Quantification of Reduced Health-Related Quality of Life in Patients with Rheumatoid Arthritis Compared to the General Population

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ABSTRACT. ***Objective.*** To compare levels of health-related quality of life (HRQOL) among patients with rheumatoid arthritis (RA) to those of the general population.

Methods. Disease burden was assessed using a generic health status instrument (Medical Outcome Study Short Form-36) for measurements of HRQOL and SF-6D to calculate utility scores in representative patients aged 20 to 79 years from the Oslo RA Register (n = 1052), and in individuals in the general population (n = 2323). Comparisons were performed with respect to sex and age, and standardized difference scores (s-scores) were calculated for comparisons with the norm.

Results. HRQOL in patients with RA was reduced compared to the general population on all scales of the SF-36 for both males and females and for all age groups. s-scores adjusted for age and education ranged from –1.39 for physical functioning to –0.27 for mental health. The overall difference in utility was 0.16 and ranged from 0.13 (in female patients below 50 yrs) to 0.20 (patients 50–60 years). This implies that RA of 1 year duration entails a disease burden of 14–20 quality-adjusted life-years in 100 RA patients.

Conclusion. RA inflicts a substantial disease burden, and the disease affects all HRQOL dimensions as measured by the SF-36 in both sexes and in all age groups. Physical functioning is predominantly affected, but RA has social and mental consequences. (First Release May 15 2007; J Rheumatol 2007;34:1241–7)

Key Indexing Terms:
RHEUMATOID ARTHRITIS QUALITY OF LIFE BURDEN OF DISEASE
UTILITY GENERAL POPULATION

The effect of musculoskeletal disorders on individuals and on society is expected to increase dramatically as a consequence of an aging population[1]. Rheumatoid arthritis (RA) is the most frequent inflammatory rheumatic disease, with a prevalence of 0.5–1%[2] and an annual incidence of 25–50/100,000[3], and affecting all dimensions of health-related quality of life (HRQOL)[4]. However, few studies have attempted to quantify this effect on HRQOL in representative RA patients based on sufficient sample size to explore the age- and sex-specific levels of involvement.

Even healthy individuals report some functional disability with increasing age, but less so than patients with RA[5]. Thus, the burden of disease per se is best considered in comparison with the general population. Generic health status measures, e.g., the Medical Outcome Study Short Form Survey (SF-36)[6] can be used to assess HRQOL in individuals drawn from the general population as well as in patients with a variety of diseases. Some studies have used this opportunity to compare the effect on HRQOL across different health conditions[7-9].

Economic evaluation of medical treatment is increasingly used by governments for priority setting and decisions on reimbursement of therapies. In health economics, utility is used to express the value of health states in order to value health improvement and subsequently use the valuation for priority setting. Utility is in principle measured on a cardinal scale where zero denotes death and 1 denotes perfect health[10]. This means that a health state of for example 0.7 is preferred to a health state of 0.6. It also means that if a medical treatment improves a patient's health state from 0.6 to 0.7, this improvement is 1/10 of taking a patient from dying to perfect health. The health benefits of treatments can then be expressed in terms of quality-adjusted life-years (QALY). If the improvement from 0.6 to 0.7 in utility lasts for 3 years, the health benefit would be 0.3 QALY [(0.7 – 0.6)*3 = 0.3]. Subsequently, treatments can be compared by comparing how many resources are needed for each treatment to generate one QALY. Treatments are consequently compared by estimating the cost per QALY for each of them. In principle, society would prefer to prioritize treatments with low costs per QALY

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in order to get maximum health benefits from limited budgets. The use of utilities and QALY allows the comparison of cost-effectiveness of treatments across diseases and patient groups[11].

The aim of our study was to quantify disease burden in RA by comparing SF-36 scores and utility weights by sex and age, between RA patients and the general population.

