was measured by the HAQ-DI ($P < 0.001$).

Both approaches (HUI-3 and the EQ-5D utilities) showed the same decreasing trend for utility values with respect to increasing degrees of severity. This resulted in similar values for each HAQ-DI category. The scatterplots reflecting each utility measure with respect to the HAQ-DI confirm the existence of a relationship between pairs of variables (Figs. 2 and 3).

Table 3 – Patient sociodemographic variables according to severity of rheumatoid arthritis assessed by the HAQ-DI.

	HAQ-DI < 0.5		0.5 ≤ HAQ-DI < 1.1		1.1 ≤ HAQ-DI < 1.6		1.6 ≤ HAQ-DI < 2.1		HAQ-DI ≥ 2.1		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Age (P = 0.065)												
ND	—	0.0	1	1.5	—	0.0	—	0.0	—	0.0	1	0.4
<40 years	9	12.9	8	11.8	3	7.5	2	5.4	—	0.0	22	9.0
40–49 years	15	21.4	12	17.7	9	22.5	3	8.1	4	13.8	43	17.6
50–59 years	22	31.4	19	27.9	12	30.0	10	27.0	7	24.1	70	28.7
60–69 years	17	24.3	17	25.0	8	20.0	9	24.3	5	17.2	56	23.0
≥70 years	7	10.0	11	16.2	8	20.0	13	35.1	13	44.8	52	21.3
Gender (P = 0.006)												
ND	—	0.0	1	1.5	—	0.0	1	2.7	—	0.0	2	0.8
Female	45	64.3	48	70.6	37	92.5	31	83.8	24	82.8	185	75.8
Male	25	35.7	19	27.9	3	7.5	5	13.5	5	17.2	57	23.4
Ethnic origin (P = 0.169)												
ND	—	0.0	1	1.5	—	0.0	—	0.0	—	0.0	1	0.4
White	70	100	62	91.2	39	97.5	36	97.3	27	93.1	234	95.9
Latin American	—	0.0	5	7.4	1	2.5	1	2.7	2	6.9	9	3.7
Education (P = 0.246)												
UNK/NR	1	1.4	1	1.5	—	0.0	—	0.0	—	0.0	2	0.8
None	2	2.9	6	8.8	2	5.0	5	13.5	6	20.7	21	8.6
Primary	30	42.9	30	44.1	24	60.0	16	43.2	14	48.3	114	46.7
Secondary	20	28.6	20	29.4	11	27.5	10	27.0	6	20.7	67	27.5
Third level	17	24.3	11	16.2	3	7.5	6	16.2	3	10.3	40	16.4
Occupational status (P = 0.001)												
UNK/NR	—	0.0	1	1.5	—	0.0	—	0.0	—	0.0	1	0.4
Unemployed	—	0.0	1	1.5	—	0.0	—	0.0	2	6.9	3	1.2
Homemaker	16	22.9	22	32.4	18	45.0	11	29.7	9	31.0	76	31.2
Retired	13	18.6	14	20.6	4	10.0	11	29.7	9	31.0	51	20.9
Active	36	51.4	21	30.9	15	37.5	9	24.3	1	3.5	82	33.6
Sick leave	—	0.0	1	1.5	1	2.5	—	0.0	1	3.5	3	1.2
Disability	4	5.7	8	11.8	1	2.5	6	16.2	7	24.1	26	10.7
Other	1	1.4	—	0.0	1	2.5	—	0.0	—	0.0	2	0.8
Total	70	100	68	100	40	100	37	100	29	100	244	100

HAQ, Health Assessment Questionnaire; ND, not determined; UNK/NR, unknown/no response.

In Figures 2 and 3, the relationships between the specific HAQ-DI scores and the generic HUI-3 and EQ-5D utility values were analyzed using linear regression, with utility values (HUI-3 or EQ-5D) as the dependent variables, and with HAQ-DI score and patient's age and gender as independent variables. This analysis of the relationship between HAQ-DI scores and both HUI-3 and EQ-5D utilities revealed that patient age and gender had no bearing on utility function. The Shapiro-Wilks test ruled out the possibility of a normal distribution of residuals for both equations (Table 5).

