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Original article

# The impact of different rheumatic diseases on health-related quality of life: a comparison with a selected sample of healthy individuals using SF-36 questionnaire, EQ-5D and SF-6D utility values

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**Summary.** *Background:* Given the high prevalence of rheumatic diseases, there is a need to determine which conditions have the greatest impact on health-related quality of life (HRQoL). The main aim of this study was to explore the HRQoL scores among 14 different rheumatic diseases and to compare them with the results of a selecting sample of healthy controls. *Methods:* 2633 patients of an ongoing cohort have been enrolled. Rheumatic diseases were classified into five diagnostic groups: inflammatory rheumatic diseases, connective tissue disorders, symptomatic peripheral osteoarthritis, soft tissue disorders, and osteoporosis. For comparison were used 649 healthy controls. The HRQoL was evaluated with the Medical Outcomes Study Short-Form 36 Health Survey (SF-36), the EuroQol five Dimensions (EQ-5D) questionnaire, and the Short-Form six Dimensions (SF-6D) questionnaire. *Results:* The five major rheumatic disease groups, compared to healthy people, significantly impaired all eight health concepts of the SF-36 ($p < 0.0001$). Similar results were found for EQ-5D and SF-6D. The patients with inflammatory rheumatic diseases have poorer self-reported health status than those without arthritis in all domains of living, but particularly with respect to scales measuring aspects of physical functioning or mobility, role limitation due to physical health problems and usual activities, and bodily pain. Rheumatoid arthritis had the largest negative impact on HRQoL, followed by fibromyalgia, vertebral fractures due to osteoporosis, hip osteoarthritis, and systemic sclerosis. *Conclusions:* Our results indicate that rheumatic diseases have a clearly detrimental effect on the HRQoL, and physical domain is more impaired than mental and social ones. (www.actabiomedica.it)

**Key words:** health-related quality of life, rheumatic diseases, SF-36, EQ-5D, SF-6D, patient-reported outcomes

**List of abbreviations**

BP: bodily pain; EQ-5D-3L: 3-level EuroQol five Dimensions questionnaire; GH: general health; HRQoL: health-related quality of life; MCS: Mental Component Summary; MH: mental health; OA: osteoarthritis; OP: osteoporosis; PCS: Physical Component Summary; PF: physical functioning; RE: role limitations due to emotional health; RP: role limitations due to physical function; SF: social functioning; SF-36: Medical Outcomes Study Short-Form 36 Health Survey; SF-6D: Short-Form six Dimensions questionnaire; SPA: spondyloarthritis; VAS: Visual Analogue Scale; VT: vitality.

## Background

Rheumatic diseases complaints represent a heavy burden on primary care services and are the most common medical causes of longterm absence from work, accounting for more than half of all sickness (1-4). This burden has been recognized by the United Nations and World Health Organization Study Group endorsing the Bone and Joint Decade 2000-2010 (5). The prevalence of rheumatic diseases in the general population ranges from 9.8% to 33.2% (6-10), and it has been estimated that 15-45% of primary care physician consultations are for musculoskeletal problems (11). The prevalence of locomotor disability rises from 3.1% in those aged less than 60 years to almost 50% in those aged more than 75 years and, in older patients, almost one third has a significant rheumatologic problem (12). A survey carried out in Italy showed a prevalence of 27% of chronic pain caused by a rheumatic disorder in the general adult population (13).

A comprehensive assessment of the multiple symptoms domains associated with rheumatic disease and their impact on aspects of health-related quality of life (HRQoL) should be a routine part of the care of patients. HRQoL has become an important measure when studying health status and health outcomes and its consideration has increased in relevance, playing a key role in decisions regarding resource allocation, intervention design, and pharmacological treatment of individuals with rheumatic diseases (14, 15). It includes physical function, pain, general health status, side effects, medical costs and other factors. Traditional methods of evaluation may fail to describe the extensive multi-dimensional issues associated with rheumatic diseases. Patient-reported outcomes are attractive options in a busy medical practice since they are easier to administer and less expensive than physician-observed disease activity and process measures. Although in Italy the use of the instruments is still quite limited, the validity and usefulness of patient-reported outcomes data in evaluating and monitoring patients with rheumatologic conditions have been well documented (16, 17).

There are several preference-based HRQoL measures including the Medical Outcomes Study Short-Form 36 Health Survey (SF-36) or the derived Short-Form Six Dimensions (SF-6D) questionnaire, and the EuroQol Five Dimensions (EQ-5D) questionnaire, that contribute to our understanding of the influence of rheumatic disease complaints and treatment associated improvements on health outcomes and quality-adjusted life-years (17, 18).

Their applicability is largely recommended by the US Panel on Cost-Effectiveness in Health and Medicine and the Outcome Measures in Rheumatology Clinical Trials Consensus-Based Reference Case for Economic Evaluation in Rheumatoid Arthritis (18-20).

The impact of different rheumatic conditions on HRQoL is widely unknown despite the growing number of studies conducted on the topic. Differences in methodology have resulted in greatly varying estimates for specific conditions (20). Considering the high prevalence of rheumatic diseases, there is a need to determine which of these chronic conditions have the greatest impact on HRQoL and identify if additional intervention may be required.

The aim of this study, therefore, was to explore the impact of individual common rheumatic diseases on HRQoL in a cohort of adult community-dwelling population, measured by SF-36 and utility indices (3-level EQ-5D [EQ-5D-3L] and SF-6D).

## Methods

### *Study population*

Patients involved in this study are part of an ongoing longitudinal project measuring rheumatic diseases outcomes conducted from April 2009 in the Rheumatology Departement of the Università Politecnica delle Marche, Jesi (Ancona), Italy. The cohort of patients is represented by consecutive adult patients suffering from different rheumatic disorders. Of the 2820 patients of our longitudinal cohort, 187 individuals were excluded through this procedure: 51 individuals had left the practice, 19 had dementia or mental illness, 21 were terminally ill, and 96 individuals had no reason given. The remaining 2633 individuals (93.4%) have been considered in the final evaluation due to the inclusiveness of all data (medical history, questionnaires

and imaging). The age and sex distribution of the sample were similar to those of the Italian population from the 2001 census (21).

For the purposes of this study, rheumatic diseases were classified, by a team of three experienced rheumatologists, into five diagnostic groups: inflammatory rheumatic diseases, systemic connective tissue disorders, symptomatic peripheral osteoarthritis, soft tissue disorders and osteoporosis. Inflammatory rheumatic diseases included patients examined by two rheumatologists and fulfilling the 2010 American College of Rheumatology classification criteria for rheumatoid arthritis (572 patients) (22), the Assessment of SpondyloArthritis international Society classification criteria for diagnosis of ankylosing spondylitis (251 patients) (23, 24), the ClASsification criteria for peripheral Psoriatic ARthritis (150 patients) (26). Peripheral psoriatic arthritis involvement was defined as synovitis of at least one large joint (wrist, elbow, shoulder, hip, knee, ankle) or three or more small joints (hands, feet, sternoclavicular joints) (26, 27).

