EULAR’s “Toolbox” for Patient-Reported Outcomes (PRO) and other Indices and Measures in Rheumatology

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The European League Against Rheumatism (EULAR) is the organization which represents the patient, health professional, and scientific societies of rheumatology of all the European nations. EULAR endeavors to stimulate, promote, and support the research, prevention, treatment, and rehabilitation of rheumatic diseases. To manage and promote its goals effectively, EULAR has set up a structure of committees and managerial bodies. One such committee is the Epidemiology and Health Services Research Committee; it is responsible for the toolbox.

In November 2009, a workshop on EULAR’s priorities in PROs was held in Zurich. A research call on PRO projects came out of that workshop, which is now on-going. Additionally, it was then established that the European researchers, rheumatologists, health professionals, and patients should be acquainted with all cross-cultural validated instruments that measured constructs of PRO with a potential use in rheumatology. Furthermore, it was proposed to generate a toolbox or catalog with the available instruments that should be available on the EULAR website. EULAR could act as an ongoing clearinghouse for providing informed opinions on validated instruments on PROs and other sorts of measures with support from the national societies. This initiative would be also useful in detecting major gaps in PRO instruments (e.g., the need for cross-cultural adaptation).

Such an initiative could have an effect on several important strategic aspects: 1) to reduce variability across Europe—the use of instruments in research based on scientific grounds, this is the level of validation achieved and appropriateness for the clinical situation; it will improve the scientific level of projects and will reduce variability among those countries with lower development or support on methodological matters; 2) to increase transparency—the methodology for including instruments will be explicit, and a way to capture instruments with validation in all European languages will be designed; 3) to increase the awareness of researchers outside the field of rheumatology—EULAR has the opportunity to become a leader on the evaluation and dissemination of PROs, as the toolbox will have open access; and 4) to educate the rheumatology community on the concepts of measure and validation of instruments, and on the importance of using the right tool in the appropriate way.

The main objective of this project is to develop a structured design “toolbox” freely available online which would include a comprehensive database of validated instruments (indices, questionnaires, scales, or others), with an emphasis on PROs used in rheumatology. The aim is to elaborate a database with a detailed description of each instrument, including the instrument itself, its versions in the EU languages; a description of the population(s) or settings where it has been validated; recommendations and rules for use (data collection and scoring method); a guideline for interpretation of the results in clinical practice or in research;
references and validated translated versions in the EU languages with a download (if possible) or a link to an access page; and a measure of the level of validation achieved or grade of recommendation.

As a secondary objective, we aim to improve the knowledge and interest of the European rheumatology community on quantitative measurement and validation by including educational tools, such as a glossary of specialized terms or materials explaining the process of validation. If deemed feasible, we aim to establish a central methodological support system for the trans-cultural validation of instruments.

The toolbox is led by two junior researchers, Isabel Castrejon, Hospital for Joint Diseases, New York, US; Laure Gossec, Cochin Hospital, Paris, France; and by Loreto Carmona, Universidad Camilo José Cela, Madrid, Spain. Many other participants from more than six European countries so far are collaborating in the project, including a patient representative and assessors from previously launched catalogs, such as PROQOLID or BiblioPro.

**On-going work**

The proposal includes several work packages (WP) that run in parallel or consecutively (See Figure 1).

The first such work package is aimed to develop the toolbox, and up to 15 methodological collaborators participate in it. The work package includes three actions: a half-day meeting, the development of the requirements, and a call for an IT solution.

The launch meeting already took place in Madrid in December 2011. There it was decided the toolbox’s aims and scope, items to include, and basic requirements. The meeting was extremely productive and the main decisions for the basis of the toolbox were taken (See Table 1 for a list of decisions).

At this moment, the data collection form is being developed by some of the researchers and will soon be sent out for validation by the rest of the team. Since some requirements for the IT solution were already set at the first meeting, once the data collection form is finished and validated, IT companies will be approached for proposals.

In a second work package, the aim is to feed the toolbox; there will be two phases. In the first step, we will feed the toolbox based on systematic reviews of the literature on the most relevant quantitative clinical measures in rheumatology, including questionnaires, scales, and indices. Some projects in the EULAR PROs call already include such reviews, and therefore will be used for the feed. Additionally, we are already searching for instruments developed in lupus, which are not covered by the on-going projects (See Figure 2).
An important aspect of the toolbox is its sustainability. In the Madrid meeting, it was thought useful to establish a system for feeding and updating the toolbox to resemble the Cochrane Collaboration. This system implies developing clear instructions and identifying contacts, which will be responsible for keeping a domain, a disease, or an instrument updated, whatever they propose.

The initial proposal of the project contemplated a third work package on education, preferably both through materials uploaded in the web page plus methodological support. In Madrid, it was decided that the educational tool should be mainly static, without formal support besides revising the contents eventually. The educational tool will cover the following aspects: a glossary, which will include explanations on the different psychometric concepts, the explanation of how the color-scale grid was created, generic warnings on common misuses of PROs, and validation issues. The proposal of a central facility to help researchers methodologically was not supported.

In summary, the toolbox is an on-going project led by rheumatologists and related professionals and patients that should help to choose the right PRO for projects in rheumatic diseases. It is foreseen that, compared to other available PRO catalogs, this toolbox will be more restrictive in terms of instruments (only those used in rheumatology) but with more languages available. Eventually, the toolbox may find what gaps exist on diseases, domains, or validation completeness.

Table 1.

Decisions taken about the toolbox in Madrid, December 2011.

| Aim | The aim of the toolbox is to provide and to advise on PROs on a user-friendly manner albeit based on sound scientific measurement principles. |
| Scope | Despite a will to be reactive to what the rheumatology community may wish to see included in the catalog, it must be understood that the toolbox needs some framing of its use and mission. |
| | • The toolbox will include PROs; that means it will contain instruments that measure constructs that are important for the patient, whether they are separated questionnaires, scales, or profiles, or they are part of a composite measure. |
| | • The PROs to be included will cover any domain, with an emphasis on those framed on the ICF (International Classification of Functioning), whether they are generic or specific; being the target all the rheumatic diseases, with an initial focus on rheumatoid arthritis (RA), osteoarthritis (OA), spondylarthritis (SPA), low back pain (LBP), systemic lupus erythematosus (SLE), gout, osteoporosis (OP), and fibromyalgia (FM). |
| | • Since the toolbox will be a repository of instruments available in EULAR countries, the PROs included should have been validated in at least one of the EULAR languages, and it will be recommended that at least a communication version in English be published. |
| | • Any PRO included should have any level of documented validity, be this complete or not, as long as it is available in a peer-reviewed journal. |
| Users | The intended users of the toolbox are rheumatologists, health professionals, patients, researchers, practitioners, etc; in other words, any potential user of PROs in rheumatology. |
| Information to include | • Concept or construct being measured by the PRO |
| | • Explanation and conditions of use with references |
| | • Disease(s) for which it may be used (some validation exists), including a category generic / all diseases |
| | • Domain |
| | • Instrument (original and validated versions) |
| | • Validation completeness and appropriateness by means of a color grid based on the COSMIN* checklist |
| | • Importance for patients |
| | • Interpretation and scoring if available |
| External researchers |

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During 2011, the Australian Health Outcomes Collaboration completed a major project on the clinical validation of the revised incontinence and patient satisfaction tools for the Department of Health and Ageing.

These tools include the Revised Urinary Incontinence Scale (RUIS) and the Revised Faecal Incontinence Scale (RFIS), which are short, five-item measures suitable for both epidemiological and clinical applications.

Data analyses indicated that the RUIS and the RFIS have excellent psychometric properties. The RUIS and the RFIS performed well in clinical settings demonstrating:

- Adequate to good internal consistency reliability and test-retest reliability in both clinical and population samples (>0.70)
- High and significant correlations with other measures of incontinence
- Good evidence that these instruments were sensitive to changes in continence status as a result of treatment, making them suitable for outcome evaluation.

The RUIS and RFIS items and the scale total scores also discriminated well in relation to other clinical indications of severity and between people with differing levels of incontinence severity. The measures both had superior psychometric properties when compared with other commonly used measures for incontinence assessment.1

The Short Assessment of Patient Satisfaction (SAPS) is a short, reliable, and valid seven-item scale that can be used to assess patient satisfaction with their treatment. The SAPS is a generic measure of patient satisfaction. In 2006,2,3 a study was undertaken to examine a number of the leading patient satisfaction scales with urinary incontinence patients. The items from all these patient satisfaction scales were pooled and the SAPS was developed by selecting the items with best measurement properties and the most comprehensive coverage of the domains of patient satisfaction. The SAPS consists of seven items assessing the core domains of patient satisfaction which include treatment satisfaction, explanation of treatment results, clinician care, participation in medical decision-making, respect by the clinician, time with the clinician, and satisfaction with hospital/clinic care. Response scales are five-point scales.

The recent study has shown that the SAPS is a valid and reliable measure of patient satisfaction. Reliability is Cronbach’s alpha $\alpha = 0.85$; it correlates highly with other measures of patient satisfaction, and correlates well with other indicators of treatment outcomes. The findings concerning the SAPS also indicate that it is sensitive to changes in patient status as a result of treatment with those patients reporting the greatest levels of improvement also reporting higher levels of satisfaction with their treatment.

The scales and the associated validation report and the technical manual have been added to the PROQOLID database to enable access and further information is also available from Associate Professor Janet Sansoni at janet.sansoni@grapevine.com.au.

As a result of recent National Health Reforms, the Australian government now has sole responsibility for the provision of aged care to people over the age of 65 years across most of Australia. With this increased responsibility, the opportunity to improve care arrangements and to streamline aged care assessment processes is available so it is now timely to use this opportunity to align the levels of aged care assessment with a continuous record, and do this in a planned and systematic way. Currently we are working with the Australian government to streamline and revise assessment processes for aged care. This ranges from the assessment of those elderly people who require a few low-level community support services to those who need access to more substantial community support packages, transitional or respite care, and/or to be assessed for eligibility for residential care. For those interested in this project, further information is available from the e-mail contact above.

Highlights from the EORTC 50th Anniversary Conference
50 Years of Progress Against Cancer
March 15-16, 2012 in Brussels, Belgium

A perspective and focus on progress in quality of life

Prof. Jean-Yves Blay, then discussed the challenges facing the EORTC after a half century and, remarking that medicine is becoming more and more a hard science with multidimensional complexity, he pointed out that medicine needs to define its problems in a way similar to how the mathematics community has defined its problems over the centuries and has tried to solve them together. He then offered 20 questions that need to be addressed by the medical community over the next 20 years. Some of them are organizational, such as how to organize the healthcare systems to ensure optimal care for all patients; and some are scientific, such as how to recognize the driving mutations in individual patients to guide treatment.

Patients were well represented by Mr. Peter Kapitein from Amsterdam. His inspiring message was that while we have achieved a lot in oncology, we still need to work hard to continue to move forward. His motivating talk, which contained visually stimulating slides, was brilliant and moved many of the attendees. Prof. Meunier then made an excellent presentation about the history of the EORTC and how the organization came into existence; She also discussed the key issues of European cooperation and future challenges and directions that the EORTC could address in the future.

