

# Patient Perspective: Reasons and Methods for Measuring Fatigue in Rheumatoid Arthritis

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**ABSTRACT.** The experience of fatigue has been reported by a large proportion of people with rheumatoid arthritis (RA), and it is often the most important problem for individual patients. A systematic analysis of patient focus group discussions revealed 3 overarching themes: fatigue is overwhelming and different from normal tiredness; it permeates every sphere of life; and self-management is variable, but professional support is rare. A systematic search for articles measuring fatigue discovered 23 scales, 6 of which have sufficient evidence of validity to pass the OMERACT filter. Some preliminary data indicate that fatigue measurement is sensitive to change induced by some interventions in RA. This issue, and the question of whether measuring fatigue adds additional information to measurements made using the current core set of measures, will be addressed at OMERACT 8. (J Rheumatol 2007;34:1171–3)

*Key Indexing Terms:*

PATIENT CENTERED VALIDITY OUTCOMES FATIGUE RHEUMATOID ARTHRITIS

## Patient perspective and outcome assessment at OMERACT

Rheumatoid arthritis (RA) is a systemic, inflammatory condition causing joint pain and swelling, disability, and psychological distress<sup>1</sup>. The experience of fatigue has been reported by a large proportion of people with RA, and its causality is likely to be multifactorial<sup>2–4</sup>. However, it was not included in the 7 internationally agreed core outcome measures in RA clinical trials<sup>5</sup>. Indeed, even though many potential outcome measures were considered in the series of international meetings that developed the core set, fatigue is not mentioned at all. The OMERACT group (Outcome Measures in Rheumatology Clinical Trials) was, with others, instrumental in developing the core set in RA, and at OMERACT 5 in 2000 the meeting turned its attention to the scores required in the core set measures for them to be considered to have truly changed in response to treatment. There were many technical arguments, but perhaps the most important development was the recognition that taking a patient perspective was required<sup>6</sup>.

At the following meeting, OMERACT 6 in 2002, specific provision was made for patient participants. At the Patient Perspective Workshop there were 11 patients from 7 countries, 5 organizing group members, and 41 other participants

from those attending the OMERACT 6 meeting. The workshop consisted of 3 formal sessions each of 2 hours, working group meetings between and after the formal sessions, and an unscheduled meeting of the patient participants<sup>7</sup>. One factor to emerge from the workshop was the clear message that other outcomes of importance to at least some patients include a sense of well-being, fatigue, and disturbed sleep. This stimulated new work on the prevalence, experience, and measurement of fatigue in RA.

## Is fatigue important in RA?

Much progress was made in several research areas identified by the Patient Perspective Workshop at OMERACT 6 when it came to reporting back to OMERACT 7 two years later<sup>8</sup>. From the point of view of fatigue, a quantitative study carried out in Ireland highlighted the importance of including fatigue as an outcome measure in RA. Women (n = 58) who participated in a quality of life cross-sectional study<sup>9</sup> were asked to rate the importance of various symptoms of RA. Pain emerged as the most important in the group as a whole. The authors reevaluated these women after 4 years' followup. Patients had not been asked to consider the importance of fatigue at baseline, but in light of the OMERACT 6 meeting this was included at the followup assessment. On this occasion, fatigue rather than pain emerged as the health status measure that patients now prioritized for improvement<sup>10</sup>.

This work illustrates the benefits of involving patients as partners in our research endeavors and highlights fatigue as an important outcome measure. Further support for this comes from a qualitative study that was performed using focus groups in 5 clinical centers in different UK locations<sup>11</sup>. Each group contained 6 to 9 patients with RA who were purposely

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sampled from local populations of patients to include men and women and a range of age, disease duration, functional disability, work disability, and current disease activity. Each group was facilitated by a researcher and lasted around 1 hour, and the discussions in each group were recorded and transcribed verbatim. The groups were asked to address 3 questions: What outcomes from your treatments are important to you? What makes you satisfied or dissatisfied with a treatment? How do you decide that a treatment is working?

The transcripts were read and reread, and themes were systematically identified and organized into groups and then into a report giving the meaning of the patient's experience that is grounded in their own words. In general there was strong concordance of central themes across all 5 groups. Fatigue was consistently mentioned as an important outcome, and patients distinguished between tiredness and a complete, systemic fatigue that was related to their arthritis. This outcome was seen as important because it affected other outcomes (functional activities, work, social activities) and contributed to an overall sense of well-being.

One of the conclusions from the Patient Perspective Workshop at OMERACT 6 was that the importance of outcomes should be checked across different cultures. In response to this, a Swedish group undertook a study<sup>12</sup> similar to that in the UK. Four focus groups in different geographical areas addressed the same questions. The broad thrust of the conclusions was in agreement with the findings in the UK study. Patients sought a reduction in oppressive fatigue, i.e., invisible and difficult to describe and quantify but acting to screen off reality.

In another study<sup>13</sup> a questionnaire listing the outcomes raised by the UK focus groups was sent to 323 patients in 3 UK centers. Fatigue and well-being were ranked as the most important issues after pain and independence, and as more important than joint symptoms.