Connective tissue disorders were further classified into three subgroups, including systemic lupus erythematosus (83 patients), systemic sclerosis (75 patients), and Sjögren syndrome (50 patients). The diagnosis of the connective tissue disorders was based on the international criteria available for a each single condition (28-30).

The symptomatic peripheral osteoarthritis group included patients with symptomatic osteoarthritis of the knee (176 patients), hip (136 patients), and hand (87 patients), according to the American College of Rheumatology criteria (31-33).

The soft tissue disorders group included fibromyalgia (226 patients), low back pain (141 patients), and shoulder tendinitis/adhesive capsulitis (shoulder pain) (112 patients). The presence of fibromyalgia was classified on the basis of the 2010 American College of Rheumatology criteria, which include the widespread pain index and a symptom severity scale. The sum of both scores was used as a measure of fibromyalgia (34). Low back pain was defined as pain localized in the back area between the lower limits of the chest and the gluteal folds, either radiating or not along the lower extremity (35). Patients with low back pain satisfied 3 screening criteria: (i) report of ever having had low back pain, (ii) a health care provider visit for low back pain in the previous six months, and (iii) low back pain that began more than 3 months previous (13, 35). For shoulder pain, separate classification criteria based on the main clinical manifestations (36) and in some instances on radiological or ultrasonographic findings were set for the purposes of this study.

The osteoporosis group included 172 women (mean age 69 years, range 48-89) who had vertebral fractures due to osteoporosis, and a group of 402 asymptomatic osteoporosis women without vertebral fractures. Osteoporosis was defined as a T-score lower than -2.5 (the difference between the measured bone mineral density and the mean value of young adults, expressed in standard deviations), according to the World Health Organization Study Group definition (37). Radiographic evaluation was performed centrally (at the Department of Radiology of the Università Politecnica delle Marche) by an experienced musculoskeletal radiologist. Total spine radiographs in lateral standing views in neutral/flexion/extension and in the lateral decubitus position in flexion/extension were taken with a film-tube distance of 1.8 m. The anterior, central, and posterior heights of each of the vertebral bodies from T4 to L5 in a neutral standing radiograph were measured using calipers. Vertebral fracture was considered present if at least one of 3 height measurements (anterior, middle, posterior) of one vertebra had decreased by more than 20% compared with the height of the nearest uncompressed vertebral body (38, 39).

Data for the healthy control group were collected from a previous cross-sectional population-based study, called MAPPING (MArche Pain Prevalence INvestigation Group). This study has been described in detail elsewhere (13, 40). In total, 3664 individuals were sampled and contacted by mail in 2004. The data collected from 649 healthy controls were used in this study. This sample reflects the age/sex related stratification/distribution of the Italian population.

*Demographics and disease-related characteristics*

A comprehensive paper questionnaire package including socio-demographic data, HRQoL questionnaires, and disease-related variables was administered to the patients. The socio-demographic variables were

age, sex, and level of education. Disease-related characteristics included disease duration and number of comorbid diseases. The presence of the following comorbidities was assessed: (1) hypertension, (2) hypercholesterolemia, (3) digestive diseases, (4) allergies, (5) cardiac diseases, (6) pulmonary diseases, (7) diabetes, (8) neurological diseases, (9) psychiatric disorders, (10) cancer, and (11) eye diseases (41). The algebraic sum of positive responses was calculated for each subject, giving a comorbidity factor with a possible range from 0 to 11. Data were collected by trained research associates during the hours of 8 AM to 16 PM on selected days.

*HRQoL assessment*

Trained rheumatologists collected the SF-36 questionnaire (42, 43), and the EQ-5D-3L questionnaire (44) by structured face-to-face interview. The SF-6D questionnaire was derived from the SF-36 questionnaire. Utility scores are provided by the EQ-5D and SF-6D, whereas the EuroQol Visual Anologue Scale (EQ-VAS) summarizes HRQoL on a 0-100 scale (45).

*SF-36 questionnaire*

The SF-36 is generic measure that is designed to capture health status in many different conditions (42, 43). The SF-36 contains 36 items, organized into eight scales covering the dimensions physical functioning, role limitations due to physical function, bodily pain, general health, mental health, role limitations due to emotional health, social functioning, and vitality. One additional item pertains to health transition. Raw domain scores are converted to a 0-100 scale, with higher scores indicating better health. These scores are Z-transformed and weighted to yield values used to calculate Physical (PCS) and Mental Component Summary (MCS) scores (42). SF-36 has demonstrated reliability, validity and responsiveness to change in patients with rheumatoid arthritis (42, 43). A standard 4-week recall validated Italian translation of the self-administered SF-36 (IQOLA SF-36 Italian Version 1.6) was used (46).

*SF-6D questionnaire*

The SF-6D was derived from the SF-36 questionnaire. The SF-6D focuses on six of the eight health domains covered by the SF-36 health survey: physical functioning, role participation (combined role-physical and role-emotional), social functioning, bodily pain, mental health, and vitality. The SF-6D was calculated from SF-36 by using a definite scoring function in order to create a weighted index score ranging from 1.0 (no difficulty in any dimensions or perfect health) to 0.296 (severely impaired levels in all dimensions). SF-6D has demonstrated construct validity and responsiveness for use (47, 48).

*EQ-5D-3L questionnaire*

The EQ-5D-3L version consists of two pages: the EQ-5D descriptive system and the EQ-VAS (44). The EQ-5D descriptive system is composed by five dimensions – mobility, self-care, usual activities, pain/disconfort, and anxiety/depression, and each dimension has three levels ("no problems", "some problems", "extreme problems"). Respondents classify and rate their health status on the day of the survey. The Italian population-based values have been used to convert patient responses to the health state classifier into a single index, which produces scores from 0.92 to -0.38 (49). A perception of "own health state" is also part of the EQ-5D-3L but is scored separately. This second part of the EQ-5D-3L, namely the EQ-VAS, ranges from 0 (worst possible health state) to 100 (best possible health state), on which the respondents rate how they perceive their health on that particular day (44).

*Statistical analysis*

Baseline demographics, clinical characteristics, and HRQoL measures were summarized using descriptive statistics. Mean domain scores of the SF-36 are displayed using spydergrams (50). Spydergrams offer the ability to view differences more easily across all domains as a pattern recognition profile, depicting disease and population specific patterns, compared with matched normative data. Student's t test was used to compare differences associated with health status groups for the

SF-36, EQ-5D and SF-6D. All analyses were adjusted for age and sex. All data were entered into a Microsoft Access database, which had been developed for management of cross-sectional study. All the statistical analyses were performed using the SPSS version 15.0 (SPSS Inc, Chicago, USA), and the MedCalc® version 16.0 (MedCalc Software, Mariakerke, Belgium).

## Results

*Demographic and clinical data*

Of the 2633 participants, the majority of the subjects were women (75.5%), married or living together with someone else (62.5%), with primary or secondary educational level (79.5%). The respondents' age ranged from 19 to 80 years, with a mean of 59 years (standard deviation, SD=14.2 years). They were most frequently retired or manual workers, and living in urban areas. Of the subjects enrolled, 952 (36.1%) reported one or more medical comorbidities. The frequency of multimorbidity was higher in those subjects classified with fibromyalgia (62.4%) followed by that of those classified as rheumatoid arthritis (52.6%) and with osteoporosis (43.3%). The most prevalent combinations were with arterial hypertension (8.8%), with hypercholesterolemia (6.9%), digestive diseases (5.3%), cardiologic diseases (4.4%), and diabetes mellitus (3.1%). Characteristics of the participants of the total sample are depicted in Table 1.