A comprehensive talk from DG Research of the European Commission was given by Dr. Ruxandra Draghia-Akli, regarding the high cost of research in drug development. She raised the important topic of public-private initiatives, the importance of linking European researchers and fostering translational trials, and referred to the creation of the Innovative Medicines Initiative (IMI).

The former EORTC President, Prof. Alexander Eggermont, currently Director General of the Gustave Roussy Cancer Institute, France, gave an excellent and scientifically based presentation on the changing paradigms for melanoma cancer care and research. He stressed that cancer medicine needs to advance in line with improved technology, and much of this can lead to improvements in patients’ QOL.

Prof. Emiel Rutgers then spoke about the importance of surgery in breast cancer studies and the need to standardize procedures. He maintained that this can both help save lives and improve outcomes. He also discussed the importance of training surgeons and also of volume and outcome relationships.

The eminent Prof. Jean-Claude Horiot made an excellent overview of the last 50 years of EORTC achievements in radiation therapy. He presented dozens of ground-breaking Phase III trials that have set the standards for the care of patients across many disease sites. His presentation clearly showed the significant achievements radiation oncology has had over the entire span of the EORTC’s existence.
Prof. Patrick Schöffski, Head of the Department of General Medical Oncology and the Laboratory of Experimental Oncology at the University Hospitals of Leuven, Belgium, presented an historical overview of key EORTC achievements with a focus on the use of drug treatments for solid tumors. He highlighted that as history has unfolded, EORTC trials have led to significant improvements in cancer treatments, such as improved treatments for lymphoma, Hodgkin’s disease, and many other treatments such as the key trial on larynx preservation and how this massively improved patients’ QOL.

Prof. Michel Henry-Amar presented the impressive research history of the EORTC Lymphoma Group and the significant work they have conducted, including many long-term studies on fatigue and QOL.

While each speaker touched on QOL issues, the main conference speaker concerning QOL was former EORTC Quality of Life Group (QLG) Chair Galina Velikova. Prof. Velikova noted that Health-Related Quality of Life (HRQOL) is an integral part of EORTC clinical trials and has been implemented in the EORTC for 30 years. The QLG was created in 1981 with the mission of developing measures of patient-reported outcomes in cancer, including HRQOL, and of promoting and coordinating clinical studies concerning the quality of life of cancer patients. In parallel, the EORTC Quality of Life Department (QLD) has provided support to all cooperative groups and has enabled them to conduct clinical trials that implement HRQOL measures. Prof. Velikova remarked that this excellent partnership and the dedication of the QLD have led to the success of QOL across EORTC studies.

Prof. Velikova went on to explain that the QLG is a leader in the development, validation, and implementation of the EORTC QLQ-C30, a general cancer HRQOL questionnaire whose development and validation is the most notable achievement of the QLG. First published in 1993, it has since then been validated in many European countries, translated into over 70 languages, and is the most widely used cancer questionnaire in randomized trials in oncology, as demonstrated by several systematic reviews. User agreements for the EORTC QLQ-C30 have been signed off in more than 9,000 clinical trials or academic studies worldwide. In addition to the EORTC QLQ-C30, there is also a portfolio of supplementary modules that are cancer site-specific or treatment-specific.

Prof. Velikova mentioned that there are many examples of practice-changing EORTC trials that have included QOL measurements using the EORTC QLQ-C30. HRQOL is an integral part of most EORTC clinical trials, and has been systematically implemented over the last 15 years. Over 170 clinical trials, many of which were designed by Dr. Andrew Bottomley, head of the QLD and EORTC’s Assistant Director, have contained an HRQOL element, but typically as a secondary endpoint study. However, most regulatory bodies, such as the European Medicines Agency and the United States Food and Drug Administration, now fully accept HRQOL as a valid endpoint.

A study in glioblastoma conducted by the EORTC Brain Cancer Group investigated the addition of concomitant and adjuvant temozolomide to the standard treatment with radiotherapy and demonstrated that temozolomide significantly improved survival without a negative effect on HRQOL.1 This treatment is now the standard of care in newly diagnosed patients with glioblastoma.

Prof. Velikova also highlighted the EORTC’s largest ever performed meta-analysis of HRQOL data from the EORTC QLQ-C30, a study designed and conducted by Dr. Bottomley. The data in this study were based on information provided at baseline by 7,417 patients. This large-scale study took over three years to complete, but the results, published last year in Lancet Oncology, provide the most robust and compelling evidence to date that HRQOL scores can provide additional prognostic information and can be used to assist in the prediction of survival in cancer patients.

The final day of the conference offered excellent presentations. Prof. Martine Piccart presented details of the progress achieved in clinical trials in breast cancer and highlighted the complexity that we can expect in newer clinical trials given current advances in personalized medicine. She highlighted the challenges often encountered when trying to carry out international studies and pointed out that, unfortunately, many of the barriers encountered ten years ago are still in place today.

Dr. Denis Lacombe, EORTC Headquarters Director, made an exemplary and comprehensive presentation of the current state of the EORTC and the challenges it faces. He stressed that the EORTC is unique as a Pan-European multidisciplinary clinical trial infrastructure. A key message from Dr. Lacombe was that his loyal staff is essential for the effective operation of the highly complex, multinational, and multidisciplinary organization which is the EORTC.

The last session of the conference focused on the future challenges and perspectives for the EORTC and included an excellent talk by EORTC President-elect Prof. Roger Stupp. Under Prof. Stupp’s guidance, the EORTC’s future looks bright, and that of QOL research even brighter. He has been a long-term supporter of QOL and, certainly, his efforts in glioblastoma...
in this regard have been well recognized. Overall, the EORTC 50th Anniversary Conference was a landmark in the history of the EORTC and a complete success. Congratulations must go out to Prof. Meunier, the entire organizing committee, and internal conference management team, who pulled together such a successful and smooth-running conference.

Without question, QOL assessment is now fully integrated into the EORTC, and the future of QOL looks promising. The EORTC QLG and QLD will be leading the way in terms of instrument development, training, education, as well as policy making and working with key legislators. The dedication of the management, staff, and volunteers within the EORTC headquarters, and of the clinicians, founders, and supporters, means that the EORTC will move forward into the next 50 years in a strong position, one that can only lead to improved collaboration and benefits for patients in terms of better survival and, importantly, better understanding of QOL.

Finally, all of this would not have been possible without the vision of Prof. Françoise Meunier, EORTC Director General, who set up the QLD over 20 years ago. She and the QLD proved the importance of QOL; she turned a dream into reality. Her vision was spot on, the QLD certainly proved Prof. Meunier right, and she would certainly not expect anything less.

All EORTC 50th Anniversary Conference presentations can be viewed online (www.eortc.org) as can a short film, The Energy of Hope, about the EORTC.

**Highlights from the EORTC 50th Anniversary Conference pp. 5-7**

**Obesity in childhood and adolescence is a growing public health concern in China. In 2010, the prevalence of obesity was 13.33%, 5.64%, 7.83%, 3.78% and that of the overweight was 14.81%, 9.92%, 10.79%, 8.03% for urban boys, urban girls, rural boys, and rural girls-ages 7-22 years old,respectively.**

As the obesity rates have increased, finding out what the perceptions of Chinese youth are regarding their weight is an important step for intervention planning and for developing outcome measures to test the effectiveness of these interventions.

QOL is a broad and global concept affected in complex ways by the person’s physical health, psychological state, level of independence, social relationships, and the person’s relationships to salient features of the environment, such as, living in a safe neighborhood, or availability of parks or opportunities for recreation. QOL is of particular importance to assess in overweight and obese youth because perceived QOL impacts are more prevalent than somatic comorbidities at younger ages.

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Youth quality-of-life research in China is still emerging. Most studies simply translate English instruments without qualitative content research and validation. Some studies have used QOL instruments designed for adults. Quality-of-life measurement for obese/overweight youth using generic instruments has been reported. However, youth weight-specific QOL has been little reported in China.

**NEWS FROM...**

Progress of Chinese Adaptation of Youth Quality of Life Instrument – Weight Module (YQOL-W)

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A recent review found that obesity is associated with lower QOL in children and adolescents across multiple domains including overall health-related quality of life, social functioning, physical functioning and psychological well-being. Little qualitative research has evaluated how adolescents of different sexes, age, and ethnicities define their weight-specific QOL and even few QOL instruments have been developed based on qualitative research with obese and overweight youth.

Youth quality-of-life research in China is still emerging. Most studies simply translate English instruments without qualitative content research and validation. Some studies have used QOL instruments designed for adults. Quality-of-life measurement for obese/overweight youth using generic instruments has been reported. However, youth weight-specific QOL has been little reported in China.
The aim of the study is to develop Chinese adaptations of the Youth Quality of Life Instrument – Weight Module (YQOL-W) developed by Seattle Quality of Life Group\textsuperscript{1,6,12,14} to facilitate relevant research in China and cross-cultural comparison through linguistic validation, qualitative research, and establishment of cross-sectional and longitudinal measurement properties. This will help in designing effective weight management and obesity prevention strategies that are informed by what is considered important to youth; translating and applying established research evidence to practical solutions within China.

So far, linguistic validation of the Chinese YQOL-W version has included two forward translations, a back translation, and participant cognitive interviewing. In the following qualitative research, an adaptation of the grounded theory method guided data collection and analysis. In testing the existing conceptual model in the Chinese context, 22 semi-structured individual interviews were conducted with Chinese youth aged 11–18 exploring areas of life, goals, concerns, and worries associated with weight and weight management. Adolescents were recruited and interviewed until little new information was added and subject matter became redundant with previous interviews. The interviews were audio recorded and transcribed verbatim for use in analysis. A thematic analysis was conducted to identify and match themes in the data to the existing YQOL-W items. Five Chinese culturally relevant items were developed: “Because of my weight, I feel I am not as good as others my age,,” “I feel upset when people my age tease me about my weight,” “Because of my weight, it is difficult for me to get a good grade in physical education class,” “Because of my weight, I am uncomfortable around people I do not know,” “Because of my weight, I worry that other people will limit my opportunities in life.”

The next step will evaluate the measurement properties of the Chinese YQOL-W including reliability, validity, responsiveness, and interpretability.

ACKNOWLEDGMENTS

This work was supported by a grant of China Medical Board Young Faculty Seed Grant in Health Policy and Systems (HPSS).


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NEWS FROM...
The Patient-Reported Outcome Measurement Information System (PROMIS®): International Update

San Keller, MS, PhD, Principal Investigator

Helena Correia, Translation Manager

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The Patient-Reported Outcomes Measurement Information System (PROMIS®) seeks to provide a common language for describing lived health and the effectiveness of health interventions—a system that can be embraced universally. PROMIS is designed as a health-focus concept rather than disease-focused measurement system which includes, for example, measures of emotional distress, social functioning, pain and many other aspects of health. To be clear, PROMIS is appropriate for use in studies of a single disease and single therapy; in addition, the health-domain focus enables description of the impact of multiple comorbidities and polytherapy, which is appropriate to the experience of most patients and an aging population.