MATERIALS AND METHODS

Patients with RA. Patients with RA were recruited from the Oslo Rheumatoid Arthritis Register (ORAR)[2]. Inclusion criteria were a diagnosis of RA[12] and a residential address in Oslo (the capital city of Norway, population 0.5 million). The procedures for inclusion in the register, updates with new and deceased cases, and data collection have been described in detail[2]. Most importantly, a previous validation study demonstrated the register to be 85% complete for RA patients aged 20–79 years in the city of Oslo, thus containing representative patients with RA[2].

We used data with self-reported health status collected through a mail survey to all RA patients registered in the ORAR in 1996 [1052 respondents aged 20–79 years (response rate 75%)]. Of these patients, 39.5% were treated with disease modifying antirheumatic drugs.

Controls. Norwegian normative data for SF-36 were collected in 1996[13]. The Norwegian Government Computer Centre drew a random sample from the National Register of Norway including all Norwegian inhabitants aged 19–80 years. The sample was representative of the general population with respect to age, sex, and educational attainment. In total, 3500 individuals were sampled and contacted by mail in 1996. The data collected from 2323 individuals (response rate 66%)[14] were used in this study.

Measures. SF-36 is the most widely used generic health status measure and it has been translated into Norwegian and validated[6,15]. It is used in health surveys in the general population as well as in various populations with different diseases. The 36 items in the questionnaire are grouped into 8 multi-item subscales measuring physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, mental health, and role limitation due to emotional problems. For each subscale a score is calculated with possible values from 0 to 100, where low scores indicate poor health. The SF-36 scores correlate to a variety of disease-specific measures capturing the same dimensions of health in patients with RA[15,16]. Physical (PCS) and mental component summary scores (MCS) were aggregated from the SF-36[17]. The PCS and MCS scales are standardized to have a mean score of 50 and a SD of 10.

The utility measure (SF-6D) was derived from the responses to the SF-36 questionnaire based on an algorithm developed by Brazier, *et al*[18]. All responders to the original SF-36 questionnaire can be assigned a SF-6D score if the 11 items used in the SF-6D had been completed. The SF-6D can be regarded as a continuous outcome scored on a 0.30 to 1.00 scale, with 1.00 indicating "full health." The SF-6D is a utility or preference-based measure of HRQOL. The primary use of such measures is to adjust life-years saved by quality for use in economic evaluations and decision models by expressing outcomes in terms of QALY.

Disease duration data (years since fulfilment of the classification criteria of RA[12]) were collected from the ORAR. The level of education was measured by years of formal education on the basis of the questionnaire, and the education variable was dichotomized into low (≤ 12 yrs) and high levels (> 12 yrs) and was used in analyses as a binary variable.

Statistical methods. Descriptive statistics are presented as means with standard deviation (SD) for continuous data or as percentages for counts. Comparisons between groups were performed with chi-square tests for categorical variables and t-tests for continuous variables. Analysis of covariance was used for group comparison, adjusting for age and also for education, although the level of education had only a very limited influence on HRQOL. Disease duration had only minimal explanatory value when already adjusting for age, and was thus not kept as a covariate in the final analyses.

Standardized difference scores (s-scores) for SF-36 scales were calculated for sex and age groups as the difference between mean scores for patients and the population, divided by the SD of the same scale for the normal population[14,19]. The s-score thus gives the number of SD by which a HRQOL mean score differs from the reference population. The sizes of s-scores were interpreted after Cohen's effect size index, where the range 0.2–0.5 refers to a small difference, 0.5–0.8 to a moderate difference, and s-scores > 0.8 refer to a large difference[20].

QALY express utility over time and were calculated as differences in SF-6D utility between RA patients and population per 100 persons over 1 year.

The Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 12.0 was used for all analyses. p values ≤ 0.05 were considered significant. No correction for multiple testing was performed.

RESULTS

As expected, our RA patients were older and predominanty female compared with the general population (Table 1); their age, disease duration, education level, and gender distribution were similar to nonresponders (data not shown). Table 1 also shows that the sample of RA patients had disease characteristic data similar to those most frequently seen in cross-sectional cohorts of RA patients.