*Severity of pain and HRQoL*

Table 2 summarizes the mean ± SD for each of the aspects of health status covered by the SF-36, EQ-5D and SF-6D for the different diagnostic groups and controls. The five major rheumatic disease groups, compared to healthy people, significantly impaired all eight health concepts of the SF-36 ($p<0.0001$) (Figure 1-5). Similar results were found for EQ-5D, and SF-6D (Figures 6 and 7). The three inflammatory rheumatic diseases, compared to healthy controls, significantly impaired all eight health concepts of

**Table 1.** Sociodemographic variables and clinical characteristics of 2,633 patients with rheumatic diseases and 649 healthy controls

| | Sex (F/M) | Age (years) | Disease Duration (years) | Educational (years) | Comorbidity (number) |
|---|---|---|---|---|---|
| **Healthy controls (n. 649)** | 401/248 | 51.88±13.90 | - | 11.2±3.9 | 0.87±1.4 |
| **1. Inflammatory rheumatic diseases** | | | | | |
| Rheumatoid arthritis (n.572) | 387/185 | 57.6±14.5 | 6.7±4.5 | 11.3±3.5 | 2.0±1.6 |
| Peripheral psoriatic arthritis (n. 150) | 79/71 | 60.4±12.1 | 4.3±3.2 | 8.5±3.4 | 1.4±1.6 |
| Ankylosing spondylitis (n. 251) | 187/64 | 53.0±10.3 | 4.5±3.2 | 8.5±3.6 | 0.9±1.1 |
| **2. Connective tissue disorders** | | | | | |
| Systemic sclerosis (n. 75) | 58/17 | 53.4±12.8 | 6.2±4.4 | 11.0±3.8 | 1.7±1.6 |
| Systemic lupus erythematosus (n.83) | 79/4 | 48.3±14.2 | 7.8±5.4 | 7.5±3.6 | 1.3±1.4 |
| Sjogren syndrome (n. 50) | 45/5 | 48.4±11.8 | 6.2±3.5 | 9.8±3.5 | 1.0±1.2 |
| **3. Symptomatic peripheral osteoarthritis** | | | | | |
| Osteoarthritis of the knee (n. 176) | 105/71 | 69.7±9.1 | 4.9±3.2 | 6.6±2.5 | 1.1±1.5 |
| Osteoarthritis of the hip (n.136) | 79/57 | 67.4±11.6 | 5.1±3.1 | 8.4±3.4 | 1.5±1.5 |
| Osteoarthritis of the hand (n.87) | 61/26 | 66.3±9.5 | 6.7±4.6 | 9.4±4.0 | 0.9±1.0 |
| **4. Soft tissue disorders** | | | | | |
| Fibromyalgia ((n. 226) | 198/28 | 50.4±10.2 | 5.9±4.0 | 9.2±3.81 | 2.2±1.8 |
| Low back pain (n. 141) | 97/44 | 59.7±14.4 | 4.7±3.6 | 7.6±3.05 | 1.3±1.5 |
| Shoulder pain (n. 112) | 59/53 | 52.4±12.4 | 3.5±2.8 | 8.2±3.64 | 0.9±1.0 |
| **5. Osteoporosis** | | | | | |
| Osteoporosis with vertebral fractures (n. 402) | 403/0 | 71.1±7.9 | ---- | 8.3±3.0 | 1.9±1.5 |
| Osteoporosis whitout vertebral fractures (n. 172) | 172/0 | 70.2±8.9 | ---- | 8.9±3.6 | 1.5±1.7 |

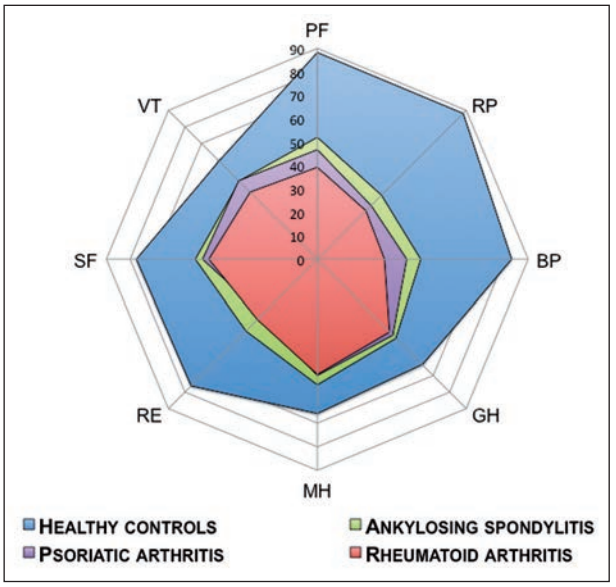


**Figure 1.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales in patients with inflammatory rheumatic diseases.
*Legend:* spydergrams with the comparison for the eight subscales of the SF-36 can vary between 0 and 100, higher values reflecting better health-related quality of life. Mean SF-36 scores of the healthy controls (n=649) are also shown. PF=physical functioning; RP=role limitations due to physical function; BP=bodily pain; GH=general health; MH=mental health; RE=role limitations due to emotional health; SF=social functioning; VT=vitality

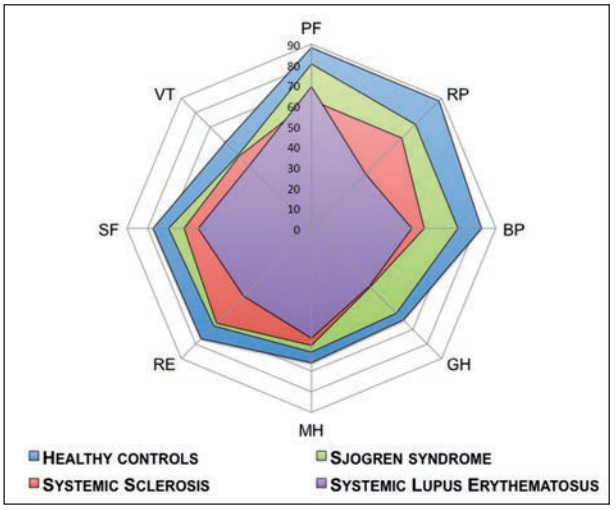


**Figure 2.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales in patients with-connective tissue disorders.
*Legend:* spydergrams with the comparison for the eight subscales of the SF-36 can vary between 0 and 100, higher values reflecting better health-related quality of life. Mean SF-36 scores of the healthy controls (n=649) are also shown. PF=physical functioning; RP=role limitations due to physical function; BP=bodily pain; GH=general health; MH=mental health; RE=role limitations due to emotional health; SF=social functioning; VT=vitality

