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SPECIAL REPORT

Expanding quantitative assessment of rheumatoid arthritis in usual care

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Reports concerning patients with rheumatoid arthritis are derived primarily from specialized sources, such as randomized clinical trials, clinical cohorts, special clinics, and from a limited number of countries. Most usual rheumatology care is conducted without quantitative assessment of patients. These considerations led to the Quantitative Patient Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA) program, undertaken to promote quantitative assessment of patients with rheumatic diseases in daily clinical practice and to establish a multinational database with a goal of 100 patients in three clinics in each participating country. Between January 2005 and July 2007, the program was established in 22 countries, including 5519 patients, to provide a general overview of patients who receive usual clinical care. Future directions include expanding the program to all consecutive patients at participating sites, and in additional clinics in other countries, with the ultimate goal of improving outcomes for patients in many countries.

Quantitative measurement in rheumatoid arthritis (RA) has been greatly advanced over the last two decades. Recent research has indicated that aiming for a quantitative target value is associated with superior outcomes to usual therapy [1–3]. However, quantitative measures have been incorporated primarily into clinical research, such as clinical trials, rather than into usual clinical care. Most usual clinical rheumatology care continues to be conducted according to 'Gestalt' impressions, with laboratory tests as the only quantitative measures.

Clinical trials have provided invaluable data to help advance the treatment of RA and other rheumatic diseases. However, these trials involve only selected patients, as inclusion and exclusion criteria frequently leave fewer than 10% of patients eligible for participation [4,5]. Therefore, the findings may not be widely generalizable concerning RA patients in usual care.

In recent years, specialized databases have been established to assess certain patients with RA, such as those taking biological agents. These databases gather quantitative data from usual clinical care, but the patients again are selected – generally fewer than 25% of all patients. Furthermore, while the variables in these databases are 90% similar to one another, the formats are sufficiently different that the data can only be pooled for analyses with great complexity.

A few rheumatology sites have approached an ideal of collecting quantitative data from each patient at each visit in a standardized database [6–12], implementing a vision advocated by Fries in the 1970s that uniform databases from usual care of patients with rheumatic diseases could enhance more rational care and improve patient outcomes [7,13]. These efforts have provided valuable observations that are not available from clinical trials or even specialized clinical databases. However, most of these databases were derived from only one or few sites, and again were not amenable to pooling data for comparisons in a larger scale. Furthermore, quantitative measures are not available at all in certain countries. Therefore, most of the reported data concerning RA are based on a small, selected minority of all patients.

These considerations led to a program called Quantitative Patient Questionnaires in Standard Monitoring of Patients with Rheumatoid Arthritis (QUEST-RA), with two objectives:

- Promote quantitative assessment of patients with rheumatic diseases in daily clinical practice
- Establish a multinational database

The initial goal was that rheumatologists in three or more clinics in different countries review 100 nonselected consecutive out-patients with RA [14]. Between January 2005 and July 2007, the program was established in 22 countries: Argentina, Canada, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Poland, Russia, Serbia, Spain, Sweden, The Netherlands, Turkey, the UK and the USA. Each patient was assessed according to a standard protocol to evaluate RA (SPERA) [15].

Keywords: QUEST-RA, rheumatoid arthritis

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The rheumatologists performed a 15–20-min clinical assessment involving three domains, each on a one-page form:

- Review of clinical features, including classification criteria, extra-articular features, comorbidities and relevant surgeries;
- Record of all previous and present DMARDs, adverse events and reasons for discontinuation if the DMARD is no longer taken;
- Undertaking of a 42 joint count including swollen and tender joints, as well as joints with limited motion or deformity [16].