RA patients had significantly poorer ($p < 0.05$) HRQOL versus the general population for all scales of the SF-36. Age-adjusted s-scores ranged from –1.39 for the physical functioning component summary to –0.27 for the mental health component summary (Table 2). The overall differences between patients and general population were consistent for both sexes, but female patients had worse scores than males. However, similar sex differences regarding HRQOL were also seen in the general population, and the s-scores were similar for both sexes (Table 2).

The largest disease impact was seen in the physical functioning subscale, with s-scores of –2.07, –2.20, –1.55, and –0.90 in the age groups < 50, 50–60, 60–70, and 70–80 years, respectively (Table 3). The mental health subscale, the dimension with the lowest impact, also had s-scores indicating a low (–0.30 in the group < 50 years of age) to moderate impact (–0.74, –0.50, and –0.81 in the other age groups) (Table 3). The scores indicated a linear decline in HRQOL, especially in the physical dimension, with increasing age in both the general population and the RA patients (Table 3, Figure 1A). For

Table 1. Characteristics of patients with RA and the general population.

	RA, n = 1052	Population, n = 2323
Age, yrs, mean (SD)	61.3 (14.1)*	44.9 (16.5)
Females, %	79*	51
Higher education, > 12 yrs, %	27	28
Disease duration, yrs, mean (SD)	13.8 (10.8)	NA
MHAQ (range 0–3)	0.7 (0.6)	NA
Rheumatoid factor-positive, %	49	NA
Pain VAS	38 (24)	NA

* $p < 0.001$. NA: non applicable. VAS: visual analog scale score. MHAQ: modified Health Assessment Questionnaire.

Table 2. Mean (SD) SF-36 and SF-6D utility scores adjusted for age and education in RA patients and the general population with computed s-scores (difference between RA and general population scores divided by SD of population scores).

		All			Men			Women		
		N	Mean (SD)	s-score	N	Mean (SD)	s-score	N	Mean (SD)	s-score
Physical function	Population	2222	86 (23)		1079	89 (19)		1143	82 (25)	
	RA	1005	56 (23)	–1.31	211	64 (19)	–1.39	794	53 (25)	–1.15
Role–physical	Population	2193	76 (39)		1081	81 (36)		1112	75 (41)	
	RA	996	36 (40)	–1.03	208	47 (37)	–0.93	788	33 (40)	–1.04
Bodily pain	Population	2270	75 (28)		1111	78 (27)		1159	73 (29)	
	RA	1014	48 (28)	–0.96	212	56 (28)	–0.81	802	46 (28)	–0.92
General health	Population	2173	76 (25)		1069	78 (23)		1104	75 (26)	
	RA	984	48 (25)	–1.13	210	53 (24)	–1.07	774	47 (25)	–1.09
Vitality	Population	2258	60 (25)		1110	64 (22)		1148	57 (26)	
	RA	1002	44 (25)	–0.68	209	49 (23)	–0.66	794	42 (25)	–0.56
Social functioning	Population	2293	85 (28)		1122	88 (24)		1171	83 (31)	
	RA	1005	68 (28)	–0.63	212	71 (25)	–0.73	803	67 (30)	–0.50
Mental health	Population	2244	79 (21)		1105	81 (19)		1139	78 (22)	
	RA	996	71 (21)	–0.41	209	71 (19)	–0.51	878	71 (22)	–0.31
Role–emotional	Population	2169	81 (39)		1069	85 (35)		1100	77 (43)	
	RA	982	56 (40)	–0.63	203	62 (36)	–0.67	779	55 (42)	–0.52
SF-6D	Population	2062	0.803 (0.142)		1021	0.829 (0.137)		1041	0.777 (0.134)	
	RA	952	0.645 (0.135)	–1.11	199	0.675 (0.141)	–1.12	753	0.636 (0.132)	–0.98
PCS	Population	2003	51 (11)		994	52 (10)		1009	49 (12)	
	RA	936	35 (12)	–1.39	196	39 (10)	–1.30	740	34 (12)	–1.29
MCS	Population	2003	50 (12)		994	50 (11)		1009	48 (13)	
	RA	936	46 (13)	–0.27	196	46 (12)	–0.38	740	46 (13)	–0.16

All differences between patients and the general population were significant, $p < 0.001$. s-scores give the numbers of SD by which a mean score differs from the reference poulation.