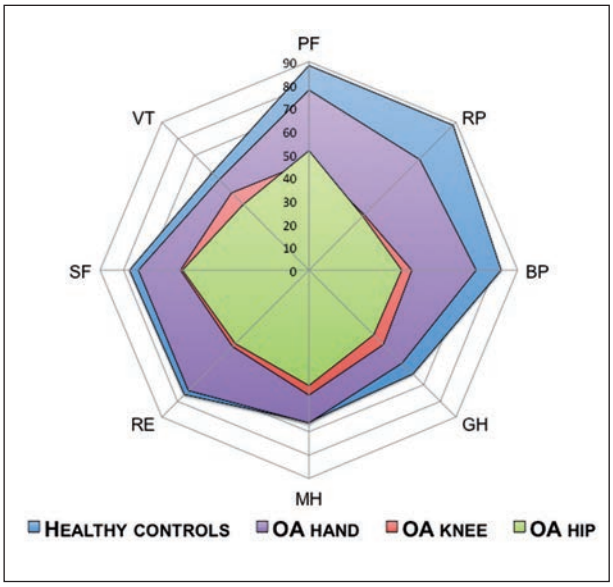


**Figure 3.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales in patients with symptomatic peripheral osteoarthritis.
Legend: spydergrams with the comparison for the eight subscales of the SF-36 can vary between 0 and 100, higher values reflecting better health-related quality of life. Mean SF-36 scores of the healthy controls (n=649) are also shown. OA=osteoarthritis; PF=physical functioning; RP=role limitations due to physical function; BP=bodily pain; GH=general health; MH=mental health; RE=role limitations due to emotional health; SF=social functioning; VT=vitality

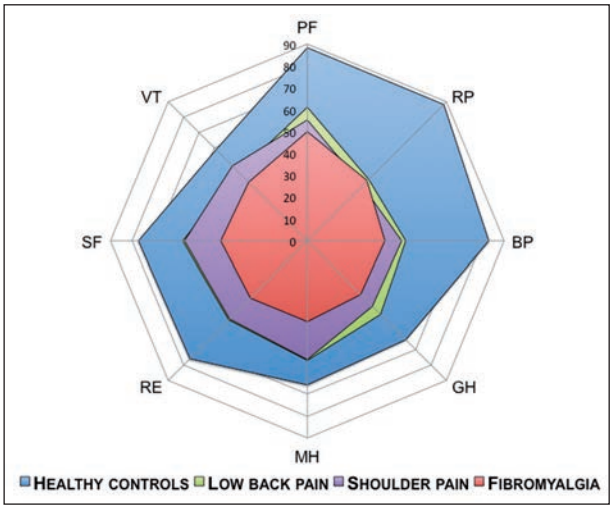


**Figure 4.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales in patients with soft tissue disorders.
Legend: spydergrams with the comparison for the eight subscales of the SF-36 can vary between 0 and 100, higher values reflecting better health-related quality of life. Mean SF-36 scores of the healthy controls (n=649) are also shown. PF=physical functioning; RP=role limitations due to physical function; BP=bodily pain; GH=general health; MH=mental health; RE=role limitations due to emotional health; SF=social functioning; VT=vitality

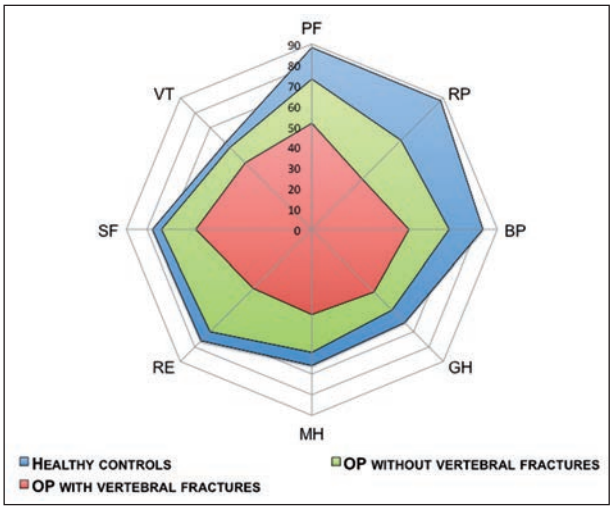


**Figure 5.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales in patients with-osteoporosis.
Legend: spydergrams with the comparison for the eight subscales of the SF-36 can vary between 0 and 100, higher values reflecting better health-related quality of life. Mean SF-36 scores of the healthy controls (n=649) are also shown. OP: osteoporosis; PF=physical functioning; RP=role limitations due to physical function; BP=bodily pain; GH=general health; MH=mental health; RE=role limitations due to emotional health; SF=social functioning; VT=vitality

the SF-36 ($p<0.0001$) in both component PCS and MCS scores ($p<0.0001$), and in utility scores (Table 2). Figure 1 compares the scores in each domain of the SF-36 health survey for the three inflammatory rheumatic diseases, compared to healthy controls. Overall, the dimensions typically affected were physical functioning, role limitations due to physical function, and bodily pain. The disease with the worst HRQoL for those dimensions was rheumatoid arthritis. The mean PCS score of rheumatoid arthritis patients was 30.65 (SD=6.21). The mean MCS score of rheumatoid arthritis patients was 44.74 (SD=12.23). The means EQ-5D and SF-6D scores were 0.43 (SD=0.14) and 0.57 (SD=0.8), respectively. The EQ-VAS score was 48.07 (SD=15.31) (Table 2). Regarding the HRQoL dimensions involving mental health problems, patients with psoriatic arthritis scores were generally lower than the rheumatoid arthritis patients scores (Figure 6).

The analysis of the results of the connective tissue disorders patients group demonstrated that, both systemic lupus erythematosus and systemic sclerosis,