Begun in 2004, and sponsored by the US National Institutes of Health (NIH) Common Fund (http://commonfund.nih.gov/promis/),1 PROMIS item banks for each health concept are scored according to Item Response Theory (IRT) to enable administration via Computer Adaptive Testing (CAT) technology for ease of use and reduction of respondent burden.2 The objective is to standardize the metric of the health domain, even though patients are asked questions customized to their level of health.3 Studies to date demonstrate the success of this method in maintaining precision while reducing the number of questions asked of the respondent.4 The PROMIS network is in its second funding cycle and has expanded to include 13 primary research sites supported by three centers of excellence (for more information, see: http://nihpromis.org).

Since the last publication about PROMIS in this newsletter five years ago,5 the PROMIS system of five item banks has expanded to include IRT calibrated assessment of 21 health concepts for adults, and nine for children, with many more item banks under development (see first column of the table below for a list of calibrated item banks). A multi-cultural perspective was incorporated into PROMIS item-bank development at the outset by requiring each item to undergo a systematic evaluation protocol called “translatability and cultural harmonization review.”6 This assessment identifies potential conceptual or linguistic difficulties inherent in the proposed item design which may be addressed through item revisions or, in rare cases, may require that the item not be used because it is highly specific to a particular culture.

The translation method used by the PROMIS network is a systematic, multistage process of forward and backward translations and multiple reviews that are characteristic of the most effective multinational translation protocols.7 A universal approach to translation has been adopted, seeking to produce one language version for multiple countries instead of country-specific versions of the same language.8 The initial focus of this approach is to identify the commonalities rather than the differences, ensuring that the translation does not contain wording that is offensive or inappropriate to a particular subgroup. Pre-testing with cognitive debriefing in the target country/countries confirms the appropriateness of the translation or results in modifications.

Nearly all PROMIS banks have been translated into Spanish and a few are also available in German. Currently, almost all calibrated adult item banks as well as the pediatric item banks are being translated into Dutch, Portuguese, and Mandarin Chinese. The Emotional Distress adult and pediatric item banks are also being translated into Hebrew. Groups of researchers in Canada and Japan have initiated collaborative arrangements to seek funding and coordinate item bank translations into French and Japanese respectively. PROMIS translation activities are coordinated by the PROMIS Statistical Center (PSC) which seeks to ensure uniform quality across these efforts and harmonization between languages. While the PSC is involved in most of the measure translations, it grants permission to other organizations to conduct translations and/or collaborates in translation projects initiated by other investigators or organizations.

The table below summarizes the status of PROMIS adult and child item-bank translations. PROMIS also includes fixed-format assessments for most item banks in a variety of lengths. The fixed-format assessments encompass fewer items than the item-bank assessments and so many more language translations are either available or in process for those including Italian, Danish, Norwegian, Swedish, Korean, Afrikaans, many Slavic languages (e.g., Bulgarian, Hungarian, Lithuanian, Latvian, Polish, Russian, Romanian), and many Indian languages (Bengali, Gujarati, Hindi, Kannada, Marathi, Malayalam, Punjabi, Tamil, and Telugu). As might be expected, the most translated item banks are those that were developed first: anger, anxiety, depression, fatigue, pain behavior, pain interference, physical and social functioning: each of these has four or more translations complete or in process.

During this second funding cycle, the PROMIS network of investigators is engaging with investigators from other countries to promote the development of PROMIS internationally. Investigators in Germany have received funding from the German government to clinically validate the PROMIS pediatric item banks when translated versions are available. The 18th Annual Conference of the International Society of Quality of Life Research (Denver, Colorado, USA, October 2011) was the occasion of an informational exchange and brainstorming session among PRO investigators from Australia, Canada, France, Germany, Spain and the UK, many of whom had been involved in the IQOLA and Who-QOL projects.
This meeting gave rise to a partnership including the six countries and associated institutions. This collaboration is applying to the European Union for funding to adapt and integrate PROMIS for use in comparative effectiveness research in countries belonging to the EU. Other international collaborations are in the planning stages. These include the integration of PROMIS Sexual Functioning item banks with EORTC measures to develop a culturally harmonized sexual functioning item bank, and the development of a standard multicultural PROMIS short form by a team of investigators from 10 different countries, planned for the coming year. An important consideration for multinational collaborations will be the investigation of Differential Item Function (DIF) across cultures. Statistical evaluation of the validity of cultural adaptations of PRO health assessments is not new; however, standard procedures for investigating DIF cross-culturally require further research and development. The conduct and interpretation of such analysis is complicated by differences among comparator groups in addition to language and culture which must also be evaluated in selecting anchor items.10 Also under consideration by the NIH are country-specific PROMIS websites. Details to enable this possibility are currently being resolved.

In these efforts and others to expand the development of PROMIS, we want to emphasize the importance of coordination, collaboration, and communication. Measurement is enhanced by standardization, which requires working together to protect the integrity of the measures. Contact information for the PROMIS effort is available at www.nihpromis.org.

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Table 1. Patient-Reported Outcomes Measurement Information System: Summary of Translations

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5. Ware JE Jr. The Patient-Reported Outcomes Measurement Information System (PROMIS) seek to improve and standardize measures of five generic health-related QOL domains. PRO Newsletter, 50, (fall issue 2007).
Value in Health has just published online a systematic review article aimed at assessing the current status of the research in the field of cultural adaptations of instruments measuring children and adolescent health-related quality of life (HRQOL) in several Latin-American countries (Argentina, Chile, Mexico, and Uruguay). Some of the conclusions were that there is a scarcity of instruments to measure the HRQOL of children and adolescents in the countries analyzed. In the reported studies, some psychometric properties of the instruments have been adequately tested. However, some other features, most notably sensitivity to change, have not been tested in most instruments. The authors recommended extending this research to other Latin American countries that may help to identify gaps in this area and promote the use of an HRQOL measurement in children and adolescents in Spanish-speaking cultures.

To know more about the initiative on quality of life of children in Latin America we are including a brief interview with someone who not only has led this project, but who has also contributed with his expertise and motivation. We are talking about Luis Rajmil MD, PhD from the Catalan Agency for Health Information, Assessment and Quality (Agència d’Informació, Avaluació i Qualitat en Salut or AIAQS), and collaborator at the Municipal Institute for Medical Research in Barcelona (IMIM- Parc de Salut Mar). Though Luis was born in Rosario, Argentina, he developed his professional career in Catalonia, Spain. The Associate Editor of Quality of Research and author of several articles, Luis chairs the ISOQOL Special Interest Group and the Latin American group of HRQOL of Children.

Question 1: How did you become interested in the quality of life of children and adolescents?

My interest comes from the time of my medical training and from my clinical experience as a pediatrician. Ever since then, I have thought that any intervention aimed at improving the health and well-being of children and adolescents should take into account the perspective of the target population. I think that measuring HRQOL, as well as other patient-reported outcome measures (PROMs), represents a very useful tool that can help to make more accurate clinical decisions and to better define health policies since they provide input from the perspective of those like us who are devoted to this area. Application of the results will largely depend on the competence of those like us who are devoted to this area in removing or simplifying the potential barriers that appear when those who are concerned but not familiarized with the subject try to approach it.

Question 2: Considering the results of your paper recently published in Value in Health, what is the state of the art of the research of HRQOL of children in Latin America?

Research in Latin America is in an early phase of developing in relation to this subject. In our review, we identified studies referring to basically one third of all the instruments available to assess children’s HRQOL, which were identified in a previous international systematic review. Notwithstanding this, there has been an important boost towards new studies in many Latin American countries in the last five years.

Question 3: What are the challenges and future steps to move forward to more and better studies?

As is the case in other regions of the world, it is necessary to attain a critical mass. Latin America has favorable conditions to promote high-quality research in the field of children and adolescents’ HRQOL research. This would require using similar measures across countries and regions, to depict sub-cultural or linguistic biases, and set new goals in health policies. At present, we are in a good position to apply children’s HRQOL measures in diverse clinical settings and population studies. In summary, we need to promote the utilization of HRQOL measures in clinical and epidemiologic studies and to increase the number of available well-validated instruments.

Question 4: What would be your recommendation to junior researchers willing to venture into the field of children’s quality of life, within and outside of Latin America?

I have found many young researchers enthusiastic about exploring this field, and that is a great advantage for future achievements. It is my impression that the proportion of health professionals dealing with these issues in Latin America is larger than in Europe. All the activities in relation with children’s health and well-being carried out at international meetings gather a lot of attention and acceptance from the Latin American professionals. It would be very interesting to create educational activities to provide training in the development and interpretation of children’s HRQOL measures in order to spread their use and applications.

The future of this field of research and the clinical application of the results will largely depend on the competence of those like us who are devoted to this area in removing or simplifying the potential barriers that appear when those who are concerned but not familiarized with the subject try to approach it.

For more information, please contact

Dr. Juan J. Dapueto at jdapueto@hc.edu.uy


FDA WORKSHOP
Measurement in Clinical Trials: Review and Qualification of Clinical Outcome

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The Food and Drug Administration organized a public workshop entitled “Measurement in Clinical Trials: Review and Qualification of Clinical Outcome Assessments” on October 19th, 2011. This document, which was circulated to the members of the ERIQA Group, aims to summarize what was discussed at this workshop.

The workshop included one introduction session and five specific sessions.

Introduction: Why Good Measurement Principles Matter

CDER perspective, measurement, and public-private partnership – Janet Woodcock

Dr. Woodcock started her talk by stating that the number of New Drug Applications (NDAs) increased dramatically in the past years and that in parallel the failure rate of these applications raised similarly. She explained that this “regulatory uncertainty” was related to “scientific uncertainty” (“scientific fog”), in particular in terms of clinical outcome assessments (COAs).

Need for moving forward the COA science

COA should be rigorously developed and their reliability and validity in their context of use should be demonstrated. In particular, she made the point that it is critical to understand the meaning of any COA used in a trial. In summary, she called for efforts to move forward the COA science.

Drug Development Tool (DDT) qualification

Developing COAs at the same time as conducting a study is not optimal. This justifies the efforts for the DDT qualification process, and the need for the development of collaborative works on COAs (private/public partnership, consortia). The DDT qualification will allow good tools to be publicly available. She said that when a new tool would be available and qualified, the FDA committed to update the related guidance. DDT qualification has become an international process. A worldwide harmonization between the regulatory agencies, in particular FDA, EMA and the Japanese agency is therefore needed. In addition, considering DDT qualification as a global process also means that culture needs to be considered in the development of COAs.

Objectives

Dr. Woodcock mentioned four objectives for the workshop and beyond:

- To clarify the terminology (get rid of the “tower of Babel”)
- To get feedback from the scientific community (in particular psychometrics) about how to move forward the COA science
- To facilitate the dialogue in the contexts where COA does not exist, in particular for pediatrics and rare diseases
- To encourage public/private partnerships

She concluded saying that regulators should engage the clinical and scientific community on the outcome assessment agenda.