The equations to calculate utilities equivalent to the HUI-3 and EQ-5D questionnaires from HAQ-DI scores for patients with RA are as follows:

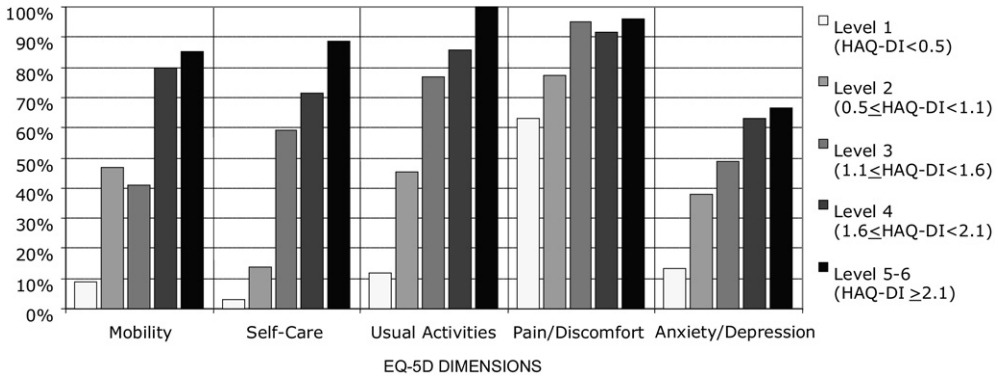

Fig. 1 – Patients with problems for each dimension in EQ-5D descriptive system according to severity of rheumatoid arthritis assessed by the Health Assessment Questionnaire Disability Index (HAQ-DI).

Table 4 – Descriptive statistics for HUI-3 and EQ-5D utility values according to severity of rheumatoid arthritis assessed by the HAQ-DI.

	HAQ-DI < 0.5	0.5 ≤ HAQ-DI < 1.1	1.1 ≤ HAQ-DI < 1.6	1.6 ≤ HAQ-DI < 2.1	HAQ-DI ≥ 2.1	Total
HUI-3 ($P < 0.001$)						
Mean	0.91	0.80	0.75	0.58	0.45	0.75
SD	0.08	0.15	0.14	0.20	0.20	0.21
Min.	0.61	0.23	0.44	0.22	0.16	0.16
Median	0.93	0.83	0.80	0.58	0.42	0.83
Max.	1.00	1.00	0.95	0.90	0.87	1.00
Valid n	62	56	31	34	23	206
EQ-5D ($P < 0.001$)						
Mean	0.87	0.74	0.62	0.42	0.17	0.65
SD	0.14	0.19	0.21	0.30	0.42	0.33
Min.	0.28	0.19	0.06	−0.24	−0.57	−0.57
Median	0.88	0.78	0.65	0.52	0.11	0.74
Max.	1.00	1.00	1.00	1.00	0.79	1.00
Valid n	68	66	39	35	27	235

HAQ-DI, Health Assessment Questionnaire Disability Index; HUI-3, Health Utilities Index Mark 3.

$$\text{HUI-3} = 0.9527 - (0.2018 \times \text{HAQ-DI}) + \varepsilon\left[\text{Adjusted } R^2 = 0.56;\ \text{Shapiro-Wilks } P < 0.001\right]$$

$$\text{EQ-5D} = 0.9567 - (0.309 \times \text{HAQ-DI}) + \varepsilon\left[\text{Adjusted } R^2 = 0.54;\ \text{Shapiro-Wilks } P < 0.001\right]$$

The model designed to estimate HUI-3 utility values obtained an R^2 of 0.56, which means that HAQ-DI is able to explain 56% of the HUI-3 scores variability. The predictive capacity of the model is similar to that obtained with EQ-5D questionnaire (R^2=0.54). Based on previous equations, utility values based on HUI-3 are obtained by multiplying HAQ-DI score by 0.2018 and subtracting the result from 0.9527.

Discussion

This study identified the relation function to use HAQ-DI scores to obtain HUI-3 and EQ-5D utility values for Spanish patients with RA, providing additional data on previous studies performed in other countries. For economical evaluation purposes the best approach is the inclusion of direct or indirect methods to obtain utility values in clinical trials. Nevertheless, due to different factors, most of the clinical trials do not include any preference measure.

In this case, relation functions enable the prediction of health state utility values at global level, for use in cost per QALY analysis when no preference-based measure has been included in the study. Due to inter-country variations, it is highly recommended that relation functions be used only in the countries in which they were derived. The relation function presented in this study reports the first functions to obtain utility values from HAQ-DI scores based on Spanish RA patients.

