

# OMERACT 5: International Consensus Conference on Outcome Measures in Rheumatology

OMERACT stands for “Outcome Measures in Rheumatology.” In all, five OMERACT conferences have now been held; this latest series of articles summarizes the work presented at the fifth meeting, held in Toulouse, France, May 4 to 7, 2000.

The acronym OMERACT was coined at the first conference held in Maastricht, The Netherlands, in 1992. OMERACT represents an international informal network, working groups, and gatherings interested in outcome measurement across the spectrum of rheumatology intervention studies. OMERACT strives to improve outcome measurement through a data driven, iterative consensus process. OMERACT has a five member Organizing Committee with members from three continents as well as a 15 member Scientific Advisory Committee composed of international opinion leaders from nine countries.

There has been substantial ongoing activity since OMERACT IV, held two years ago in Cancun. The designation of the Bone and Joint Decade has focused world attention on rheumatologic diseases. One event in this context was the meeting in January 2000 at the World Health Organization, held in conjunction with the International League of Associations of Rheumatology (ILAR), where the recommendations from a sequence of OMERACT meetings on rheumatoid arthritis (RA), osteoarthritis, lupus, and osteoporosis were presented.

In this era of evidence based medicine, agreement on the use of standardized endpoints, which have been shown to be responsive to change, is extremely important. This allows different studies to be compared and contrasted and the results combined to provide the best available estimates of benefit and safety and provide the basis for “best practices” to maximize the opportunity of improving the health of populations with musculoskeletal disease.

There continues to be close linkage to the Cochrane Collaboration in musculoskeletal diseases, since standardization of validated endpoints and designation of minimally clinically important differences for both benefit and adverse effects are critical for meaningful systematic reviews and the ability to combine results from different studies in meta-analyses. There are now over 25 completed reviews and another 25 protocols on miscellaneous diseases registered on the Cochrane Library Database of Systematic Reviews.

OMERACT 5 was attended by 171 participants from 19

countries. The conference comprised 4 modules, which are published in 4 parts as follows: Part 1 (Module 1) focused upon revisiting the methodologic classification of Minimal Clinically Important Differences (and moving into Major Clinically Important Differences); Part 2 (Module 2) examined Health Economics, to help establish a core set of data for cost-effectiveness evaluations; Part 3 (Module 3) looked at radiographic imaging to review response criteria for radiographs in RA trials; Imaging continues in Part 4, with a closer look at Magnetic Resonance Imaging (Module 3 continued), followed by Safety (Module 4), to establish a standardized data set for recording adverse effects and seeking agreement on a protocol to allow data on rare side effects to be collected from databases in different countries.

In Module 1, chaired by George Wells, OMERACT 5 revisited the concept of minimum clinically important difference (MCID). We were fortunate that new work had been carried out by Dorcas Beaton, Claire Bombardier, and colleagues that provided a useful framework for discussions in that it separates out the contributions of changes over time, within versus across patients, using means versus individual results, and of the differentiation between statistical significance and clinical importance. The discussions focused on the importance to the clinician and patient in the context of the individual patient (it has been suggested that the term MCID be expanded to MCIID — Minimal Clinically Important *Individual* Difference) to emphasize the focus on change in individual patients rather than the traditional approach of using mean results of the group of patients in each arm of the study, which does not provide information on the distribution of the magnitude of effect in individual patients. In RA, the American College of Rheumatology 20/50/70 and the EULAR Response Criteria have established generally accepted levels of minimal clinically important differences.

The focus at OMERACT 5 was therefore to look at not minimal but “major differences.” In osteoarthritis, the new criteria for MCID based upon the attributes recommended at OMERACT III and further developed in collaboration with OARSI were presented. These include both relative and absolute changes — an issue that was actively debated. Proposals for a research agenda to establish and obtain agreement on the MCID in back pain and osteoporosis were

also developed; the details can be found in the relevant sections.