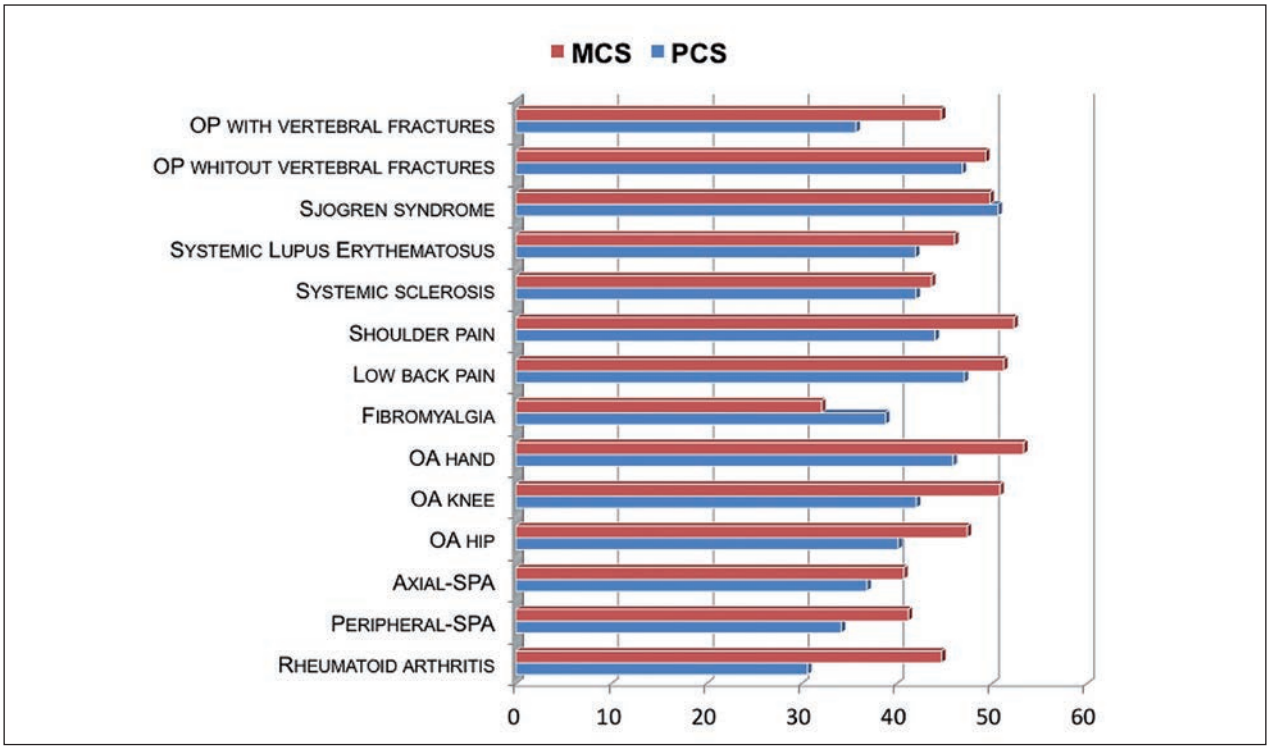


**Figure 6.** The Medical Outcomes Study Short-Form 36 (SF-36) physical component summary (PCS) and mental component summary (MCS) scores in all rheumatic diseases. Bar graph where higher values reflect better health-related quality of life. OP=osteoporosis; OA=osteoarthritis; SPA=spondyloarthritis

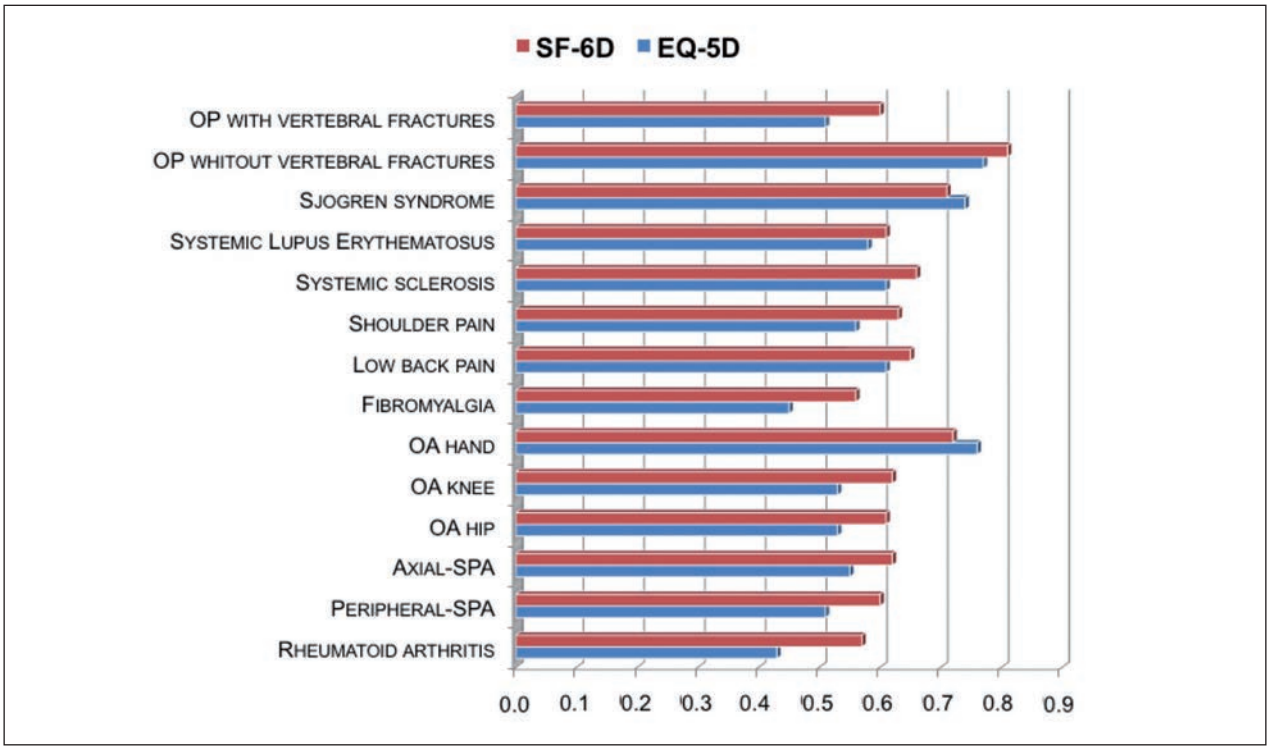


**Figure 7.** The EuroQol five Dimensions questionnaire (EQ-5D) and the Short-Form six Dimensions (SF-6D) utility scores in all rheumatic diseases. Bar graph showing the comparison between EQ-5D and SF-6D scores in all rheumatic diseases. OP=osteoporosis; OA=osteoarthritis; SPA=spondyloarthritis

showed a significant impairment in all the eight subscales of the SF-36 ($p<0.0001$) with respect to healthy controls as well as the PCS and MCS scores ($p<0.0001$), and in EQ-5D and SF-6D scores ($p<0.0005$) (Table 2). From the comparison of the eight SF-36 subscales, the mainly compromised in patients with systemic lupus erythematosus resulted the role limitations due to physical function (systemic lupus erythematosus, 37.65±37.73 vs. systemic sclerosis, 62.40±35.42; $p<0.01$) (Table 2, Figure 2). No statistical significant difference emerged from the comparison of the mean of the value of the PCS or MCS scores (Figure 6) or among the means of the values of the EQ-5D, EQ-VAS e SF-6D. Compared to systemic lupus erythematosus and systemic sclerosis, the Sjögren syndrome showed the lower impact in HRQoL, both in physical and mental dimensions of the SF-36 and in the scores of the EQ-5D, EQ-VAS and SF-6D. In comparison with healthy controls, patients with Sjögren syndrome resulted in poorer scores of vitality (50.50±17.59 vs. 59.16±15.48; $p=0.03$).