Table 3. Mean (SD) age-specific SF-36 and SF-6D utility scores in patients with RA and in the general population with computed s-scores (difference between RA and general population scores divided by SD of population scores).

		< 50 Years			50–59 Years			60–69 Years			70–80 Years		
		N	Mean (SD)	s-score	N	Mean (SD)	s-score	N	Mean (SD)	s-score	N	Mean (SD)	s-score
Physical function	Population	1418	93 (13)		346	86 (17)		260	76 (21)		211	65 (26)	
	RA	219	67 (24)	–2.07	171	49 (25)	–2.20	279	43 (25)	–1.55	369	42 (27)	–0.90
Role–physical	Population	1408	93 (29)		345	78 (36)		257	61 (41)		197	45 (44)	
	RA	218	44 (40)	–1.44	169	29 (34)	–1.36	276	21 (31)	–0.95	360	18 (31)	–0.59
Bodily pain	Population	1429	79 (24)		359	74 (26)		278	66 (27)		221	64 (29)	
	RA	220	51 (23)	–1.14	171	42 (21)	–1.20	278	42 (20)	–0.90	378	39 (23)	–0.88
General health	Population	1407	81 (20)		335	74 (22)		254	65 (25)		187	65 (22)	
	RA	219	50 (24)	–1.59	168	42 (21)	–1.35	268	42 (21)	–0.93	357	41 (22)	–1.07
Vitality	Population	1430	60 (20)		354	62 (21)		274	60 (23)		212	56 (23)	
	RA	218	46 (22)	–0.68	169	42 (21)	–0.97	272	42 (21)	–0.80	374	39 (23)	–0.76
Social functioning	Population	1439	87 (21)		362	86 (23)		283	85 (22)		227	78 (27)	
	RA	220	73 (27)	–0.67	171	64 (25)	–1.00	279	64 (28)	–0.96	378	59 (31)	–0.70
Mental health	Population	1430	78 (16)		351	80 (17)		271	79 (17)		203	80 (18)	
	RA	217	73 (19)	–0.30	168	67 (22)	–0.74	270	70 (20)	–0.58	369	65 (22)	–0.81
Role–emotional	Population	1400	84 (30)		341	86 (29)		250	76 (35)		191	64 (41)	
	RA	216	66 (34)	–0.60	168	49 (40)	–1.25	268	46 (39)	–0.85	357	37 (38)	–0.66
SF-6D	Population	1359	0.819 (0.1375)		322	0.808 (0.144)		232	0.764 (0.141)		158	0.728 (0.143)	
	RA	214	0.675 (0.1424)	–1.04	166	0.610 (0.122)	–1.38	260	0.610 (0.121)	–1.09	336	0.588 (0.134)	–0.99
PCS	Population	1350	54 (8)		299	50 (10)		207	45 (12)		156	42 (12)	
	RA	213	37 (12)	–1.98	164	32 (11)	–1.77	252	30 (10)	–1.23	330	30 (11)	–1.04
MCS	Population	1350	49 (10)		299	51 (10)		207	52 (10)		156	50 (11)	
	RA	213	38 (12)*	–0.05	164	45 (13)	–0.63	252	46 (11)	–0.53	330	43 (12)	–0.64

* NS: all other comparisons between RA and population $p < 0.001$. s-scores give the numbers of SD by which a mean score differs from the reference population.