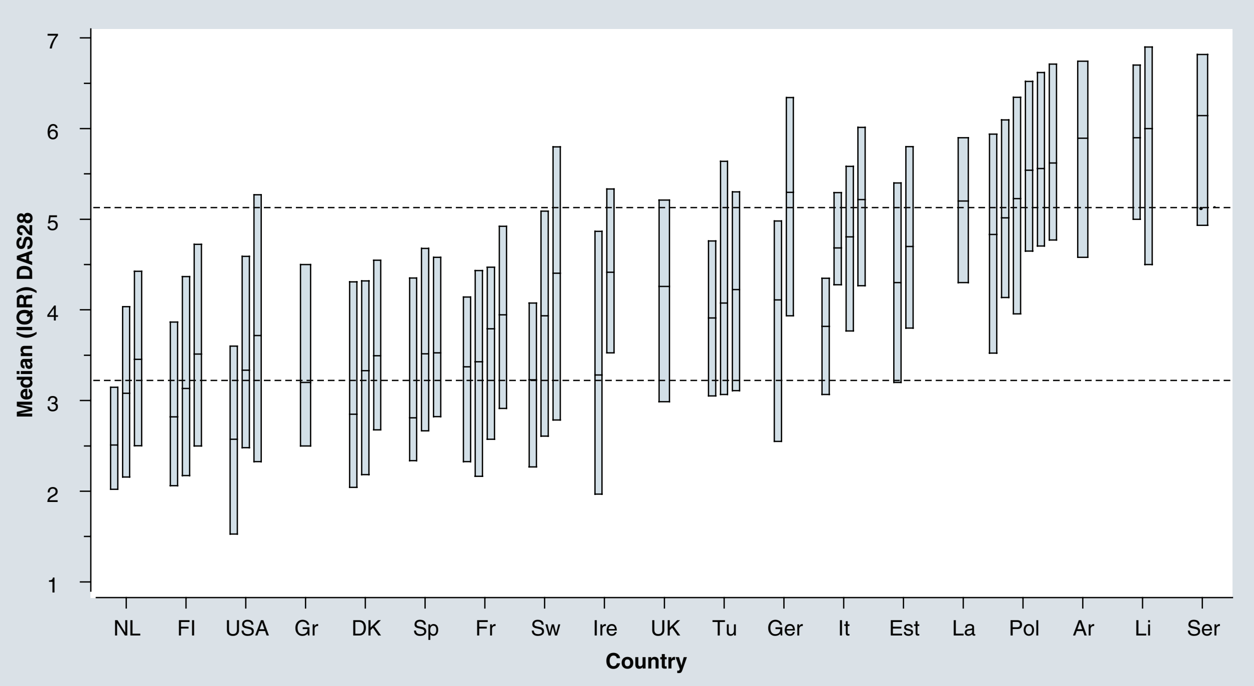
The review also included physician global estimate of disease activity, physician report whether or not the patient had radiographic erosions and laboratory tests for erythrocyte sedimentation rate (ESR) and C-reactive protein, and rheumatoid factor values. Disease activity score (DAS)28 was calculated for current disease activity [17,18].

The patients completed a four-page expanded self-report health questionnaire that was translated into the language of each participating country according to standard methodology. The questionnaire included the Health Assessment Questionnaire (HAQ) [19] to assess functional capacity in activities of daily living, visual analog scales (VAS) for pain, global status, and fatigue, self-report joint count [20], duration of morning stiffness, lifestyle choices such as smoking and physical exercise, height and weight for body mass index and demographic data including years of education and work status.

In July 2007, the QUEST-RA database included 5519 patients from 62 sites in 22 countries [14]. The demographic characteristics are those of a typical RA cohort with 79% females, more than 90% Caucasians, a mean age of 57 years and mean education level of 11 years.

In general, patients had active disease, with a median DAS28 of 4.2. Significant variation was seen between countries ($p < 0.001$), ranging from around 3 in The Netherlands and Finland to 5.7 in Lithuania and 6.1 in Serbia [14]. Among 48 sites at which more than 50 patients were enrolled, by April 2007 low disease activity of DAS28 less than 3.2 was observed in more than 50% of patients at seven sites in five countries: The Netherlands, Finland, USA, Denmark and Spain (**Figure 1**). These data extend observations that a minority of patients at some clinical sites would be eligible for most RA clinical trials due to low disease activity [4,5]. By contrast, more than 50% of patients had high disease activity of DAS28 greater than 5.1 in five countries: Latvia, Poland, Argentina, Lithuania and Serbia.

Figure 1. Disease activity according to DAS28 (median, IQR) in QUEST-RA per country and site.



Reference lines indicate low (DAS28 <3.2) and high (DAS28 >5.1) disease activity. Update from [14], with permission.

DAS28 and other outcome measures were associated with gross domestic product (GDP) in different countries [21]. These observations in QUEST-RA are consistent with extensive evidence that macro-economic variables concerning different nations provide significant explanation of variation in health outcomes. GDP predicts variation in overall mortality, infant mortality and life expectancy [22–24] in different countries, as well as outcomes of specific diseases, such as 5-year survival of cancer in 22 European countries [25].

Conclusion

The QUEST-RA program is the first study of patients with RA outside of clinical trials with an identical protocol in multiple locales, and provides an overview of patients who receive usual care in more than 20 countries. These data appear to be more generalized than data from single sites, specialized databases or clinical trials.

The QUEST-RA database contains extensive data that can be further analyzed to better understand demographic, macroeconomic, treatment and clinical variables which may contribute to differences in clinical status among patients with RA in different countries.

Future perspective

QUEST-RA may serve as an initial step towards a practice at participating sites, to assess quantitative measures in each patient at each visit. Further efforts will be directed toward quantitative assessment of all patients at all participating sites and at additional rheumatology clinical settings using electronic tools for more feasible data collection, storage and analyses. The ultimate goal of these efforts would be to improve outcomes for patients in many countries over the next 5–10 years.

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