Figure 3 shows the patients' HRQoL patterns of the SF-36 of the symptomatic peripheral osteoarthritis group. The overall impact on health was substantial for both groups of patients with osteoarthritis of the lower extremities. Compared to the healthy controls and with osteoarthritis of the hand patients, both groups showed a significant impairment in all of the eight subscales of the SF-36 ($p<0.0001$). The most striking impact was seen in osteoarthritis of the hip for SF-36 role limitations due to physical function (33.09±34.27), general health (39.76±18.69), and bodily pain (40.01±14.73) (Table 2, Figure 3). Both the PCS and MCS components of the SF-36 resulted substantially impoverished, without showing a statistical significance, in osteoarthritis of the hip patients compared to osteoarthritis of the knee subjects (PCS, 40.18±17.74 vs. 42.09±17.02 and MCS, 47.43±19.14 vs. 50.88±19.54) (Table 2, Figure 6). The EQ-5D, EQ-VAS and SF-6D values were comparable in the two groups and remarkably reduced respect to the os-

**Table 2.** The Medical Outcomes Study Short-Form 36 (SF-36) subscales and summary dimensions and utility scores in 2,633 patients with rheumatic diseases and 649 healthy controls

| | | Mean±SD | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | SF-36 SUB-SCALES | | | | | | | | SF-36 DOMAINS | | UTILITY SCORES | | |
| | n. | PF | RP | BP | GH | MH | RE | SF | VT | PCS | MCS | EQ-5D | SF-6D | EQ-VAS |
| **Healty controls** | 649 | 88.9±13.3 | 88.7±21.7 | 82.9±17.3 | 63.4±17.4 | 65.7±15.0 | 76.1±34.5 | 77.3±18.1 | 59.6±15.4 | 57.4±11.3 | 54.4±13.6 | 0.81±0.1 | 0.78±0.31 | 75.8±11.0 |
| **1. Inflammatory rheumatic diseases** | | | | | | | | | | | | | | |
| Rheumatoid arthritis | 572 | 39.1±19.8 | 29.2±14.8 | 28.6±16.3 | 43.0±19.4 | 49.6±22.8 | 36.6±40.8 | 46.7±20.8 | 40.8±20.2 | 30.5±6.2 | 44.7±12.2 | 0.44±0.14 | 0.57±0.08 | 48.7±15.3 |
| Peripheral psoriatic arthritis | 150 | 46.9±21.2 | 32.5±23.2 | 38.1±19.0 | 45.6±18.1 | 49.7±20.3 | 33.0±36.0 | 48.0±22.2 | 47.3±18.0 | 34.8±6.7 | 41.3±11.3 | 0.51±0.15 | 0.60±0.08 | 54.0±14.1 |
| Ankylosing spondylitis | 251 | 52.3±20.2 | 38.4±28.1 | 44.3±17.4 | 47.3±20.9 | 53.5±20.9 | 43.09±30.5 | 52.2±19.4 | 47.1±19.2 | 36.9±8.1 | 40.7±10.1 | 0.55±0.14 | 0.62±0.75 | 57.4±14.4 |
| **2. Connective tissue disorders** | | | | | | | | | | | | | | |
| Systemic sclerosis | 75 | 62.7±22.9 | 62.4±35.5 | 55.1±28.7 | 40.5±17.5 | 57.2±20.3 | 65.40±36.1 | 62.9±22.2 | 50.0±17.9 | 42.5±8.1 | 43.6±9.1 | 0.61±0.17 | 0.66±0.10 | 54.7±16.7 |
| Systemic lupus erythematosus | 83 | 69.2±19.4 | 37.65±37.7 | 48.9±22.3 | 39.8±17.3 | 53.3±20.6 | 47.7±40.7 | 55.9±22.7 | 43.1±17.8 | 42.0±12.5 | 46.1±16.6 | 0.58±0.15 | 0.61±0.10 | 50.5±11.5 |
| Sjogren syndrome | 50 | 80.3±19.3 | 71.5±33.5 | 71.5±26.3 | 58.8±19.2 | 60.7±19.2 | 67.2±41.2 | 69.5±22.5 | 50.0±17.9 | 50.8±12.6 | 49.2±15.2 | 0.74±0.17 | 0.71±0.10 | 62.8±14.0 |
| **3. Symptomatic peripheral osteoarthritis** | | | | | | | | | | | | | | |
| Osteoarthritis of the knee | 176 | 46.1±21.8 | 33.1±32.1 | 44.5±15.4 | 45.6±18.0 | 54.7±19.3 | 46.9±39.6 | 55.4±24.2 | 47.4±18.9 | 42.9±17.0 | 50.8±19.5 | 0.53±0.16 | 0.62±0.09 | 56.1±15.6 |
| Osteoarthritis of the hip | 136 | 51.4±24.0 | 33.9±34.2 | 40.0±14.7 | 39.7±18.6 | 49.9±21.0 | 44.6±41.5 | 54.8±22.4 | 40.6±18.5 | 40.8±17.7 | 47.3±19.14 | 0.53±0.15 | 0.61±0.08 | 51.4±16.8 |
| Osteoarthritis of the hand | 87 | 77.7±14.8 | 67.3±28.8 | 72.5±17.7 | 56.9±16.7 | 66.5±15.8 | 83.6±25.1 | 73.8±17.2 | 55.1±15.4 | 45.9±7.0 | 53.6±8.7 | 0.76±0.10 | 0.72±0.06 | 69.1±10.3 |
| **4. Soft tissue disorders** | | | | | | | | | | | | | | |
| Fibromyalgia | 226 | 49.9±17.3 | 17.2±35.0 | 35.5±9.7 | 34.4±11.1 | 36.8±13.3 | 36.7±23.9 | 36.4±13.8 | 38.2±12.1 | 38.8±4.7 | 32.3±7.5 | 0.45±0.11 | 0.56±0.05 | 45.9±11.6 |
| Low back pain | 141 | 61.2±23.7 | 39.5±34.4 | 45.1±19.2 | 47.5±19.9 | 54.6±19.5 | 50.9±36.8 | 57.6±22.6 | 44.2±17.5 | 47.1±19.5 | 51.7±18.0 | 0.61±0.16 | 0.65±0.85 | 62.5±18.1 |
| Shoulder pain | 112 | 55.3±23.6 | 35.7±35.9 | 43.1±17.3 | 41.9±14.6 | 54.9±13.7 | 50.3±43.6 | 56.2±15.2 | 48.5±13.4 | 44.0±14.5 | 52.4±16.0 | 0.56±0.12 | 0.63±0.06 | 53.4±14.3 |
| **5. Osteoporosis** | | | | | | | | | | | | | | |
| Osteoporosis with vertebral fractures | 402 | 51.7±22.7 | 34.2±35.4 | 47.2±20.9 | 42.5±18.7 | 41.1±19.4 | 40.1±38.7 | 56.4±22.3 | 45.6±16.7 | 35.4±8.8 | 44.0±9.3 | 0.51±0.14 | 0.60±0.73 | 53.2±15.7 |
| Osteoporosis whitout fractures | 172 | 73.0±21.8 | 60.1±38.4 | 66.2±23.1 | 54.9±19.2 | 59.4±18.1 | 69.6±34.0 | 72.7±22.0 | 56.3±16.2 | 46.1±8.8 | 49.3±8.6 | 0.77±0.09 | 0.81±0.06 | 67.8±11.4 |

Abbreviations. SD = standard deviation; SF-36 = Medical Outcomes Study Short-Form 36 Health Survey; PF = physical functioning; RP = role limitations due to physical function; BP = bodily pain; GH = general health; MH = mental health; RE = role limitations due to emotional health; SF = social functioning; VT = vitality; PCS = physical component summary; MCS = mental component summary; EQ-5D = EuroQol five Dimensions questionnaire; SF-6D = Short-Form six Dimensions.

teoarthritis of the hand patients ($p<0.01$) and to the healthy controls ($p<0.001$) (Table 2, Figure 7).