The sample of study patients presents a sociodemographic and clinical profile similar to that of the profile of patients included in previous studies. Compared to the EMECAR study [20], which is one of the most important and more recent RA patient studies performed in Spain, the sample of patients included in the present study is slightly younger (with a mean age 4 years younger) and with a very slightly higher proportion of women (75.8% vs. 71.3%). From a clinical point of view, both samples are comparable in terms of time of disease evolution and age at diagnosis. In terms of HAQ-DI scores, patients included in the present study report a slightly lower disability level. The 244 patients evaluated in our study had a mean

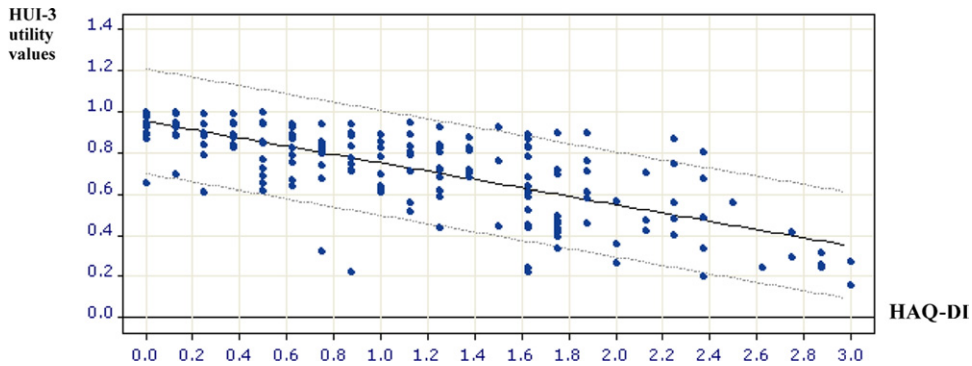

Fig. 2 – Scatter plot between Health Assessment Questionnaire Disability Index (HAQ-DI) scores and HUI-3, Health Utilities Index Mark 3 (HUI-3) utility.

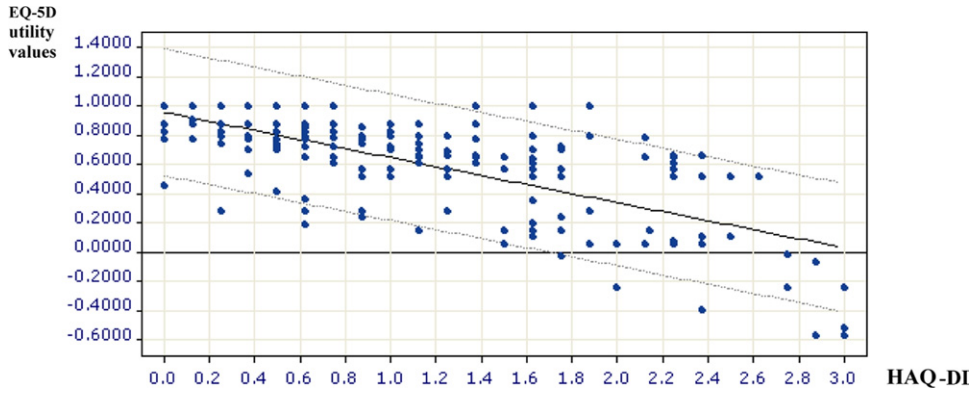

Fig. 3 – Scatterplot between Health Assessment Questionnaire Disability Index (HAQ-DI) scores and EQ-5D utility values.

HAQ-DI score of 1.02 points, whereas the EMECAR Study Group reported a mean score of 1.6 points for a sample of 788 RA patients in 2003. The difference in terms of severity scores can be attributed to differences in the patient selection methods used. The EMECAR study sample was selected from a random sample of patients with RA registered in the center at any time. According to the main study objective, the selection process was mainly focused on obtaining a minimum sample of patients covering all the HAQ-DI levels and able to respond to protocol requirements (questionnaires).

Utility values for HUI-3 and EQ-5D used in the present study to obtain HAQ-DI utility value are based on general population assessments, not on patients' assessments. Although the question about whether patient-rated utility values should be ranked higher than the general population-rated value has been discussed in several forums, it is generally accepted that economical evaluations of health interventions should be analyzed from a societal point of view. In the present study, HAQ-DI values rated by patients themselves have been used to predict utility values from a social point of view. Cost-utility analysis is based on health states assessed by the patients themselves, in order to collect self-perceived HRQoL to weight length of life. These states are generally converted to utility values evaluated from a social point of view, facilitating comparison with other health interventions that can be applicable to other conditions.