Q&A

During the Q&A session, a first point that was made was that before considering measurement issues it is important to understand what to measure: what is important to patients, and therefore what should be assessed. And this should be done early, not at the time of pivotal trials. Dr. Woodcock explained that the idea was to develop a toolbox for measurement that will then be applied to the relevant questions.

Session 1: Nomenclature and Measurement

Nomenclature for clinical outcome assessments – Marc Walton

Endpoints to address treatment benefit including replacement endpoints – Thomas Fleming

“How a patient feels, functions, or survives.”

The purpose of outcome assessment is to provide evidence of a specific treatment benefit, which was defined as “a favorable effect on a meaningful aspect of how a patient feels, functions, or survives.” If survival has well-established methods for evaluation, feels and functions are more complex. Feels is defined as “a patient’s physical sensation or perceived mental state” and function is defined as “a patient’s ability to perform specified activities that are meaningful, part of typical daily life.” Of note, function does not refer to “isolated physiologic process” nor to “ability to perform tasks that are not part of usual life.”

Evidence of treatment effectiveness should be obtained through methods of assessment that are “well-defined and reliable.” The assessment of “how a patient feels or functions” clearly raises questions.

Dr. Walton made it clear that the scope of the workshop was limited to the use of OA in adequate and well-controlled trials, and to new OAs or application of OAs in new contexts.
settings. Also, he reminded that an OA cannot be judged in isolation, but that its purpose should be clearly identified. Both presentations elaborated on a framework of four intrinsic characteristics of an assessment:

- Is the assessment Psyche influenced?
- Who is performing the rating?
- What is the relationship to true (meaningful) treatment benefit?
- What is the setting of measurement?

These four characteristics are “orthogonal” (independent), are not related to how the assessment is used in a trial, are not judgmental, and the categories of a characteristic are not graded and mutually exclusive. These characteristics create a classification designed to aid the process of evaluating whether an OA is well-defined and reliable (see Table 1).

Dr. Walton mentioned that these four characteristics are the main ones but other characteristics could be considered, such as sensitivity to change. He also mentioned that for PROs, language could be a characteristic.

Psychomodulated assessment

Psychomodulated assessments are those that can be influenced by human choice, consciously or not. They are sensitive to judgment, motivation, and cooperation. Basically they cover patient-reported outcomes, clinician-reported outcomes, and observer-reported outcomes and are opposed to biomarkers.

Direct vs. indirect assessments

An assessment can be an indirect measure of the meaningful concept of interest. They are used when the direct assessment of the meaningful concept is infeasible. There is a gradation within the “indirect” assessment category: some indirect measures are closer to the meaningful concept than others. An important aspect of indirect assessment is that the relationship between the measured concept and the meaningful concept to be inferred should be solidly demonstrated.

Dr. Fleming recalled the categorization presented by Dr. Walton as a preliminary of his talk about endpoints to address treatment benefit (see Figure 1). Dr. Fleming’s presentation showed the complexity of using replacement endpoints (=indirect assessment as endpoints?), based on the experience on biomarkers. He made it clear that the multiple pathways of the disease process can jeopardize the correct use of indirect assessment. He also showed that the intervention (=treatment) could have mechanisms of actions independent of the disease process, which might therefore not be captured by an indirect assessment. Therefore he emphasized

### Table 1.

<table>
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### Figure 1.

Categorization of Nomenclature - Outcome Assessments

- Direct Measures of Patient "Functions, Feels, Survives"
  - Patient (symptoms)
  - Clinician (PANNS for schizophrenia syndrome)
  - Observer (seizures, infant behavior, death)

- Psychomodulated – (Dependence on patient motivation or clinician judgment to perform test)
  - Patient (rescue meds for pain, alcohol presentation test)
  - Clinician (TM bulging, Limb spasticity, 6MWT, PFTs, 9-hole peg test)
  - Observer (rescue meds for pain)

- Indirect Measures
  - (e.g., HbA1c, CD-4, PSA, CEA, antibody levels, TIMI-III flow HDL, LDL, blood pressure, body temperature, urine GAG, urine KS, cardiac rhythm, blood cultures, PCR, quantitative measures from radiology imaging)

* Presumes that relationship to a direct outcome has been demonstrated

that the use of indirect measures should be based on a comprehensive understanding of the causal pathways of the disease process and of the intervention's mechanisms of action. He showed how meta-analysis can help support the use of an indirect assessment by the demonstration of its relationships with the meaningful concept.

Q&A

In the panel discussion and audience discussion, the concept of psychomodulation was extensively debated. Some feedback was that it is unclear, or ambiguous; maybe a gradation in psychomodulation will be needed. The possibility of needing it considering the inclusion of personality trait measures in trials to control for psychomodulation was raised. The notion of indirect assessment was also discussed. In particular, it was agreed that a critical point when using indirect assessment is that the ultimate meaningful concept should be clearly identified. Also, the question of relevance of indirect measures for symptomatic measures was raised. It was answered that biomarkers, which are by nature indirect, are used in symptomatic diseases. Finally, to the question whether direct measurement is better than indirect measurement, it was answered that there is no judgment in the categorization and that, for example, in many diseases, artificial assessments are the good measures, because they ensure a good sensitivity, which might not be possible with natural ones.

Session 2: Context of Use

**Clinical trial outcome assessment review: Concept definition and context of use – Laurie Burke**

**Importance of context during COA qualification – John Powers**

FDA reviews COA with two distinct processes: as part of a drug application review under the DDT qualification process. The same principles apply for the two processes with as a basis the FDA PRO guidance.

In both processes, the COAs are reviewed in a given context of use. This context of use includes:

- **Disease definition**
- **Target subpopulation (age, severity):** different stage of a disease can have different outcomes; the disease manifestations may be different in different populations; concept may be the same, but measurement may need to differ (e.g., pediatrics)
- **Study design:** outcome will be different in treatment trials than in prevention trials; similarly for non-inferiority vs. superiority trials
- **Endpoint model**
- **Geographic location of the study sites:** Language, practice of medicine may impact the COA; this is true for both patient-reported and clinician-reported outcomes
- **Targeted claim**

All these elements should be clearly defined for a COA to be considered as a well-defined and reliable measure. The definition of the concept to be measured is closely related to the context of use. Dr. Powers quoted: “Historically, concept came first, then measurement.” The definition of the concept and of context of use is an iterative process. A framework for concept definition for COA development and review was given (See Figure 2).

The question of timing and planning was also emphasized in both presentations.

![Figure 2. Concept definition for COA development and review](http://www.fda.gov/Drugs/NewsEvents/ucm276110.htm#coapresentations – adapted from http://www.fda.gov/downloads/Drugs/NewsEvents/UCM277007.pdf)

### Timeline for COA development during drug development

![Figure 3. Timeline for COA development during drug development](http://www.fda.gov/Drugs/NewsEvents/ucm276110.htm#coapresentations – adapted from http://www.fda.gov/downloads/Drugs/NewsEvents/UCM277007.pdf)
The timing of development of a COA alongside drug development was presented (see Figure 3). Cultural and linguistic issues were identified as important and part of the context of use.

Concept and context of use should be defined early to allow COA decisions (identification of measures; development of measures) and time to interact with FDA. Dr. Powers concluded by this quote: “Failing to plan is planning to fail.”

Q&A
The following points were discussed in the Q&A session:
- Can distal disease impact concepts be included in a label? These concepts convey important pieces of information to have for the patients. But concepts closer to the core of the disease are preferred.
- It was noted that a diagnostic criterion is not necessary a good COA. An instrument could be appropriate in one context of use (diagnostic) but not in another (OA).
- Context of use was said to be a complex concept, with many aspects to be considered and described. How to handle this complexity? The required level of detail of context of use definition depends on the final objective.
- When a COA is to be used in a new context of use, to what extent the COA should be evaluated again? What level of difference between the two contexts of use call for a new evaluation of a COA?
- No definitive criterion exists regarding this question.
- It was noted that in some instances, the mechanism of action of the treatment or the mode of administration could be part of the context of use definition.

Session 3: Content validity, reliability, and variability

Content validity: Important measurement principles for PROs and extension to ClinRO and ObsRO – Jeremy Hobart

Reliability, validity, and source of variability in measurement – Nathaniel Katz

All the p-values obtained in clinical trials rely on measurement, therefore having a good measurement is essential, and it is critical to be able to demonstrate that COAs have good measurement properties.

Content Validity
According to Dr. Hobart, the FDA draft guidance of 2006 was a milestone. Before 2006, there was an overemphasis on statistical tests. Content validity of a scale was considered as obviously important but difficult to demonstrate. Since 2006, qualitative tests have become more important than quantitative tests of validity and content validity has become a hot topic. For example, several publications have been recently published about content validity and how to investigate it. However, no quantitative method to support content validity has been developed and accepted yet. In the recent papers on content validity mentioned above, quantitative methods are extremely marginal. Quantitative methods to support content validity are therefore great challenges to be addressed. A framework of interest is this respect is the approach taken by Strenner and colleagues, who developed a theory-driven approach of exploration of content validity in the context of reading ability. The basic idea of this approach is to develop a theory on the concept being measured to be subsequently able to test this theory. A step forward in the development of a quantitative approach to content validity of COA may be to investigate how this theory-driven approach can be translated to health. As for its implementation, different technical paradigms may be candidates to substantiate this theory-driven measurement. Modern psychometrics obviously is a promising approach in this context.

Reliability and Variability
Assay sensitivity is a property of a clinical trial defined as the ability to distinguish an effective treatment from a less effective or ineffective treatment. It depends, among other things, on the variance of the outcome. Therefore, identifying and mitigating sources of error in experimental design and measurement can increase assay sensitivity (and thereby decreasing sample size requirements in clinical trials). Dr. Katz illustrated this using his experience on pain assessment (but most can be translated for other COAs). There are several sources of variability in an assessment: the experiment, the patient, the measure. The following formula encompasses all these aspects: Reported pain score = “True” pain score + Patient Innate Reporting Capability + measure error + experimental noise + random error.

The features of the experiment that were identified as potential sources of variability, in the context of opioid trials, were: the trial structure, dosing, concomitant analgesic, rescue, primary endpoints, and number of sites. As for the sources of variability pertaining to the patient, there is a “within patient variability of pain,” but also a “between patient variability of response to treatment,” a “heterogeneity in the appropriateness of the outcome between patients,” and finally, a “variability in the ability of patients to report their pain.”

Finally, the measure is the third source of variability, therefore the need for reliable measures. And in the case of observer-reported outcome, inter-rater is critical but also content validity, to ensure that the different observers interpret the measure in the same way.

While all these sources of variability are identified, their relative importance and the methods to control them are not clear yet. There is a need for rigorous research on these variability sources to be able to optimize assay sensitivity of trials.

Q&A
It has been asked whether it would make sense to select investigators who are using the tool the most appropriately to enhance the reliability of the measure. It was noted that it is already done in the psychiatric studies.

The question of the need for prespecification of validation of COAs in a given study, to mirror the validation step of biomarkers, has been asked. It was made clear that it is a prerequisite of any clinical trial to demonstrate that the COA is performing appropriately in the trial, and
in conformity with the existing evidence of the COA properties.