In comparison with the general population, the fibromyalgia patients showed significant impairment in relation to all of the eight scales of the SF-36 ($p<0.0001$), as well as the PCS and MCS scores ($p<0.0001$) (Table 2, Figure 6) and EQ-5D ($p<0.001$) and SF-6D scores ($p<0.01$) (Table 2, Figure 7). Figure 4 shows the patients' HRQoL patterns. The dimensions typically affected by fibromyalgia were role limitations due to physical function (17.24±35.00), bodily pain (35.57±9.70), general health (36.91±13.32), social functioning (36.64±13.83) and role limitations due to emotional health (36.87±23.99). Overall, fibromyalgia was confirmed as the disease with the higher impact on HRQoL both compared with the group of patients suffering from low back pain and with the group of patients with shoulder pain. In these two groups, the outlines of the health status on SF-36 and the utility values were essentially equivalent.

Table 2 shows overall results comparing osteoporosis patients with and without vertebral fractures. A significant difference was found between the 2 groups for all dimensions considered. SF-36 scores in patients with vertebral fractures due to osteoporosis clearly showed a more significant impairment in HRQoL not only versus healthy controls, but also in comparison with osteoporosis patients without vertebral fractures. The dimensions typically affected by osteoporosis with vertebral fractures were role limitations due to physical function (34.72±35.44), general health (42.51±18.71), mental health (41.10±19.45) and role limitations due to emotional health (40.10±38.77) (Figure 5). In patients with vertebral fracture, both the PCS of the SF-36 (Figure 2) and the utility scores (EQ-5D, EQ-VAS, and SF-6D) (Table 2, Figure 5) showed a pronounced endangerment. The comparison between osteoporosis patients without vertebral fractures and healthy controls demonstrated meaningful differences in physical functioning (73.00±21.85 vs. 88.17±21.77; $p<0.005$), role limitations due to physical function (60.91±38.46 vs. 88.39±13.33; $p<0.001$), and bodily pain (66.62±23.10 vs. 82.98±17.38; $p<0.001$).

## Discussion

This study confirms that rheumatic diseases have a clearly detrimental effect on the HRQoL, and physical domains are more impaired than mental and social ones.

Rheumatic diseases are associated with some of the poorest HRQoL issues, particularly in terms of physical functioning, role limitations due to physical function and bodily pain, where HRQoL is lower than for gastrointestinal disorders, urogenital conditions, psychiatric disorders, chronic respiratory diseases, cerebrovascular/neurologic conditions, and cardiovascular conditions (5, 51-55).

Saarni et al. conducted a study to estimate the relative effects of 29 chronic conditions on HRQoL in the Finnish population and found that rheumatic and psychiatric disorders had the largest negative impact on HRQoL at the population level (56). Branco and colleagues revealed that rheumatic and musculoskeletal diseases are highly prevalent in Portugal and are associated not only with significant physical function and mental health impairment but also with poor HRQoL, leading to more health resource utilization (10). Rheumatic disorders had the largest and rather stable impact across ages on the population level, moreover, are common reasons of claiming disability pensions, along with mental, respiratory and cardiovascular disorders (57, 58). In two Swedish works, the conditions with the largest age-adjusted HRQoL loss were depression, stroke and low back pain (59), and mental distress, low back pain and neck/shoulder pain (60). The EPISER study, an initiative of the Spanish Society of Rheumatology, showed that rheumatic diseases affect a significant proportion of the population, with various degrees of impact on HRQoL, resulting in a significant number of physician visits, work disability, and medication use. Compared with persons without any of the target rheumatic diseases, and after controlling other factors that may interfere with functional ability or with the HRQoL, three diseases – rheumatoid arthritis, low back pain, and knee osteoarthritis – were found to have a clearly detrimental effect on the lives of the affected subjects (8).

We conducted this study in order to estimate the impact of 14 different rheumatic disorders on HRQoL

in the Italian adult population. To the best of our knowledge, no other study has directly compared the relative HRQoL impact of rheumatic disorders, drawn from Italian settings, using generic SF-36 questionnaire and utility-based HRQoL measures.

*HRQoL in inflammatory rheumatic diseases*

The patients with inflammatory rheumatic diseases have poorer self-reported health status than those without arthritis in all domains of living. In particular, the disease with the worst HRQoL for physical dimensions of SF-36 was rheumatoid arthritis. The mean PCS score for rheumatoid arthritis patients was 30.5, approximately two standard deviations below the mean observed in the Italian general population (40). Based on the PCS scores alone, physical functioning of these patients is comparable to patients with congestive heart failure (55). Concerning patients with psoriatic arthritis and ankylosing spondylitis, our data confirms clinical cohort studies from Germany (61), United Kingdom (62), and Canada (63) that found similar functional disability and reduced HRQoL in patients with psoriatic arthritis compared to rheumatoid arthritis. Although patients with psoriatic arthritis had lower levels of physical functioning by the SF-36 PCS, in comparison with health controls, they have also reported more psychosocial problems than patients with rheumatoid arthritis and ankylosing spondylitis. Overall, the SF-36 MCS dimension typically affected by psoriatic arthritis was related to limitations due to emotional health. In patients with ankylosing spondylitis, the physical functioning and bodily pain are more impaired than the mental scales. Rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis have a comparable burden of disease (61, 64). Compared to rheumatoid arthritis, psoriatic arthritis showed similar disease activity, disability and reduced HRQoL in many studies (63, 65, 66). The extent of disability and the impact on physical and mental HRQoL is possibly related to the fact that these patients have the dual burden of psoriatic skin lesions and joint disease. The psychological and social effects of skin involvement have been well documented in patients with psoriasis (67). When skin disease is severe, for example, median scores on the anxiety/depression domain of the EQ-5D and HRQoL, are comparable to those of patients with rheumatoid arthritis (62, 68). It is essential to highlight the frequent coexistence of depression and/or anxiety in these patients, because their presence worsen the outcome and modifies assessment scores and the response to therapies. Indeed, depression was the most prevalent comorbidity in rheumatoid arthritis in the Comorbidities in Rheumatoid Arthritis (COMORA) study (69). Depression was associated with clinically significantly worse physical functioning (70). Also Moussavi et al. found that the combination of depression and arthritis was associated with lower health status (71). Morris and colleagued described how depression, and even intermittent depression over time, was associated with low self-reported health status and disability after 18 years (72). Depression is linked to rheumatoid arthritis and physical functioning by biological, behavioral, cognitive, and social pathways (73-75). Similarly to rheumatoid arthritis, spondyloartrhritis can affect HRQoL, morbidity, mortality, participation in paid and unpaid work, and healthcare costs (68, 76). Although psoriatic arthritis was considered a benign disease in the majority of cases given in previous reports or in population-based samples, clinical cohort studies described that this condition as a progressive and disabling disease, especially when polyarticular peripheral arthritis is present (68). Strikingly, depression is the comorbidity more often disregarded in psoriatic arthritis by both rheumatologists and dermatologists. The Canadian Initiative includes 3 recommendations (77) on the importance of this comorbidity. Recently, psychological disorders such as anxiety and depression have been frequently reported also in patients with ankylosing spondylitis. Hakkou et al. reported that more than half of the patients with ankylosing spondylitis experienced depression or anxiety (78).