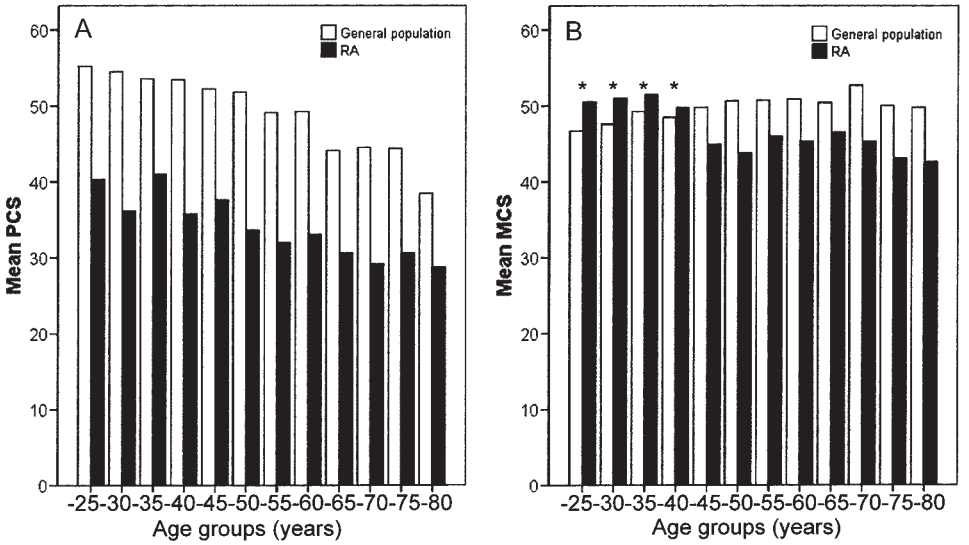

Figure 1. Age-specific physical component summary (PCS) (A) and mental component summary (MCS) scores (B) in the general population and in patients with RA (*nonsignificant; all other comparisons between RA and population $p < 0.001$). Numbers for general population/RA patients (age group): 287/9 (to 25 yrs), 236/25 (25–30), 244/32 (30–35), 217/50 (35–40), 219/53 (40–45), 188/60 (45–50), 165/70 (50–55), 112/96 (55–60), 113/118 (60–65), 95/149 (65–70), 91/181 (70–75), and 45/116 (75–80).

physical functioning, s-scores decreased with increasing age (Table 3).

RA patients had worse overall scores for physical (PCS) and mental (MCS) health across all age groups (Figure 1A, 1B). For PCS these differences were highly significant ($p < 0.001$) for all age groups, and for MCS they were statistically significant above the age of 40 years.

The difference between RA patients and the general population in mean utility as measured by SF-6D was –0.14, –0.20, –0.15, and –0.14 in the age groups < 50, 50–59, 60–69, and 70–80, respectively (Table 3), and 0.16 overall when adjusting for age and education (Table 2). The latter difference, when applied to the utility scale, expressed that 6.3 average RA patients cured of their RA (1/0.16) is equivalent to bringing one patient of similar age from death (= 0) to perfect health (= 1). Corresponding numbers for patients aged 50–69, 60–69, and 70–79 years were 5.0, 6.7, and 7.1 patients, respectively.

The differences in utility between RA and the general population were consistent across all 5-year age groups (Figure 2), and the differences in the height of the bars for RA and the general population in Figure 2 can be considered a graphic presentation of the burden of RA. Stratified to age group and sex, the loss of QALY in 100 female (male) RA patients was 13 (14) at age < 50 years, 20 (18) in the age group 50–59 years, 13 (16), in the age group 60-69 years, and 12 (13) QALY in the age group 70–80 years (data not shown).