Dr. Burke asked about the condition of use of the quantitative assessment of content validity and its appropriateness to COA. Dr. Hobart answered that there is no consensus on a standard paradigm. He called for a hypothesis-based approach. He also emphasized that quantitative and qualitative methods should be used together to study content validity and that understanding the disease is also critical in this approach.

Session 4: Measure development in pediatrics and rare diseases

Patient- and observer-reported measurement in pediatrics – Todd Edwards

The problem of instrument development in rare diseases – Nancy Kline Leidy

The importance of patient reports in both pediatrics and rare disease was emphasized, despite the specific challenges of these two fields.

Challenges and solutions in pediatrics

Child development is rapidly changing and variable across individuals making the measurement in this context challenging. Specifically, it imposes context of use and content validity to be considered extremely carefully.

There are no established guidelines on the cut-off age for self-report: age 7 was mentioned as bottom of age range; over 11 was said to be acceptable psychometrically. However, age may not be the best criterion: assessment of comprehension and motivation may be better. When a self report is not possible, verifiable observation can be used.

Challenges and solutions in rare diseases

Four challenges were identified in rare diseases: knowledge, availability, access, and variability.

The limited knowledge on the disease and patient experience makes it harder to develop good COAs. Patients are few and often difficult to identify, and when they are, to access, since they will be spread across many locations. Finally, the disease is often variable from persons to persons and given the small number of patients, it is generally needed to consider heterogeneous patients, in particular in terms of age.

To address these challenges, several potential solutions were given:

- Planning early
- Using all available information
- Selecting focus outcomes
- Preferring using or adapting existing instruments
- Being inventive at all stages
- Collaborating

Q&A

The interrelationships between the disease and the developmental process of children were discussed: it was said that it would be relevant to understand how the disease impacts growth and development, but also how growth and development impact the disease. It was asked how the challenge of explaining some difficult tasks like cognitive interviewing or difficult concepts like recall period can be managed. It was acknowledged that this is difficult with children and that no ideal solution exists: one idea can be to have the child paraphrasing the question for the cognitive debriefing and to use as short a recall period as possible.

As for rare diseases, it was agreed that efficiency is key. The potential important role of patient groups and foundation was emphasized. The understanding of the disease was also recognized as a critical question. Finally, the potential importance of communicating with the FDA early was mentioned.

Session 5: Collaborative processes for COA development and dissemination

CDER’s public-private partnership programs – ShaAvhree Buckman

FDA’s public-public partnership with NIH – Rochelle Fink

CDER’s partnership with the Foundation for NIH – David Wholley

CDER’s partnership with the Critical Path Institute PRO consortium – Stephen Coons

CDER’s partnership with EXACT-PRO – Nancy Kline Leidy

CDER’s partnership with PROOF – Patrick Marquis

FDA-EMA MOU interactions concerning COA qualification – Maria Isaac

Several experiences of collaborative projects were presented, either public-public or public-private, demonstrating that, yet challenging, these projects can lead to significant contributions to COA development. Of particular importance, the collaboration between EMA and FDA on the qualification of COAs is to be noted. The consortia presented were the following ones:

- Nancy Kline Leidy of the EXACT-PRO Initiative See http://www.exactproinitiative.com/default.php
- Stephen Coons on the Critical Path Institute and the C-Path PRO Consortium See http://www.c-path.org/PRO.cfm

Maria Isaac (EMA, Scientific Advice Working Party) presented the interactions between the FDA and EMA concerning COA qualification:
- Companies can ask for scientific advice to the EMA and to the FDA.
- They will be able to submit the same briefing packages and the same questions for discussion.
- This is an opportunity for consortia and companies to have views about the development at the same time.
- It will give a chance to have a discussion meeting with both agencies at the same time.
- Each agency will give its own advice.
Conclusion and implications

The main elements of the workshop probably are:
1) the proposed categorization of COAs;
2) the need for quantitative methods to investigate content validity; and
3) the clear push of the FDA for collaborative work and for the DDT qualification of COAs.

Categorization of COAs

The COA classification is based on four COA intrinsic characteristics. Among these characteristics, the notion of psychomodulation seems to be the most debatable, mainly because of its lack of clarity. Incidentally, this may lead to issues in the categorization, while the classification was claimed to be “non-judgmental.”

The COA categorization was proposed to aid the evaluation of COAs. However, no practical implication of this categorization has been described. It can be thought that the position of a COA in the categorization will impact the evidence to be provided for its evaluation. A few first elements could yet be spotted in the presentations and discussions:
– For indirect measures to be used as COAs, the relationship of the measure to the meaningful concept will have to be strongly supported
– For observer-reported outcomes, the inter-rater reliability will have to be supported
Other aspects remained to be identified.

Quantitative methods for content validity

The workshop confirmed the importance of content validity initiated by the FDA guidance and extended it to all COAs (not only PROs). The main question that appeared was the need for quantitative approaches to assess content validity. Some indications have been given but no consensus exists on such methods. The approach proposed by Jeremy Hobart, based on a theory-driven measurement approach and modern test theory, will clearly have to be considered carefully.

Collaboration and DDT qualification

The workshop confirmed the clear will of the FDA to encourage collaborative work for the development of COAs and the submission of COAs to the DDT qualification process.

Language Issues

It is important to note that language of COA (in particular PRO) was mentioned as an important feature at several occasions and was included as an item of context of use of COAs; in this respect, “ethical/cultural sensitivity” could be proposed as an additional intrinsic characteristic of COAs in the classification. Indeed, this concept has already been shown to be important: it is central in the ICH E5 guidance on ethnic factors in the acceptability of foreign clinical data. This would enable the need for culturally adapted tools to be emphasized.

For further information, the interested reader can consult the FDA website, from which all presentations, as well as the full transcript of the workshop, can be downloaded:
http://www.fda.gov/Drugs/NewsEvents/ucm276110.htm/coapresentations

For more information, please contact: Antoine Regnault at aregnault@mapigroup.com

Turkish Society of HRQOL (SAYKAD) will Organize the 4th National Congress (April 4-6, 2013, Izmir, Turkey)

Prof. Dr. Erhan Eser,
Turkish Society of Quality of Life Research (SAYKAD), Izmir, Turkey

SAYKAD was founded in 2002 in Izmir, the third-biggest city of Turkey, by a group of medical doctors working in the areas of public health, psychiatry, and medical oncology. The founders of SAYKAD also belonged to the core study group of the WHOQOL Project Turkish team. The main target of SAYKAD has been to introduce and disseminate the knowledge about HRQOL to diverse health disciplines and healthcare professionals in Turkey. Based on this purpose, the society participated in and organized a number of scientific meetings and workshops and has provided methodological support to the professionals working on HRQOL in clinical practice.

The organizational structure of SAYKAD has led to the establishment of a number of working groups in allergy, dermatology, urology, pneumatology, rheumatology, cardiology, neurology, endocrinology, oncology, oral health, nursing, public health, and occupational health. These working groups are in close collaboration with relevant medical specialty societies of the country. They continuously force the societies to bring HRQOL into their agenda in their regular scientific meetings by HRQOL plenary sessions and workshops.

SAYKAD started to establish a national HRQOL bibliography as well. Due to the lack of drug industry relationships, SAYKAD has no financial support except membership dues and potential international project contributions. A new emerging target of SAYKAD is to be an affiliated body of ISOQOL. A recent official application has been sent to the ISOQOL executive committee for this purpose.

SAYKAD has organized three national scientific meetings in Izmir, the first in 2004, the second in 2007, and the third in 2010. The fourth National HRQOL Meeting of SAYKAD will be held from April 4th through 6th, 2013 in Izmir. Conference information is visible at the SAYKAD website: www.saykad.org. The topic of the 4th Congress is "Adding HRQOL to Clinical Practice."

Noticeable scientific development was detected in previous meetings. In addition to the plenary sessions, there were six workshops, three of which given by invited international experts of HRQOL. The presentations (in plenary sessions and workshops) by these experts brought the international view of HRQOL to the audience. ISOQOL used to support these meetings by giving financial travel support to HRQOL experts. SAYKAD’s executive committee appreciated this very valuable support. More detailed information can be obtained from the previous meetings at the SAYKAD website: www.saykad.org.

For more information, please contact: Prof. Dr. Erhan Eser, Member of SAYKAD Executive Committee, erhanese@gmail.com

Quality of Life and Mortality Among Children
Thomas E. Jordan
Publisher: Springer - ISBN 978-94-007-4389-2
Due: May 31, 2012

This brief examines mortality among young children in the period from the seventeenth to the nineteenth century. It does so using several types and sources of information from the census unit England and Wales, and from Ireland.

The sources of information used in this study include memoirs, diaries, poems, church records, and numerical accounts. They offer descriptions of the quality of life and child mortality over the three centuries under study. Additional sources for the nineteenth century are two census-derived numerical indexes of the quality of life. They are the VICQUAL index for England and Wales, and the QUALEIRE index for Ireland. Statistical procedures have been applied to the numbers provided by the sources with the aim to identify effects of and associations between such variables as gender, age, and social background. The brief examines the results to consider the impact of children’s deaths upon parents and families, and concludes that there are differences and continuities across the centuries.
Is “Fear of Passive Movement” a Distinctive Component of the Fear-Avoidance Model in Whiplash?

Howard Vernon, DC, PhD, Rocco Guerriero, DC, Shawn Kavanaugh, DC, Aaron Puhl, David Soave, MSc
Canadian Memorial Chiropractic College, 6100 Leslie Street, Toronto, Ontario, Canada, M2H 3J1

Abstract
Aims: Modify the Tampa Scale for Kinesiophobia (TSK) for “fear of passive motion” beliefs.
Methods: With permission, a 14-item modification, the TSK-PM (passive movement), was created. Test-retest reliability and construct validity were tested in chronic whiplash patients.
Results: The TSK-PM showed high test-retest reliability (r = 0.83) and high correlation with the original TSK. Low, non-significant correlations were found with other variables. Neck Disability Index (NDI) scores were strongly correlated with ranges of motion.
Conclusions: While being reliable, the TSK-PM failed to demonstrate distinctive construct validity vs. the TSK. Modifications to the current version of the TSK-PM might improve its construct validity in future studies.

Introduction
In whiplash-associated disorder (WAD), many psychosocial factors are accounted for in the Fear-Avoidance Model. Many of these factors have been shown to correlate strongly with current self-ratings of disability and with prognosis. The Tampa Scale for Kinesiophobia (TSK) and the Fear-Avoidance Beliefs Questionnaire assess movement-related anxiety; i.e., a patient’s beliefs about the degree to which the movements they might undertake might aggravate their pain and, accordingly, whether they would perform these movements or activities. The fundamental construct being assessed is fear of moving. These active movements undertaken by the patient, and beliefs thereof, are not the only kind of movement encountered by whiplash sufferers who become patients in a healthcare setting. Passive motions are commonly applied in both the diagnostic and therapeutic settings, especially in manual therapy. If a patient had any anxiety about these kinds of movements, it would best be termed a fear of being moved. This construct has not been well studied. Given the frequency of circumstances where passive motion is applied to patients, especially in manual therapy, assessing a patient’s attitudes and beliefs about this could make an important and distinctive contribution to the overall management of their pain condition. Modifications to therapy and education could be made to address these issues.

