The importance of the patients’ experience of RA compared with clinical measures of disease activity

P.C. Taylor

The Kennedy Institute of Rheumatology Division, Imperial College, London.

Please address correspondence and reprint requests to:
Peter C. Taylor, MD,
The Kennedy Institute of Rheumatology Division,
Imperial College London,
65 Aspenlea Road,
London W6 8LH, United Kingdom.
E-mail: peter.c.taylor@imperial.ac.uk

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ABSTRACT
Improvements in rheumatoid arthritis (RA) treatment have led to an increased focus on specialised and validated outcome measures, resulting in a decrease in the use of subjective assessments such as patient perceptions. However, to achieve optimal outcomes in the treatment of RA, there is a need to balance clinical goals with those that may be more important to patients. Although the treatment goals of physicians and patients are generally aligned, the framework in which these goals are expressed differs widely, and there are pronounced differences in how patients and physicians view their interactions regarding the decision-making process about treatment and information sharing. Detailed discussion between the physician and the patient regarding the patient’s perspectives can lead to valuable insights into the patient’s unmet needs from treatment as well as enhancement of the physician-patient relationship and an overall improvement in patients’ quality of life.

Introduction
The improvement in treatment of rheumatoid arthritis (RA) in recent years has led to a greater need for, and focus on, specialised and validated outcome measures. As a consequence, the focus of physicians has been drawn away from patients’ perceptions and the subjective reporting of individual experiences in favour of more clinical, objective measures of the disease. Since the presentation and clinical course of RA are highly variable between individuals and over time, there is a need to consider a balance between patient perspectives and clinical measures when considering optimal outcomes. The symptoms and signs of RA cover a wide spectrum, varying from pain, stiffness, swelling, and functional impairment to more constitutional complaints such as general malaise and profound fatigue. With time there may be progressive joint destruction and accompanying functional loss. As a result of this variety in disease expression, a large number of outcome variables have been used in recent decades in order to evaluate disease activity, presence of remission, response to therapy, progression of structural damage to joints, and functional status. In part, these evaluations have evolved in order to allow a robust and meaningful interpretation of the therapeutic benefit of new treatment interventions in the context of clinical trials. However, current tools to assess outcomes do not capture all of the factors that are important to patients.

The physicians’ perspective – a moving target
As the list of documented, achievable benefits has grown in the course of clinical studies conducted over the last two decades and, in particular, since the biologic era began with the introduction of anti-tumour necrosis factor (TNF) agents, the physicians’ perspective on the desirability of clinical outcome following treatment intervention has evolved accordingly. Thus, the modest aspirations of earlier years, to achieve some degree of improvement in symptoms and signs of disease, in particular pain, joint swelling, and stiffness, have evolved to embrace sustained low disease activity states or even remission (1-3), significant inhibition of structural damage to joints (1, 4), maintained or improved function (5-7), improved employment status (8) where applicable, and a reduction in the co-morbidities associated with maintained disease activity in RA (9, 10).

These evolving expectations of many rheumatologists with respect to desirable treatment outcomes must be tempered with the recognition that the optimum degree of inflammation suppression that is actually achievable will vary on a patient-by-patient basis. Considerable emphasis has been placed by regulatory...
bodies on the assessment of functional outcomes in clinical trials, and well-validated tools, such as the Stanford Health Assessment Questionnaire (HAQ) and its derivatives, have been developed in order to do this. It should be noted, however, that such questionnaires do not discriminate between the extent of functional impairment due to currently active disease (that is, process related and therefore potentially reversible) and the inevitable sequelae of long-term, irreversible joint destruction. In the United Kingdom, the National Institute of Clinical Excellence formulates its opinions on the cost-effectiveness of biologic therapies for RA on a health economic modelling based largely on HAQ changes (11). However, HAQ changes do not embrace all variables that impact quality of life from the patient perspective. The overall score does not indicate which particular area of health or daily activities constitutes a priority for improvement for any given individual. Furthermore, health preferences and perception of change in status may differ between patients and physicians. Thus, it is possible to see an overall improvement in HAQ score that is not necessarily accompanied by a subjective improvement in the health domain of greatest importance to the patient and vice versa. For many patients in the established phase of RA, trying to assess the level of current function on the basis of HAQ domain questions such as “can you lift a 5 lb sack of potatoes above your head?” has little practical meaning. With respect to inhibition of structural damage, it is important to recognise that many RA patients enrolled in clinical trials do not have demonstrable progression in damage scores over the course of the trial. Furthermore, when translating trial findings to routine practice, even those rheumatologists experienced in scoring radiographs may find it difficult to accurately assess whether a drug is impacting favourably on the rate of joint damage for a given individual based on a rapid outpatient evaluation of sequential radiographs.