*HRQoL in connective tissue disorders*

Connective tissue disorders are traditionally considered conditions with great impact on all aspects of health status. The usefulness of the utility measures such as the EQ-5D and the more recent SF-6D in patients with systemic sclerosis has been reported (79, 80). Our data demonstrate that the reduction in

HRQoL in systemic sclerosis is similar to that experienced by patients with systemic lupus erythematosus. In agreement with data already reported, the scores of HRQoL, including overall score as well as the PCS and MCS, were lower in patients with systemic lupus erythematosus than in controls (81). The scores of the role limitation due to physical function, role limitations due to emotional health and vitality were lower in systemic lupus erythematosus than in patients with systemic sclerosis. The patients with Sjögren syndrome experienced a higher HRQoL level with regard to both physical function and psychological dimensions than the patients with systemic sclerosis and systemic lupus erythematosus. Despite the fact that Sjögren syndrome is a common disorder which significantly impacts health status, the effect of Sjögren syndrome on a broad spectrum of HRQoL domains has not been well studied (82, 83). Segal et al. documented reduced functioning among patients with Sjögren syndrome in every domain of the SF-36, and increased utilization of health care services including medications, hospitalization rates, provider visits and out of pocket expenses. Additionally, pain, fatigue, depressed mood and cognitive symptoms were significantly greater in patients compared to controls (83).

*HRQoL in osteoporosis*

Fragility fractures are an increasingly important contributor to the burden of rheumatic conditions (38, 84). Patients with prevalent vertebral fractures were found to be associated with a significant decline in HRQoL for most of the SF-36 domains analyzed and utility scores. In particular, it has significantly reduced role limitations due to physical function, bodily pain, general health, vitality, social functioning, role limitations due to emotional health, and PCS and MCS scores. HRQoL scores were lower in women with lumbar fractures. Pain is a common problem after vertebral compression fractures. In a study, one-third of the patients with vertebral compression fractures still had severe pain, necessitating pain medication and physical therapy (85). Psychological problems often occur in patients with osteoporosis vertebral fractures. They express substantial anxiety, especially about the possibility of future fractures and physical deformity.

*HRQoL in soft tissue diseases*

Regarding the soft tissue disease group, the patients with fibromyalgia showed an impact on all aspects of health status that are as severe as those reported by patients with rheumatoid arthritis (86), and more severe than those reported by patients with osteoarthritis or other painful condition (87, 88). Fibromyalgia may represent either comorbidity or a continuous phenotypic spectrum associated with variations in central pain processing (89). Our recent findings confirm previous reports (90, 91) that 10-20% of established rheumatoid arthritis and spondyloarthritis patients, satisfied fibromyalgia classification criteria (92, 93). Furthermore, the mental health of subjects suffering from fibromyalgia is more severely affected than that of rheumatoid arthritis patients (94-96). The dimensions typically affected by fibromyalgia are role limitations due to physical function, general health, mental health, and social functioning, whereas physical functioning is more impaired in the rheumatoid arthritis patients. Our results are consistent with previous studies using the SF-36 and highlight the substantial health burden associated with fibromyalgia (97-99). The mean EQ-5D index value of 0.45±0.11 calculated in the current study for the fibromyalgia population is comparable to the 0.44±0.33 reported in a population of French and German fibromyalgia patients (99), but less than 0.61±0.22 that has been estimated for an fibromyalgia population in the US derived from the National Data Bank for Rheumatic Diseases (100). This resembles the pattern of restrictions generally found in patients with rheumatic disorders (6, 40) or other chronic conditions such as congestive heart failure, chronic obstructive pulmonary disease, hypertension, recent acute myocardial infarction, type II diabetes and malignancy (41, 100). Our results also confirm that all physical and mental subscale scores and utility scores were significantly lower in both chronic low back pain and shoulder pain group. The enormous global burden of low back pain has gone largely unrecognised by many policymakers. Shim et al. documented that the SF-36 subscale score and summary score in subjects with chronic low back pain were significantly lower than the healthy controls (101). Shoulder pain is common in the general

population and affects 18-26% of adults at any point in time, making it one of the most common regional pain syndromes (102).

*HRQoL in symptomatic peripheral osteoarthritis*

Large joint clinical osteoarthritis is a major cause of disability, a growing proportion of which is borne by people who regard themselves still of working age, is associated with frailty and pre-frailty in older adults in European countries, and pose a significant economic burden on the community (103-105). Recent publications found an independent association between hip osteoarthritis and frailty or pre-frailty in men aged 65 and over and knee osteoarthritis has been shown to be associated with a greater prevalence and risk of developing frailty (106, 107). Our findings showed that the physical functioning and role limitations subscales of SF-36 are significantly more impaired in patients with osteoarthritis of the hip. Consequently, also the PCS scale of the SF-36 showed a slightly higher impairment in osteoarthritis of the hip. The greatest differences in SF-36 scores in patients with osteoarthritis of the hip, compared with knee osteoarthritis, were seen for bodily pain and vitality.

This study has several limitations that should be taken into account in interpreting the results. Firstly, because of the nature of the sample, the results are not generalizable beyond patients being treated in rheumatology practices. A second limitation is related to the cross-sectional study design which does not allow test-retest reliability evaluation and does not provide information on the sensitivity to change after treatment. Finally, in this study we have not examined the role of other components such as comorbidity, psychological variables (i.e. anxiety and depression), and certain sociodemographic variables (i.e. lower education) that may be indicators of more severe pain disability (108-110).

## Conclusions

The five major rheumatic disease groups, compared to the healthy controls, significantly impaired all eight health concepts of the SF-36. Similar results were found for EQ-5D, EQ-VAS and SF-6D. The patients with inflammatory rheumatic diseases had poorer HRQoL than those without arthritis in all domains of living, but particularly with respect to scales measuring aspects of physical functioning or mobility, role limitations due to physical function or usual activities, and bodily pain. Rheumatoid arthritis had the largest negative impact on HRQoL at the individual level, followed by fibromyalgia, vertebral fractures due to osteoporosis, osteoarthritis of the hip, and systemic sclerosis. These findings may help clinical decision making and priority setting for management of individuals with rheumatic diseases. Further longitudinal research is needed to confirm the impact of rheumatic diseases on health resources and employment suggested by our data.

**Ethics approval and consent to participate**

This study is in accordance with the 1964 Helsinki Declaration and is approved by our institutional research committee (Comitato Etico Zona Territoriale 5 ASUR Marche). All the subjects provided a written informed consent to participate.

**Authors' contribution**

FS has been the principal investigator, responsible for the coordination and management of the study. MDC, MC, SF and AC participated in the conception of the study, in the acquisition of the data, provided clinical support, and contributed in writing the manuscript. MG participated in the acquisition of data and has been involved in revising the paper for intellectual content. All authors have read and approved the final manuscript.

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