Mortimer and Segal [21] completed a systematic review of algorithms for converting descriptive measures of health status into QALY-weights. They concluded that, although the techniques used are quite different, the sensitivity and validity of derived QALY-weights could be more dependent on the coverage and sensitivity of measures and the disease area/patients' group under evaluation than on the technique used in derivation [21]. In this sense an important point to be analyzed is the validity of the EQ-5D, HUI-3, and HAQ-DI questionnaires in RA patients. Both generic preference questionnaires used in the present study (EQ-5D and HUI-3) have been widely used and validated in RA patient populations [22-24]. Based on a comparison of methods to obtain utility values, the EQ-5D showed a better association with RA outcome measures than the TTO [24]. Despite the validity of all three questionnaires in RA population, a ceiling effect affected discriminant validity of the EQ-5D and HUI-3 questionnaires and revealed the high proportion of patients with no problems in any dimensions. This ceiling effect could have had a negative impact on the adjustment obtained with the relation function to convert HAQ-DI scores to utility values, due the low variability of scores obtained in a significant group of patients. HAQ-DI is a disease-specific questionnaire widely used and accepted to be used in RA patients to assess the disability level.

Another factor to be considered to understand the relation functions obtained is the difference in dimensions or factors assessed by general HRQoL questionnaires and the HAQ-DI. HAQ-DI is a functional questionnaire and does not assess some HRQoL factors, for example, mental health or pain, which are usually included in generic questionnaires

Table 5 – Functions obtained between HAQ-DI and utility values assessed using the HUI-3 and EQ-5D.

Variable	*df*	Parameter estimate	SE	T for H0: parameter=0	Prob > |T|	95% confidence limit	
Estimators for regression function coefficients for HUI-3 = f (HAQ-DI)							
Intercept	1	0.9527	0.0159	59.92	<0.0001	0.9214	0.9841
HAQ-DI	1	−0.2018	0.0125	−16.10	<0.0001	−0.2265	−0.1771
Estimators for regression function coefficients for EQ-5D = f (HAQ-DI)							
Intercept	1	0.9567	0.0238	40.15	<0.0001	0.9098	1.0037
HAQ-DI	1	−0.3090	0.0187	−16.46	<0.0001	−0.3460	−0.2720

HAQ-DI, Health Assessment Questionnaire Disability Index; HUI-3, Health Utilities Index Mark 3; SE, standard error.

used to obtain utility values. Differences in dimensions or factors assessed by each kind of questionnaire probably have a relevant impact on goodness of fit. Nevertheless, each questionnaire was developed and validated to respond to specific objectives.

The approach used in the present study and the relation functions obtained are consistent with previous studies reported in the literature using the HUI-3 [10], and EQ-5D questionnaires [11]. An analysis of adalimumab trial data of almost 2000 patients permitted transformation from HAQ-DI to HUI-3 (HUI-3 utility = 0.76 – 0.286HAQ-DI + 0.056FEMALE), with an R^2 measure of 0.49 [10]. Despite the inclusion of gender, the R^2 obtained in the referenced study was slightly lower than that obtained in the present study (0.56). The comparison of the EQ-5D function with that reported previously is not directly due to the different methodological approaches used. Although the final HAQ-DI scores in the present study has been used to obtain the relation function, in the referenced study, the individual scores were used. The methodology used in the present study resulted in a really simple model with an acceptable R^2 (0.54), only slightly lower than that obtained in the referenced study. The added value of the utility equations calculated in our study is that they reflect cultural differences in how patients with RA self-report their health state and utility [25]. This generates more accurate estimates, given their grounding in studies with samples of patients conforming to national, cultural, and disease characteristics.

There are some limitations in the current study. First, the sample of RA patients was selected by 14 rheumatologists throughout Spain in order to obtain a more representative sample of patients. The lower disability level presented by patients, in comparison with the EMECAR study, suggests a possible bias to a healthy population of RA patients. This is probably due to the requirement to include at least one patient per each HAQ-DI level and also due to patient requirements (such as the completion of three questionnaires) in order to be included and complete the study. Second, relation functions were obtained for the total sample of patients. A separate sample of patients was not used to validate the relation functions obtained, comparing estimated with observed values. This approach was not used due to the limited number of patients included in the study. Further research about the validity and goodness of fit of the relation functions obtained would provide additional information about the capacity to estimate utility values based on HAQ-DI at the global and patient levels. Third, the study was designed to be cross-sectional in order to focus on the relationship between preference-based questionnaires and the HAQ-DI. The follow-up of the study patients and a second administration of the study questionnaires would allow analysis of the reliability of the obtained scores and the derived relation function, as well as detection of possible changes over time. This additional information derived from a prospective study has been analyzed only in some previous studies to estimate relation functions. Further research into the reliability and sensitivity to change the relation functions obtained would provide additional understanding of the strengths and weaknesses of the relation functions.

Acknowledgment

The authors acknowledge the contribution of Carlos Polanco in prior versions of this article.

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