The patients’ perspective
The viewpoint expressed by patients regarding their preferred goal of therapy may differ depending on the time point in his or her disease course during which the patient is questioned. In the case of recent-onset joint symptoms or an acute flare on a background of otherwise well-controlled inflammation, a commonly articulated desire is the wish to “feel well again,” or to “get back to normal” (12). However, many patients with persistently active RA become remarkably accepting of disease activity that when assessed as objectively as possible, for example by DAS28 or other criteria, would be considered moderately severe and meriting a change or escalation in drug therapy. This may reflect a number of processes, not least a learned coping mechanism and possibly a form of central nervous system modulation related to persistent inflammatory cytokininemia. It also represents a practical clinical problem for those rheumatologists who prefer to base their evaluation of the patient’s overall health on what is reported on questioning rather than on a quantifiable and more objective measure of disease activity. In such a case there is a real danger of under-treating inflammation that may otherwise be coupled with articular destruction and the evolution of co-morbidities. For example, a proportion of patients with established RA who respond well to biologic anti-TNF administration will report that they feel as if a persistent “flu-like” state had disappeared but that they had grown so accustomed to living with it that they had forgotten the subjective feeling of well-being. Another important element with respect to the patients’ experience concerns the factor of time. The primary concern of many patients is the subjective sense of well-being, or otherwise, as experienced in the present and recent past. In the early stages of RA, fewer will make the conceptual link between optimising the treatment of inflammation in the present, and thereby improving their sense of well-being as much as is feasible, with a reduction in longer term joint damage and loss of function but with the increasing risk of non-articular complications and, if relevant, employment status. However, once progressive disability has been experienced, many patients then experience considerable anxiety about their future. A further concern commonly expressed by patients relates to the perceived side effects of medication and also tolerability problems that have actually been experienced. If a physician fails to explain to the patient that any symptomatic benefit and, even more so, any advantage with respect to long-term outcome may not be immediately appreciated, then willingness to put up with a tolerability issue such as nausea will be greatly diminished.

Productivity and participation are also important patient-focused quality of life outcomes. Recent advances in the treatment of RA have extended the range of benefits to include productivity at work both outside and within the home. Certolizumab pegol is the most recently available therapy for RA, and has been shown to benefit patients on the traditional measures of signs and symptoms, radiographic progression, and physical function in combination with methotrexate (MTX) or as monotherapy (13-15). In addition, however, significant and clinically meaningful improvements in pain with certolizumab pegol plus MTX are rapidly reported 1 week after starting therapy (16, 17). Furthermore, certolizumab pegol improves work productivity outside the home and within the home, and participation in family, social, and leisure activities (18).

Shared goals, but varying emphasis
Although in reality the physicians’ and patients’ viewpoints are aligned and might broadly be expressed as focused on achieving the best overall state of well-being that is possible in both the short and long term, the framework in which this goal is expressed differs very widely. Despite physician goals having been met in terms of clinical outcomes, the patients’ overall treatment experience and well-being may not necessarily improve. Detailed discussion between the physician and the patient regarding the patient’s perspectives can lead to valuable insights into the patient’s unmet needs from treatment that may not otherwise be captured, particularly regarding pain and fatigue. Not surprisingly, pain is a
major concern for many patients. In a recent survey conducted via structured face-to-face interviews with 756 adult RA patients from the United Kingdom, France, Germany, Spain, and Italy, 34% of patients were very dissatisfied with the level of arthritis pain experienced in the past 30 days, and 75% reported experiencing moderate or severe pain in the past 2 months (19). There was a strong correlation between patients’ satisfaction with arthritis pain and with the other health areas such as fatigue (p<0.01). Increased pain across joints was the main reason that would prompt patients (83%) to make an unscheduled visit to their rheumatologist. When asked about how they believed RA would affect their lives, 31% agreed/strongly agreed, how they believed RA would affect their rheumatologist. When asked about increased pain across joints was the past 30 days, and 75% reported experiencing arthritis pain experienced in RA patients from the United Kingdom, face-to-face interviews with 756 adult recent survey conducted via structured pain control in RA in particular is an unmet need, since despite treatment with currently available agents, pain levels remain unacceptably high for more than one third of patients (19). Thus, in an extreme case, confusion might be anticipated for the patient who is under the impression that he or she is starting to take a “powerful” and perhaps “more risky” drug in order to prevent “Sharp score progression.” In distinction, the majority of patients will rapidly grasp the importance of controlling inflammation that might cause joint damage if left unchecked. The perspectives simply need to be communicated on a level of common understanding and within a framework of balanced and honest presentation of benefits and risk with respect to treatment interventions.

Summary
As recently shown in a survey of 756 RA patients and 501 rheumatologists across five European countries, there are pronounced differences in how patients and physicians view their interactions regarding the decision-making process about treatment and information sharing (20). It is very useful for physicians and patients to work together to set management goals that will permit a quality of life outcome from the perspective of the individual patient. Examples might range from being able to undertake work activities without physical difficulty, complete a round of golf, comfortably walk the dog, or stand in the kitchen for long enough to comfortably cook a meal through being able to undertake dressing and self-care activities independently. When the means to achieve such ends are presented in appropriate language to patients, with a realistic appraisal of likely outcome that maintains a positive focus, enhancement of the physician-patient relationship and overall patient satisfaction is the likely result. Thus, there are benefits as well as limitations to validated health outcome measures. Furthermore, patients’ reporting of needs varies over time and with their own individual experiences, and benchmarks to disease improvement may differ between the physician and the patient. In order to enhance the physician-patient relationship and improve the overall quality of life of the patient, it is important to identify and address patients’ unmet needs, not only by using health outcomes measures, but also by considering the overall state of well-being that may not be captured by the currently validated measures.

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