The Cost Effectiveness Module was chaired by Sherine Gabriel and Mike Drummond. This subject was first discussed at OMERACT II in Ottawa in 1994. Sherine Gabriel has been leading a task force to follow up, which has resulted in a series of recent editorials in *The Journal* reviewing key issues including the value of utilities, the interface between economic evaluation and health policy, statistical problems in cost-effectiveness analyses, the use of trial versus observational study data, and the implications of using estimates based on single versus multiple endpoints, and from single trials versus metaanalyses. The task force discussions were also a stimulus to the interesting work presented by Maria Suarez-Almazor and colleagues, who look at the similarities and differences between health utilities derived from patients versus those derived from the general public; the latter allow utilities to be derived from generic questionnaires such as the York Tariffs that are used for the EQ5D (formerly known as the EuroQol). This OMERACT 5 module focused on applying generic strategies developed by the Institute of Medicine in the US to establish reference cases for economic evaluations for the major classes of intervention in rheumatoid arthritis, osteoarthritis, osteoporosis, and lower back pain. A survey was sent to a number of opinion leaders asking them to identify the items that should be included in any cost-effectiveness study. There was broad agreement on most items, but a number of controversial issues were identified when applied to these specific rheumatologic areas; these formed the basis for small group discussions at this meeting. It is proposed that the results of these small group discussions be applied to developing case studies in the relevant rheumatologic categories.

The Imaging Module was chaired by Desirée van der Heijde, Marissa Lassere and John Edmonds. The module consists of two sections, one on x-ray imaging and the other on MRI. In the x-ray imaging component several approaches to defining an MCID were discussed. The discussions on the smallest detectable difference (SDD) approach and an approach where MCID were derived from expert panels were supported by studies performed since OMERACT IV. Participants agreed that these approaches were valuable as a starting point, but are most likely setting-specific. A predictive, data-driven MCID is the ultimate goal but is not available now. At present, analyses based on the group results (i.e., differences in means or medians) should remain primary in clinical trials. Reporting the SDD in each study is useful as a quality measure; reporting the number of patients meeting that threshold is useful as a secondary outcome measure. Much useful data on the SDD and the extent to which it is influenced by variables such as the different observers and changing the order of films divided into an important database would ensure that these discus-

sions were “data driven.” The research agenda set up at OMERACT IV includes many other issues not discussed at this conference. All these research questions would benefit enormously from the establishment of a database of radiographs of clinical trials. It may be worthwhile having the OMERACT participants re-examine the basic attributes (i.e., how many clinicians will change their behavior on the basis of a change in new erosions, erosion scores vs joint space narrowing). The same discussions also need to take place in other diseases such as osteoarthritis.

Magnetic resonance imaging is a fast moving field and part of this OMERACT’s focus on imaging was to review the center where work is now being done to meet the requirements of the OMERACT filter. Agreement on scoring is pivotal if studies are to be comparable and the current status of different approaches to establish a reproducible method based upon a series of MRI images were compared and recommendations for taking this further were made.

The fourth module, Drug Safety, was chaired by Peter Brooks and Ric Day. This area has been a focus in OMERACT III and IV. Two major initiatives were discussed in detail at OMERACT 5. The first was a proposal to develop a large patient population cohort for longterm safety monitoring in RA. This would consist of a combination of product-specific registries to follow a cohort of RA patients who receive a newly approved therapy, and the development of a much larger cohort of RA patients treated with multiple second line agents, to enable case-controlled determinations of the relative incidence of events in the treated registry patients versus the larger disease population. This involves developing agreement of linkage between a number of large databases worldwide to develop standardized data collections to allow a systematic approach to detecting events that occur rarely or over a longer period of time than will be detectable during the preregistration Phase III clinical trials. Good progress was made in this regard.

The other initiative was the standardization of the assessment of adverse effects in rheumatology clinical trials, so that they meet the new international guidelines as well as allowing for easy comparison of results. Those developing new studies are encouraged to incorporate this instrument so that experience can be obtained on how well it performs.

Much was achieved during this OMERACT, and there was general agreement that the research agenda requires ongoing work by the appropriate task forces and needs to maintain momentum in the interim before the next OMERACT meeting.

As before, we would thank the many individuals who have contributed to making OMERACT 5 a success. We also take this opportunity to thank our corporate sponsors for their ongoing support of the OMERACT process and for their input into both content and financial matters to ensure the continuity of the OMERACT process. OMERACT

committee members and sponsors are listed in Acknowledgments. We look forward to working with the Scientific Advisory Committee and Business Advisory Committees to ensure broad input into the future OMERACT agenda.

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