Accordingly, we undertook a modification of the TSK to assess “fear of passive movement” beliefs (TSK-PM (passive movement)). We first modified the TSK for this purpose. Then, the test-retest reliability of this modified version was established in a sample of neck pain patients. Then, we explored its validity in a sample of chronic WAD patients by comparing TSK-PM scores with scores on the Neck Disability Index (NDI), the original TSK, and active cervical ranges of motion. We predicted that the TSK-PM would only mildly correlate with the TSK and that it would more strongly correlate with ranges of motion and with cervical non-organic signs (C-NOS) than the original TSK.

Methods
Revision of TSK
We asked permission to modify the TSK from Prof. J. Vlaeyan. All items were reviewed by the authors for applicability. Fourteen of 17 items were retained (original items #2, 4, 9, and 12 were excluded).

Figure 1.
Tampa Scale for Kinesiophobia – PM

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I’m afraid that I might be injured if someone moves me</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2.</td>
<td>My body is telling me that I have something dangerously wrong if it hurts when someone moves me</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3.</td>
<td>My pain won’t be made worse if someone moves me</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4.</td>
<td>People aren’t taking my medical condition seriously enough</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5.</td>
<td>My accident has put my body at risk for the rest of my life</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6.</td>
<td>Pain always means I have injured my body</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>7.</td>
<td>Just because it hurts when someone moves me does not mean that it is dangerous</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>8.</td>
<td>Being careful not to have anyone move me is the safest thing I can do to prevent my pain from worsening</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>9.</td>
<td>I wouldn’t have this much pain if there weren’t something potentially dangerous going on in my body</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>10.</td>
<td>My pain will let me know when to stop someone from moving me so that I don’t get injured</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>11.</td>
<td>It’s really not safe for a person with a condition like mine if someone moves me</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>12.</td>
<td>I can’t do all the things normal people do because it’s too easy for me to get injured</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>13.</td>
<td>Even though something is causing me a lot pain, I don’t think it’s actually dangerous</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>14.</td>
<td>No one should have to be moved by someone when they are in pain</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Four items were retained in their original form (original items 6, 7, 15, and 16). The remaining nine items were revised by changing the wording from an active to a passive voice, principally by using the phrase “if someone moves me.” The scoring was the same; responses ranged from 1- strongly disagree, 2 – disagree, 3- agree, 4- strongly agree. Items 3, 7, and 13 are reversed in scoring as a validity check (See Figure 1).

Study 1: Reliability

Subjects were recruited if they presented with neck pain of at least two weeks duration. Both males and females ages 18-70 were included. After providing informed consent, subjects completed the TSK-PM. Upon return to a treatment clinic for a follow-up visit within 48 hours, they completed the TSK-PM for a second time. Descriptive data were also obtained. A sample size estimate for Pearson’s Coefficient of 0.90, with beta level of 0.80 determined that 19 pairs of data were also obtained. Data was analyzed with intraclass correlation (ICC) for test-retest reliability.18

Study 2: Validity

Males and females, ages 18-65 were recruited with whiplash-related complaints of chronic neck pain (with or without headaches). Neck pain was defined as from C0-T3, anterior or posterior to the neck and laterally to the lateral scapular border. Subjects were excluded if they had radiating pain into the arms or if they had sustained a closed head injury and were exhibiting signs and symptoms of post-concussion syndrome. No WAD IV subjects were included. Subjects were not excluded if they had additional pain elsewhere in the body.

Outcome measures

In addition to the TSK-PM, the following outcome measures were used.

1. NDI: Developed in 1991, the NDI is the most commonly used measure of self-rated disability due to neck pain.19 It has excellent reliability and validity.20 It is composed of 10 items; each item is scored out of five for a total score out of 50.

2. TSK: The TSK was developed in 1990 by Kori, Miller, and Todd to measure fear avoidance beliefs. Its reliability and validity have been well-documented.21-23 It is composed of 17 items; each item is scored out of four for a total score out of 68.

3. Ranges of motion (ROM): Cervical ranges of motion were measured with the CROM goniometer. Head goniometers have good reported test-retest reliability.24,25 Two trials were obtained and averaged. The data point was the total ROM (degrees) summed from six individual ranges.

4. Age, gender, duration of complaint (time since WAD injury), and pain severity on a 100 mm VAS were also obtained.

Sample Size Estimate

At an alpha level of .01 and a beta level of 0.80, for r = 0.70, 18 pairs of data are required. Given that two primary analyses were performed (TSK-P/TSK and NDI/TSK), 40 subjects were required.

Data Analysis

Pearson’s correlation coefficients were used to assess the univariate associations of the NDI, TSK, TSK-PM, total range of motion and pain severity scores as well as with age, gender, and duration [months]. Next, a linear regression analysis was conducted to assess the importance of variables in relation to one another when predicting self-rated disability. A multivariable analysis was planned if any univariate correlations were significant. A p-value of 0.05 was considered statistically significant. Post, hoc analyses for any significant findings were performed with t-tests with Holm’s correction.

Results

Eleven subjects completed the test-retest study and 49 subjects completed all the required measures for Study 2 (31 males, 18 females). The mean age and duration of symptoms were 39.9 (12.5) years and 9.7 (6.2) months, respectively.

Study 1: The test-retest reliability was 0.83.

Study 2: The mean NDI, TSK, pain VAS, and ROM scores are shown in Table 1. The mean total ROM represents approximately a 20% reduction in total ranges of motion (normal = 360 degrees). Univariate correlations are shown in Table 2. The highest and only significant correlation found was TSK / TSK-PM = 0.84 (p = 0.0000). As no other important univariate correlations with the TSK-PM were obtained, a multiple regression analysis was not performed. Both forms of non-organic signs as well as the NDI had significant correlations with other variables.
TSK and TSK-PM had no significant correlations with any of the other variables.

Discussion

This study produced a modified version of the TSK to account for the construct of “fear of being moved” or “fear of passive motion” beliefs. We found a high degree of test-retest reliability in the TSK-PM. However, in this sample of chronic WAD subjects, we failed to find a strong distinction between the original and modified versions of the TSK. This finding may have occurred because the TSK-PM does valid measure “fear of passive motion” beliefs, but these are simply not different enough from “fear of active motion” beliefs. Contrarily, the modifications made to the TSK may not have been adequate enough to permit valid measurement of a distinctive set of beliefs. The creation of a different instrument, not the minor modification of an existing one may be required to resolve this issue.

Our findings can be interpreted as supporting the original TSK in assessing motion-related anxiety for both active and passive movements. Should a clinician be concerned about “fear of being moved” in their patients, the original TSK probably provides an adequate measure of that attribute. We also failed to find strong correlations between scores of either version of the TSK with scores of self-rated disability, current pain intensity, ranges of cervical motion, and standard or novel cervical non-organic signs. This is contrary to other studies, and may be a statistical issue, as we found that TSK and TSK-PM scores were considerably higher and less varied than NDI scores and scores for ranges of motion and non-organic signs. It may also be due to the fact that our subjects suffered with chronic whiplash-related pain. The situation may be different in subjects with sub-acute pain whose pain-related beliefs may not have become so entrenched. In addition to the findings directly related to the TSK-PM, our study has other important results. The significant correlation between NDI scores and ranges of neck motion confirms the results of Howell et al., although the correlation between ROM and pain VAS scores was slightly higher.

The limitations of this study pertain to the limits of interpretation of the negative results with respect to the TSK-PM: chronic WAD patients with relatively high fear avoidance beliefs. As noted above, replication in acute WAD patients is recommended.

Conclusion

Despite being found to be reliable and internally consistent, a modified version of the TSK to account for fear of passive motion beliefs has failed to demonstrate construct validity in a sample of chronic WAD patients. In fact, we have found that this construct is likely incorporated into the original TSK. Secondarily, validity of the C-NOS tests for cervical non-organic pain behavior in WAD patients has been given support.

For more information, please contact: Howard Vernon at hvernon@cmcc.ca.

Standards were high—even somewhat higher than usual—and the task of judgment extremely interesting and by no means easy. However, all four judges agreed that the winning entry for the $10,000 US award was "The Use of Personal Ritual among Hospice Staff Following the Death of a Patient" by Lori Montross. A description of her project is in this issue of the PRO Newsletter.

"Pyridostigmine in Cancer Patients with Constipation and High Anticholinergic Loads," by Katherine Clarke, and "A Controlled Trial Of Glycopyrrolate for the Treatment of Noisy Respiratory Secretions at the End of Life," by Caitlin Sheehan, were both considered worthy of Honorable Mention, to which the authors might refer in their future CVs.

"I keep a small silver angel on my bookshelf at home. It holds a white votive candle in its wings. Whenever one of my patients dies, I light that candle when I get home and keep it burning all night." — Nancy, Hospice Social Worker.

After the death of someone close to us, whether they were family, friends, colleagues or even patients we cared for, we often feel the instinctual need to have a sacred ritual to honor their lives.

This study will examine the use of personally meaningful rituals among hospice staff and volunteers as they cope with the death of their patients. Hospice staff will be asked to describe their ritual practices, to elaborate on how they created such practices, and to express how these practices impact their work, with particular attention to whether these rituals enhance meaning or "compassion satisfaction" at work.

One innovation of this study is that all hospice staff and volunteers will be invited to participate—including housekeepers, cafeteria workers, social workers, chaplains, music therapists, nurses, office staff, as well as physicians. This inclusive design will offer a unique window into the practices of all team members involved in care of the dying.

The results will have several implications. First, new staff will be able to learn from more established staff, possibly leading to reduced frustration, isolation, or burnout as they cope with the death of their patients. Second, administrators will be able to gain new ideas for meaningful organizational practices, ones that enrich staff and their desire for positive patient remembrances.

Finally, the wider medical community will benefit from hearing about the practices of hospice staff. Although other medical professionals such as oncologists or surgeons may experience patient deaths less frequently than hospice staff, many still struggle with how to make meaning of those difficult experiences.

This study will start a beneficial dialogue across medical professions, with the aim to share how the use of personally meaningful rituals may bolster coping and compassion in one’s work.

For more information, please contact: Lori P. Montross, LMontross@SDHospice.org
The entry by Sigrid Frey-Revere, “An Interactive Internet-based End-of-Life Decision-Making Matrix,” is the subject of discussion between MAPI Institute and the author.

Perhaps because the conditions of application for the 2011 Award were broadened to permit the entry of competitors outside scientific disciplines, more entries than ever before were received (nine from North America, five from the UK, two from Australia and one each from China, the Republic of the Congo and the Philippines. Some applicants were –presumably for a period of research or study– working outside their countries of origin). Five were MDs, four PhDs, three Registered Nurses and three had Master’s or Bachelor’s degrees. Four did not specify a scientific discipline. Thirteen applicants were women. One entry appeared not to have noticed the basic requirement for entry, for the proposal in question was unrelated to terminal care.