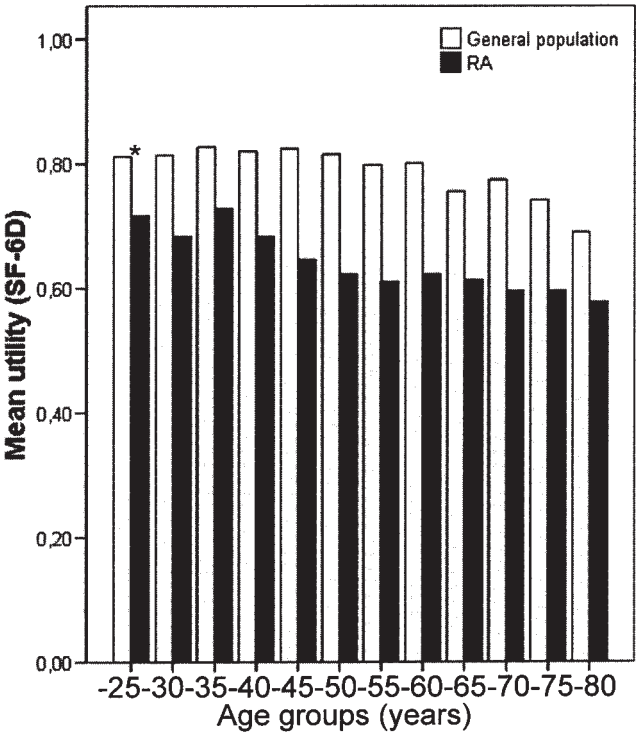

Figure 2. Utility as measured by SF-6D in the general population and in RA patients and by 5-year age groups (*$p < 0.05$; all other comparisons between RA and population $p < 0.001$). Numbers for general population/RA patients (age group): 287/9 (to 25 yrs), 232/25 (25–30), 245/32 (30–35), 222/51 (35–40), 219/54 (40–45), 196/59 (45–50), 173/69 (50–55), 130/98 (55–60), 120/120 (60–65), 112/159 (65–70), 89/179 (70–75), and 46/121 (75–80).

DISCUSSION

Our study reports a considerable disease burden of RA in terms of lowered HRQOL in patients compared to the general

population, and these differences were consistent across both sexes and in the whole age range 20–80 years.

The disease effect as measured by s-scores was high for physical functioning and low to moderate for mental health. The decrease of the s-scores for physical functioning with increasing age would indicate a lower relative effect of RA on physical health in older age groups. However, differences in s-scores for SF-6D utilities were of similar magnitude across the age groups, indicating that the overall disease effect compared to the general population did not change with age (Table 3).

The RA-induced SF-6D utility reductions compared to those of the general population were similar across age groups, but the effects on physical function and mental function were different, in that the loss in physical function increased with increasing age while the loss in mental function remained stable or declined.

The QALY combines utility with time, and assuming that the average reduced health state utility of 0.16 in RA patients is maintained over 1 year, it can be interpreted as follows. The disease burden experienced among 100 RA patients over 1 year corresponds to a health loss of 16 QALY. This health loss is equivalent to 16 healthy individuals losing 1 year of their life[10], a number translating disease burden to face value. This study, with its large number of patients, made it possible to calculate similar QALY estimates in subsamples stratified for age and sex. The reductions in 1-year QALY among 100 RA patients (13–20 QALY depending on age and sex) represent a consistent and relevant burden of disease.

The assessment of disease burden in musculoskeletal diseases, as conducted in our study, is crucial for priority setting by decision makers who aim at maximizing health benefits within budget constraints[21]. By estimating the cost (in terms of euros, dollars, crowns, etc.) per QALY gained from medical treatments, decision makers are able to devote scarce resources to treatments and patient groups with the greatest potential for health improvement. The burden of RA could be compared to that of other chronic diseases by using the same index and making subsequent calculations. Our results indicate that RA inflicts a considerable burden upon RA patients, and consequently society would devote resources to treatment of this disease when treatments are effective and reasonably priced.

Generic instruments capture health status aspects independent of an existing disease and may detect disease consequences not assessed by disease-specific instruments[22]. The SF-36 was used in this study and is a widely used generic instrument with similar responsiveness when used as disease-specific instruments in RA[16]. As information is provided from 8 different important dimensions of health, SF-36 scores can also be presented as component scores for physical and mental health.

The interpretation of HRQOL and indicators of disease burden may be difficult. The clinical significance of high or low scores is not universal, and SF-36 scores have limited face value for clinicians. The utility score, however, represents an estimation of the preference-based valuation of health states. The concept of the QALY is useful when differences in valued health states are evaluated on a population-based and economic level, but they present no information on individual health. Comparisons of QALY across patients and therapies should be interpreted with caution, however, as different utility measures are not interchangeable, and sensitivity analyses or standardization of scores should be performed before calculations of QALY[23].

