

## It's Good to Feel Better But It's Better to Feel Good



A lot of effort has been made by the scientific rheumatology community to standardize the clinical evaluation of musculoskeletal disorders using a rational and scientific approach. The first step was to make a list of domains of interest (for most musculoskeletal disorders, the domains considered most important from a patient's perspective were pain and functional impairment, and from a doctor's perspective, inflammation and structural damage). The second step was to propose tools allowing evaluation of each domain [for example, a 0–100 mm visual analog scale (VAS) for evaluation of the domain "pain"]. Such tools are usually continuous variables and have intrinsic excellent metrological properties in terms of validity, reliability, and discriminant capacity.

Because of these characteristics, these tools have been largely used in clinical trials for evaluation of treatment modalities. The results of therapeutic trials using them are usually expressed at a group level as mean changes [for example, pain (VAS) decreased from  $62 \pm 12$  to  $34 \pm 15$  and from  $63 \pm 13$  to  $58 \pm 12$  in the active and placebo groups, respectively;  $p < 0.001$ ]. The difficulty for the clinician is interpretation (in terms of clinical relevance) of the results obtained and presented. In order to facilitate his or her critical appraisal of presented results, the clinician strongly favors presentation of results not at a group level but at an individual level, as a percentage of improved patients in each study group. To be able to present the results at an individual level while using a continuous variable, it is mandatory to determine a cutoff value of change in this variable above which a patient can be classified as "improved."

The methodology allowing definition of such a cutoff is not easy. Concerning symptomatic variables, one has to keep in mind the definition given by Jaeschke, *et al*: "the smallest difference in score in the domain of interest which patients perceive as beneficial and which could mandate... a change in the patient's management"<sup>1</sup>. If one can easily consider a longitudinal study with a baseline and a final visit to calculate the "difference" in the variable, the choice of the gold standard at final visit allowing us to classify a patient as improved is more debatable. Based on the above definition,

this gold standard could be either the decision to change the symptomatic therapy at final visit, or the overall patient opinion. This methodological question was debated during the OMERACT 2000 meeting in Toulouse and the conclusion strongly favored the patient's perspective<sup>2</sup>. Another difficulty also arises from the definition of "smallest difference" and "beneficial."

In this issue of *The Journal*, Pavy, *et al* report results of a study on ankylosing spondylitis aimed at proposing a cutoff for symptomatic outcome variables frequently used in ankylosing spondylitis (i.e., the Bath indices) based on the definition of a minimum clinically important difference<sup>3</sup>. In their study, the authors consider as a gold standard the overall patient opinion at end of study using a 15 point scale; for the statistical analysis, they converted the 15 point scale into a dichotomous variable: improved yes/no, where "good deal better," "great deal better," or "very great deal better" was considered as "improved." Several remarks can be made concerning this approach:

- The difference in score that patients perceive as beneficial is probably different from the difference in the score patients perceive as deterioration. The value of the minimum clinically important deterioration is usually of lower magnitude than that of minimum clinically important improvement<sup>4</sup>.
- Since the objective is to detect the "smallest" difference, one can argue that determination of the cutoff should not be extrapolated from the score obtained in the whole group of patients who perceive improvement (whatever the magnitude, from a "little" to "very great deal"); it should be derived from the score obtained in the subgroup of patients who perceive a clinically relevant improvement, even of moderate magnitude.
- Several studies have shown that such a cutoff is usually closely related to the baseline score<sup>5,6</sup>. Patients with a high score at baseline need a broad level of change to consider themselves clinically improved.
- Probably the most important point is to clearly define the concept under evaluation. In other words, is the main objective of the patient to be in better condition (concept of

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See Establishment of the minimum clinically important difference for the BASDI, page 80

improvement) or in good condition (concept of state)? Based on results obtained in osteoarthritis evaluating these 2 concepts (minimum clinically important improvement and patient acceptable symptom state) it appeared that the minimum clinically important improvement values for the symptomatic outcome variables (e.g., pain, patient global assessment, functional impairment) were closely related to the baseline scores but not the patient-acceptable symptom-state values<sup>6,7</sup>. In other words, whatever the level of symptoms at baseline, the main objective for the patient seems to be to reach a state they consider acceptable. It is obvious that the best condition is the absence of symptoms. This concept (absence of any symptom) is one of remission. For many musculoskeletal disorders and especially for specific domains such as pain and/or fatigue, this objective is very difficult to achieve. Therefore, alongside this concept of remission, the concept of low disease activity state is emerging.

For symptomatic outcome variables, the concept of patient-acceptable symptom-state is similar to the one of low disease activity state. When considering a disease as an entity (e.g., rheumatoid arthritis) the objective is to merge both the patient's and the doctor's perspectives. For this purpose, as we have seen, domains other than subjective symptoms have to be included in the definition of low disease activity state, for example, inflammation (e.g., C-reactive protein, number of sites of synovitis in rheumatoid arthritis). This concept was discussed during the OMERACT 2004 Monterey meeting and the results should appear soon in this journal<sup>8</sup>.

In conclusion, concepts of improvement and state are both important to consider. They enable us to present results of clinical research studies and, in particular, therapeutic trials at an individual level. This presentation is more meaningful for the clinician, especially since it allows the calculation of the number needed to treat. In this respect, the data presented in this issue by Pavy, *et al* are important to consider. These results should be compared across different sets of patients for a specific outcome variable (e.g., Bath Ankylosing Spondylitis Functional Index for evaluation of functional impairment in ankylosing spondylitis), as well as across diseases for a common outcome variable (e.g.,

patient's overall assessment, pain, etc.). The data obtained in different studies will, I hope, be discussed during international meetings such as OMERACT; such discussions should result in proposals of endorsed cutoffs for the concepts of improvement and state, for outcome variables to be used in evaluation of the most frequent musculoskeletal disorders.

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