For the 2012 Catherine Pouget Award, competitors should adhere more closely to a minimal size of font (12 pt.), and both competitors and judges should no longer overlook the requirement that not more than four double-spaced pages should be submitted.

Background

Between 2007 and 2010 we conducted a large study on preferences for information and participation in medical decision-making of advanced lung cancer patients in Flanders, Belgium. We found that a lot of recently diagnosed patients who wanted to be informed about prognosis, palliative care, and end-of-life decisions with possible life-shortening effects (ELDs), were not informed. Patients who wanted to share the medical decisions with their physician often did not achieve this degree of involvement and were less involved than they preferred.

Objectives and methods

The goal of this follow-up study was to discuss these problems with pulmonologists and oncologists and to list their suggestions for improvements in order to develop an intervention. The methodology of focus groups was used. At this moment in the study, a first focus group with experienced pulmonologists has taken place. A focus group is a qualitative research method that consists of a group discussion and is oriented at gaining additional insights. The discussion has been audio-taped and analyzed.

Results

The mean age of the pulmonologists was 45 (SD=6.0), 60% were male. The mean number of treated terminally ill patients in the last year was 70. There was considerable variability in the degree the pulmonologists gave prognostic information to their patients: some gave little or no information because they viewed this as too burdensome for their patients, while others gave specific numbers, i.e., mean life expectancy and spread. There was a consensus between the pulmonologists that giving information regarding palliative care and ELDs shortly after diagnosis was premature. With regard to shared decision-making, the pulmonologists reported that they were unaware about how this should be done. They also reported that decisions were often made in previous meetings with several other physicians and healthcare professionals, but without patient involvement. The pulmonologists suggested several structural interventions that could improve communication: regular interdisciplinary meetings to discuss psychosocial issues, support of physicians by psychologists, and delegation of routine tasks to other healthcare professionals.

Conclusion

This focus group provided several explanations for the existing communication problems, and suggested that structural interventions might be effective to improve communication. In two follow-up focus groups, it will be evaluated whether these findings are corroborated and whether new insights arise.

For more information, please contact: Koen Pardon,
A focus group study of the End-of-Life Care Research Group,
Ghent University & Vrije Universiteit Brussel, Belgium - koen.pardon@vub.ac.be
This edition is a revision and update of the book first published in 2004.

In addition to the linguistic validation process presented in 2004, this edition offers revised procedures, new examples, and three new chapters:

**New examples and revised sections** in Chapter 1 (Linguistic Validation Procedures) reflect MAPI Institute's leadership in linguistic validation sustained by strong experience and continued growth through an increased volume of projects undertaken since 2004:

- The Institute has considerably increased the number of instruments translated by its teams (from 300 to 2500), widely developed its network of experts (150 to more than 300), and expanded its area of intervention (from 65 to over 90 countries), especially in Asia and Africa.

- The Institute has broadened its scope to major Health Outcome Assessments (HOAs) such as Patient-Reported Outcome (PRO), Observer-Reported Outcome (ObsRO), and Clinician-Reported Outcome (ClinRO) measures.

**Three new chapters** highlight the developments of a new tool, a new technique, and the importance of copyright issues:

- **A new tool presented in Chapter 2, the MI Checklist**: To aid in the review of translations of HOAs, the Institute has developed a checklist that addresses FDA requirements for evidence that HOAs have been adequately translated, ensuring content comparability and validity for the combined analysis of data from two or more language versions. The checklist helps to organize all information generated during translation and linguistic validation as well as record reviewer comments.

- **A new technique in Chapter 3, the Translatability Assessment (TA)**: It covers the translatability of instruments during the development phase. Results from unpublished data from MAPI Institute studies suggest that the use of a TA on an original instrument can optimize its formulations in view of subsequent translations and ultimately contribute to an enhanced cross-cultural comparability of data.

- **Copyright issues in Chapter 4**: In this section questions about the copyright of original measures and their translations are clarified. Also included are recommendations for users and developers.

This manual is a valuable source of information that answers any question you may have about the cross-cultural adaptation of Health Outcome Assessments.

For more information, please visit:
www.mapi-institute.com/linguistic-validation/manual
In 2011, MAPI Research Trust celebrated the 20th year of the PRO Newsletter

Created in 1991 by Dr. Catherine Acquadro, the PRONL celebrated its 20th anniversary in 2011. Initially known as the “Quality of Life Newsletter,” it allowed the MAPI group – which at the time was made up of about thirty people – to create a network of PRO experts. Through the collaboration of dozens of PRONL authors, we were able to develop our group’s expertise in quality of life and PROs and become leaders in this domain.

The newsletter has undergone a few changes along the years. One was changing its name to “PRO Newsletter” in 2005; another was the 2007 launch of an online version. Today it is published twice a year and offers a combination of scientific articles and brief news articles to over 5,500 readers around the world.

Some of these experts have been with us right from the start, contributing to MAPI projects over two decades and authoring articles in our special PRONL 20th anniversary edition.

This special publication was produced for the ISOQOL conference last October and provided the opportunity for us to toast the anniversary with these experts with a glass of champagne. At this occasion, Prof. Donald Patrick paid tribute to both Catherine Acquadro and Bernard Jambon for the creation of this means of communication which, even today, remains unique within the PRO domain.

The MAPI Group also hosted a champagne reception to honor the PRONL’s 20th anniversary at last November’s ISPOR congress in Madrid. The event provided the occasion to remind attendees about MAPI Group’s PRO expertise and leadership.
In 2012, the Patient-Reported Outcome and Quality of Life Instruments Database (PROQOLID) Celebrates a Major Feat: Its 10th Anniversary!

Martine Caron, Laure-Lou Perrier, Marie-Pierre Emery

MAPI Research Trust, Lyon, France

This year marks the 10th anniversary of PROQOLID, the world's first and still the only comprehensive database dedicated to Patient-Reported Outcomes and Quality of Life Instruments.

MAPI Research Trust (MRT) originally launched the database in 2002 as QOLID (see Figure 1)—describing only 313 instruments. It was renamed PROQOLID in 2005 to reflect the FDA’s shift in terminology from Quality of Life (QOL) to Patient-Reported Outcomes (PRO) (see Figure 2). The basis of the database was the randomly collected information available at MRT and information collected by the late Marcello Tamburini of the National Cancer Institute in Milan, Italy.

PROQOLID currently contains detailed information on over 710 instruments and is constantly growing. PROQOLID offers a free level that provides essential information: the author’s name, the instrument’s objective, mode of administration and a list of existing translations. In addition, database subscribers have direct access to review copies of the instruments, conditions of use, descriptive information, content validity documentation, measurement properties, bibliographic references, regulatory use information, scoring manuals, authors’ contact information, and links to useful websites—all consistent with current FDA terminology. No wonder PROQOLID has become THE reference source for PRO and Clinician-Reported Outcomes (ClinROs) information and currently has nearly 900 regular subscribers (64% are pharmaceutical companies, 34% from academia, and 2% from health authorities). Over 8,000 visitors freely consult the database every month.

To celebrate PROQOLID’s decade of service we have revised the website and added numerous new features. On the technical side, you will find a new Google-type search engine for more user-friendly browsing. Very soon all users will be able to search for instruments by the domain assessed. They will also have direct access to contact information, review copies, and user agreements for all the instruments distributed by MAPI Research Trust. We have also added the main bibliographic references to PROQOLID’s free level (see Figure 3).

Honoring PROQOLID’s anniversary milestone, MRT will hold special events throughout the year. Event information will be posted on the PROQOLID website (www.proqolid.org).

For more information, please contact:
- Andrea Murison
  amurison@mapigroup.com (North America)
- Marie-Pierre Escanez-Virieux
  mpvirieux@mapigroup.com (rest of the world)
In 2012, the Patient-Reported Outcome and Quality of Life Instruments Database...

**Figure 2.**

PROQOLID home page

Developed and managed by NAPRTCS (National Advisory Research and Training Center onemploi), PROQOLID aims to identify and describe PRO and QOL instruments to help users choose appropriate instruments and facilitate access to them.

**Figure 3.**

PROQOLID new home page

The content of the PROQOLID database is based on information taken from scientific literature and validated by the authors of the instruments. The accuracy of the study methodology and psychometric properties is not evaluated.
An electronic survey was conducted among PROQOLID users. This survey had two main aims: first, to assess the level of satisfaction with the database, and, second, to better understand the different patterns of use of PROQOLID. Additionally, it also served at collecting users’ expectations in terms of further developments of the database.

Results
Some 270 surveys were sent out and 52 users’ answers were received, a very favorable 19% response rate.

In total, 94% of the respondents were satisfied with PROQOLID (there was one missing answer) – see Figure 1. Only two users were dissatisfied; one of them expressing concerns about the clarity of the information provided (“I personally don’t think it is clear what assessments require licenses/fees and who the correct contact person is”). Satisfaction rates were excellent and ranged from 87 to 95% on items such as the ease of use of the PROQOLID database, the reliability of the information displayed, or the support provided by the team – see Tables 1 and 2. The most frequent points of dissatisfaction reported by users were “the information covered” (13% dissatisfied), “the way the information is displayed” (12% dissatisfied), and “the search options” (10% dissatisfied). The types of information considered most important were the availability of a copy of the questionnaire (n=41), the conditions of use (n=24), the list of available translations (n=23), and the contact information (n=21).

Finally, two suggestions to improve the database included a more robust search function, and a more flexible (e.g., Google-type) search engine.

KEYWORDS
PROQOLID, SATISFACTION SURVEY

Conclusion
This survey helped to identify areas for improvement which are available in the new version of the website online at the occasion of PROQOLID’s 10-year anniversary (May 2012).

For more information, please contact: Laure-Lou Perrier, MAPI Research Trust, llperrier@mapigroup.com

Table 1.
Answers to “How are you satisfied...”

<table>
<thead>
<tr>
<th>How are you satisfied</th>
<th>Very satisfied</th>
<th>Somewhat satisfied</th>
<th>Somewhat dissatisfied</th>
<th>Very dissatisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>with the ease of use of the PROQOLID database?</td>
<td>52% 27</td>
<td>40% 21</td>
<td>12% 6</td>
<td>0% 0</td>
</tr>
<tr>
<td>with the way information is displayed in the PROQOLID database?</td>
<td>40% 21</td>
<td>48% 25</td>
<td>6% 3</td>
<td>0% 0</td>
</tr>
<tr>
<td>with the search options of the PROQOLID database?</td>
<td>25% 13</td>
<td>65% 24</td>
<td>6% 3</td>
<td>4% 2</td>
</tr>
<tr>
<td>with the reliability of the information provided in the PROQOLID database?</td>
<td>48% 25</td>
<td>44% 23</td>
<td>13% 7</td>
<td>2% 1</td>
</tr>
<tr>
<td>with the current information covered in the PROQOLID database?</td>
<td>31% 16</td>
<td>56% 29</td>
<td>0% 0</td>
<td>0% 0</td>
</tr>
<tr>
<td>with the flexibility of the MAPI Research Trust staff in adapting to your needs?</td>
<td>37% 19</td>
<td>58% 30</td>
<td>0% 0</td>
<td>0% 0</td>
</tr>
<tr>
<td>with the support provided by the MAPI Research Trust staff (general assistance and response to your information requests)?</td>
<td>44% 23</td>
<td>50% 26</td>
<td>0% 0</td>
<td>0% 0</td>
</tr>
</tbody>
</table>
The aim of this encyclopedia is to provide a unique, comprehensive reference work on scientific and other scholarly research on the quality of life, including health-related quality of life or patient-reported outcomes research. Springer will publish a dynamic and living version of this treatise on SpringerReference.com, where authors and editors can update and add articles at any time.