To clarify the nature of fatigue, a qualitative study explored RA patients' descriptions of the nature of fatigue, and its cause, consequences, and management<sup>14</sup>. The systematic analysis revealed 3 overarching themes: fatigue is overwhelming and different from normal tiredness; it permeates every sphere of life; and self-management is variable, but professional support is rare. Vivid descriptions tell how daily life can be halted by the sudden onset of both physical components ("heaviness" and "wipeout") and cognitive elements ("enthusiasm's gone"). Patients believe fatigue is linked to RA inflammatory activity, poor sleep, and strain from working disrupted joints and muscles harder. Consequences are widespread ("It dumbs down everything") and affect not only physical activities but also normal social roles.

These advances in understanding the importance of fatigue formed the foundation of the Patient Perspective Workshop at OMERACT 7. Financial and organizational commitments ensured a wider representation of patients, so that participants included 19 patients from 10 countries, 5 organizing group

members, and about 155 other participants from those attending the OMERACT 7 meeting. The workshop consisted of 3 formal sessions each of 2 hours and working group meetings between and after the formal sessions. All participants heard an overview presentation on fatigue, summarizing what is reported above, and all discussion groups considered some aspect of fatigue (as well as other allocated topics)<sup>15</sup>.

The outcome of the workshop<sup>15</sup> was the clear conclusion that fatigue is an important and intrusive issue for patients. There was an urgent need to clarify measures of fatigue, ensure they are valid for use in RA, and introduce them more widely. The Patient Perspective Workshop took several questions to the final plenary session at OMERACT 7, where all participants in the conference had the opportunity to hear the main points emerging from individual workshops and modules and to pass a collective opinion about them. For fatigue it was argued that: the majority of patients have fatigue for the majority of the time; we do not yet have the evidence that measurement tools have been validated in RA; there are some treatments that seem to alter fatigue when it is measured; and omitting fatigue reduces the face validity of the core set of outcome measures in RA. Three motions were proposed, and the conference delegates voted substantial support for them: Fatigue is an important symptom in RA (95% agreed); measures of fatigue should be validated in RA (100% agreed); after further work, fatigue may warrant consideration for inclusion in the core set for RA (86% agreed).

### **Can fatigue be measured in RA?**

Once again, firm endorsement of the rheumatology outcomes research community helped to move the agenda forward, and a systematic review of fatigue scales used in studies of RA patients was carried out<sup>16</sup>. Articles measuring fatigue in RA were searched for using the terms RA and fatigue, and RA and tiredness, plus scale, questionnaire, inventory and checklist. Index papers reporting identifiable RA fatigue data were examined for the fatigue scale used. Index and validation papers for each scale were reviewed for evidence supporting scale validation to measure RA fatigue using a standardized checklist of content, face, criterion and construct validity, and sensitivity to change.

The search<sup>16</sup> identified 23 different scales that had been used to measure fatigue in RA patients. For most of these the authors could find no or limited evidence of validation. However, reasonable evidence of validation was found for 6 scales, indicating that suitable measuring instruments are available, although additional work on validity would be desirable. These included ordinal scales (which have not been used frequently), the SF-36 vitality subscale<sup>17</sup> (although this may measure a different concept than fatigue), the Multi-dimensional Assessment of Fatigue (MAF) scale<sup>18</sup>, the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) scale<sup>19</sup>, the Profile of Mood States (POMS)<sup>20</sup>, and visual analog scales (but these probably require some standardization).

## Is fatigue explained by other core measures? Can fatigue be changed in clinical trials?

These data on the validity of fatigue measures in RA have facilitated a new analysis of some existing databases where fatigue has been measured in RA patients in longitudinal studies and in some recent clinical trials. Results of this analysis were used to answer the 2 remaining questions about the measurement of fatigue. First, does the measurement of fatigue add additional information to measurements made using the current core set of measures? Second, are fatigue measures sensitive to change, particularly to changes that might occur in clinical trials? Some preliminary data on this were reviewed as part of the search for appropriate scales for measuring fatigue in RA<sup>16</sup>. Measures of fatigue are sensitive to changes induced by nonsteroidal antiinflammatory drugs<sup>21</sup>, following cognitive-behavioral therapy intervention<sup>22,23</sup>, following the treatment of anemia<sup>24</sup>, after exercise<sup>25</sup>, and after treatment with biologic agents<sup>19</sup>. One scale consistently showed fatigue was least at noon and worst in the evenings when measured 7 times per day over 7 days<sup>26</sup>. Taken together and after consideration of the detailed evidence available<sup>16</sup>, these studies strongly suggest that fatigue does change and that this change can be measured.

## Patient Perspective Workshop — Fatigue at OMERACT 8

The aim of the fatigue workshop at OMERACT 8 was to consider the evidence for the importance and measurability of fatigue as summarized here, and to take account of new data on the relative contribution of fatigue measurement to the overall assessment of RA. It scrutinized the validity of the concept and of the instruments available to measure it, and reviewed their performance in clinical trial and other data<sup>27</sup>.

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