By using standard difference scores we applied the advantage to present direct reductions in HRQOL and utility of RA across sexes and age groups, thus providing estimates of the burden of RA. We have published similar data in patients with ankylosing spondylitis[19].

The burden of musculoskeletal diseases compared to chronic respiratory, gastrointestinal, and cardiovascular conditions has been attributed in particular to the dimensions of pain and physical functioning[24]. A large multinational European study demonstrated that arthritis had greater effects on HRQOL than other chronic conditions due to a combination of high prevalence and poor scores for physical functioning[25].

Worse HRQOL in individuals with musculoskeletal diseases versus the general population has been described in a Dutch study[7], which also applied SF-36 and measured utility (EQ-5D) in persons with one or more self-reported musculoskeletal diseases. The difference between individuals with musculoskeletal diseases and the population was most pronounced for physical functioning[7]. The patients with RA were generally in better health than in our study, although a discrepancy between the Dutch findings and our findings could be due to self-reported diagnoses in the Dutch study. Self-reported RA is not a reliable diagnosis and may include individuals with a variety of non-RA musculoskeletal conditions[26].

Other studies showing worse health in patients with RA than in the general population have generally been small and unable to describe the burden of disease in subgroups based on age and sex. In a small cohort of patients with RA from Sweden, HRQOL was reduced in most dimensions compared to normative data[27]. In a Spanish study physical function measured by the SF-12 was lower in RA patients than in the population, but there were no differences in the psychological component of the SF-12 between the population and patients with RA and other musculoskeletal conditions[28].

A clue to the reliability and robustness of our findings is apparent in the representativeness of the ORAR patient sample, which contains representative RA patients[2]. Further, the sample sizes, with more than 1000 RA patients examined and more than 2000 individuals from the population, were sufficiently strong statistically to also examine the burden of RA in men and in younger age groups.

Limitations of our study include that comparisons are

based on one quality of life instrument (SF-36), and the same instrument was also used to derive utility with an algorithm to "translate" SF-36 scores into utilities derived by a function of the preference for the health states according to the UK population. Calculation of SF-6D results in a "floor effect" in that the algorithm produces few utilities close to zero[18]. This characteristic could thus lead to an underestimation of the QALY burden of RA in our study. The cross-sectional design of this study prevented us from examining changes in HRQOL over time, and age and cohort effects could have contributed to the differences that were observed. Longitudinal assessments and application of additional instruments could have been used to confirm our findings.

Characteristics of the respondents with RA and those in the general population were not different compared to nonrespondents, but generally some caution is appropriate for the interpretation of responses from individuals in the highest age group[13]. The data collection was performed in 1996, making it difficult to extrapolate to the present state. We could have compared the data from the general population with a more recent data collection from ORAR, taking into account that the HRQOL of average RA patients may have improved by about 0.03 SF-6D units between 1996 and 2004, due to more effective treatment and better management[29,30]. This improvement of 0.03 roughly corresponds to the reported minimally important difference for health-state utility values within patients with early RA[31]. While it is thus possible that our analysis overestimates the burden of disease to some degree, it is not known whether the health status in the general population has improved over recent years. We have previously shown that patients with RA in Oslo had better health status than patients from Vilnius, which could indicate a larger disease burden of RA in other geographic settings[32]. It is also known that another widely used measure of utilities, the EQ-5D, on average yields lower utilities than the SF-6D[33]. Thus the gap in utility scores and QALY compared with the general population is more conservatively estimated with SF-6D than with EQ-5D.

In summary, our results reveal a considerable disease burden in patients with RA. In order to allocate resources in healthcare budgets and to gain a global perspective, estimates such as those obtained in our study may contribute to acknowledging the effect of RA on health. More data on disease burden would be useful for comparison between different rheumatologic conditions. Disease-specific registers in the same population area could enable such comparisons of disease burden in representative patients across different rheumatic diseases, and comparisons with population data are mandatory to have a clear picture of the effect on HRQOL.

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