Since the 1960s two overlapping but fairly distinct research communities and traditions have developed concerning ideas about the quality of life, individually and collectively, one with a fairly narrow focus on health-related issues and one with a quite broad focus. In many ways, the central issues of these fields have roots extending to the observations and speculations of ancient philosophers, creating a continuous exploration by diverse explorers in diverse historic and cultural circumstances over several centuries of the qualities of human existence. What we have not had so far is a single, multidimensional reference work connecting the most salient and important contributions to the relevant fields.

Entries will be organized alphabetically and cover basic concepts, relatively well-established facts, law-like and causal relations, theories, methods, standardized tests, biographic entries on significant figures, organizational profiles, indicators and indexes of qualities of individuals and of communities of diverse sizes, including rural areas, towns, cities, counties, provinces, states, regions, countries, and groups of countries.

Articles will range from short entries and biographies, to intermediate summaries, and to major overviews. All articles will be cross-referenced and electronically accessible to relevant articles in this encyclopedia. Selected scientific and scholarly journals will be linked to relevant articles in the encyclopedia. In effect, this encyclopedia will be a one-stop shopping center for research on quality of life in all its dimensions. Assuming approximately 2500 articles, there will be about eight volumes in the set.

With Alex C. Michalos serving as Editor in Chief, all articles will be refereed by members of an Editorial Board consisting of about 150 experts drawn from the disciplinary fields that have made the greatest contributions, including anthropology, applied mathematics, arts, biometrics, economics, ecology, education, environmental studies, demography, development studies, epidemiology, geography, management studies, marketing, neuroscience, nursing, pharmacology, philosophy, planning, political science, public/population health, psychology, psychiatry, religion, social work, sociology, and statistics.

The encyclopedia is intended to serve the needs of graduate students, scholars, researchers, clinicians and therapists, elected government officers and unelected public service workers, as well as small and large private-sector practitioners.

Find more information at:
The focus of the PRO methods group (PROMG), an entity of the Cochrane Collaboration, is on patient-important outcomes self-reported by participants in treatment trials. This year, the PROMG is continuing a focus on methods for pooling continuous data from outcome measures in meta-analyses. A recently published article described summarizing data as minimal important difference units. A second article, extending the method to situations in which some studies use instruments without an established minimally important difference, is in press. A paper just published in Research Synthesis Methods describes, from a statistical point of view, 12 available approaches to summarizing evidence from multiple trials using different instruments measuring the same construct. Another paper, recently submitted, is part of series of articles describing the GRADE approach to rating confidence in estimates of treatment effect that has been adopted by Cochrane. The article places the 12 approaches into five categories that will be informative from the point of view of Cochrane review groups, and illustrates how each can be presented in Summary of Findings tables. Finally, we are preparing an article that expands on the information available in the Cochrane Handbook PRO chapter and describing a number of aspects related to collecting, analyzing, and summarizing data from PROs in systematic reviews and meta-analyses.

Another continuing activity is to provide evaluations of PROs in the actual Cochrane treatment review areas; you can locate them at www.cochrane-pro-mg.org/index.html.

The next Cochrane Collaboration meeting will be held in Auckland, New Zealand. Gordon Guyatt will facilitate the workshop entitled “Making results of patient-reported outcomes interpretable.” The Patient-Reported Outcomes Methods Group Annual Meeting will also take place at the Auckland meeting.

If you wish to join our Methods Group, please complete the membership form on this website at www.cochrane-pro-mg.org/index.html. We thank MAPI Research Trust for providing funds and superb administrative support for our activities, as well as their assistance in setting up our website. Please join us at the next Cochrane Colloquium in Auckland September 30 - October 3, 2012!


October 17–19, 2012: 3rd EORTC QOL Conference “Quality of Life, Symptom Research and Patient Reported Outcomes in Cancer Clinical Trials”

The EORTC is holding a conference on QOL and cancer clinical trials which will be hosted at the European Commission, October 17-19, 2012. Visit the website for information on the complementary registration and to apply for a travel award. (http://www.eortc.be/probe/conference2012.htm).

There will be 40 travel awards granted (400 euros each) to early stage career investigators and those from developing countries. Uniquely in 2012, abstracts can be submitted to this QOL conference (register online at http://www.eortc.be/probe/Registration.htm).

Awards for best early career investigators, speakers, and research will be presented.

Attendance is free, due in part to this conference being co-funded by the European Union Public Health Program grant, but sponsorship opportunities still exist. To learn more, please contact Dr. Andrew Bottomley (Andrew.bottomley@eortc.be).

ISOQOL’s mission is to advance the scientific study of health-related quality of life and other patient-centered outcomes to identify effective interventions, enhance the quality of healthcare, and promote the health of populations. It carries out its mission primarily through the sponsorship of scientific conferences, its journal Quality of Life Research, and its special interest groups and chapters.
**ANNOUNCEMENTS**

Since its beginning in 1993, ISOQOL has been an international collaborative network including researchers, clinicians, patient advocates, government scientists, industry representatives, and policy makers who have unique perspectives and interests in HRQOL research. The backbone of ISOQOL is its methodologists, who concentrate on integrating qualitative and quantitative methods to improve the measurement and application of patient-reported outcomes (PROs) data in research, healthcare delivery, and population surveillance.

ISOQOL’s 19th Annual Conference will take place in Budapest, Hungary, on October 24-27, 2012. The scientific program will have great interest to all, including:

1. The use of PROs in clinical practice
2. The use of PROs in comparative effectiveness research
3. The use of technology for the delivery of clinical information, care and services

### The Translation and Cultural Adaptation Special Interest Group (TCA-SIG)

Katrin Conway1, Donald Patrick2, Mona Martin3, Sonya Eremenco4

1 MAP Research Trust, Lyon, France, 2 University of Washington, Seattle, WA, USA, 3 Health Research Associates, Inc., Seattle, WA, USA
4 United BioSource Corporation, Bethesda, MD, USA

The Translation and Cultural Adaptation Special Interest Group (TCA-SIG) of the International Society for Quality of Life Research (ISOQOL) was established in 2004. The TCA-SIG membership strives to identify needs and advance research in the fields of translation and cultural adaptation of Patient-Reported Outcomes (PRO) measures.

**How we are organized**

The TCA-SIG is chaired by Katrin Conway and Donald Patrick. Its 25 active members are divided into three subgroups, each pursuing individual objectives to meet the overall aim:

1. **The Cross-Cultural Issues Subgroup** is led by Sonya Eremenco, and addresses issues related to the access of copyrighted instruments, the translation of PROs and their use in e-format.
2. **The Translation Methodology Subgroup** is chaired by Mona Martin, and pursues a research agenda for the development of methodologies in the field of translation and cross-cultural research.
3. **The PRO Translation Certification Subgroup**, coordinated by Mona Martin and Katrin Conway, aims at developing and establishing an international certification program for PRO translations.

### 2011 Annual Meeting in Denver, Colorado, USA

The annual meeting of our group took place on October 27, 2011, during ISOQOL’s annual meeting in Denver, Colorado. Forty-seven participants attended the meeting. The primary focus was the following two invited presentations that gave rise to lively discussions:

1. “Spanish DTSQ: multiple translations and same language adaptations” by Annarita Felici from Health Psychology Research Ltd, University of London, London, UK; and,
2. “Pilot testing translations of PRO measures with populations who are difficult to interview” by Darren Clayson from PharmaQuest, Banbury, Oxfordshire, UK.

Come and participate at TCA-SIG 2012 Meeting in Budapest, Hungary

In preparation for this year’s TCA-SIG annual meeting during the ISOQOL gathering in Budapest in October 2012, we are soliciting ideas for presentations. If you are interested in participating, please submit your suggestions by email to Tatiana Gauchon at tgauchon@mapigroup.com outlining the following elements:

- (1) title of the talk
- (2) name of the presenter, his/her affiliation, and contact details,
- (3) three main points of the talk,
- (4) explanation of the topic’s relevance to the objectives of the TCA-SIG.

Please submit your proposals by June 15, 2012. All proposals will be reviewed by the TCA-SIG Steering Committee—composed of the two chairpersons of the SIG and the Sub-Group leaders—and two presentations will be selected. We look forward to your participation and suggestions and hope you will join us in Budapest. Information on the time and location of our annual meeting will be communicated in the ISOQOL program.

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**Call for Articles**

**PRO Newsletter 48**

Any news and information on Patient-Reported Outcomes are welcome (e.g., short articles on on-going Quality of Life research, announcements of publications, meetings, websites, etc.)

Deadline for submission: August 15, 2012

Please send your article by e-mail to Mathilde Charnay at mcharnay@mapigroup.com

More information on www.pro-newsletter.com/submission.html
CALENDAR

June 2-6, 2012
ISPOR 17th Annual International Meeting
Washington, DC, USA
Hilton Washington
http://www.ispor.org/Events/Index.aspx?eventid=38

June 12-14, 2012
PRO & ePRO Congress
Annecy, France
Les Trézos hotel
http://www.phtcorp.com/EU_PRO_ePRO_Congress_2012/

June 24-28, 2012
DIA’s 48th Annual Meeting
Philadelphia, PA, USA
Pennsylvania Convention Center

July 8-12, 2012
World Federation of Hemophilia World Congress 2012
Paris, France
Palais des Congrès

August 23-26, 2012
28th ICPE
Barcelona, Spain
Barcelona Convention Center
http://www.pharmacoepi.org/meetings/28ICPE/index.cfm

September 1-5, 2012
22nd Annual Congress of the European Respiratory Society (ERS)
Vienna, Austria
Reed Messe Wien
http://www.erscongress2012.org/

September 2-4, 2012
ISPOR 5th Asia-Pacific Conference
Taipei, Taiwan
Taipei International Convention Center

October 11, 2012
Universités de Pharmaco-Epidémiologie
London, UK
Venue to be confirmed
For more information please contact rogunfojuri@mapigroup.com

October 24-27, 2012
ISOQOL 19th Annual Conference
Budapest, Hungary
Marriott Hotel
http://www.isoqol.org/2012conference/

November 3-7, 2012
ISPOR 15th Annual European Congress
Berlin, Germany
ICC Berlin
http://www.ispor.org/Events/Main.aspx?eventid=39

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Patient Reported Outcomes (PRO) NEWSLETTER

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