

2007 ISOQOL Workshops ~ October 10, 2007

Morning Workshops (1-8)

9:30 am - 12:30 pm

Workshop 1

METHODS FOR CROSS-CULTURAL DEVELOPMENT, TRANSLATION/ ADAPTATION, AND EVALUATION OF HEALTH OUTCOMES MEASURES

Instructors: Sonya Eremenco, Evanston Northwestern Healthcare/Northwestern University, USA and Ramona Lucas, Universitat Autònoma de Barcelona, Spain

Cross-cultural translation of existing instruments has become an essential component of research methodology in preparation for multinational clinical trials. However, to improve cross-cultural equivalence, it is important to incorporate an awareness of cross-cultural issues prior to beginning translation work. This workshop will cover: 1) cross-cultural instrument development including a comparison of sequential, parallel, and simultaneous approaches with a special focus on WHOQOL methods; 2) types of cross-cultural equivalence and possible threats to validity if equivalence is not achieved; 3) instrument translation and adaptation methodologies; 4) use of qualitative evaluation methods such as cognitive interviewing techniques to assess linguistic validity and cross-cultural equivalence of translated questionnaires. Finally, we will discuss strategies to use to improve equivalence, such as the decentered model to refine the source instrument and alternatives when modification of the original instrument is not feasible. Workshop structure includes 65% lecture, 25% Q&A and 10% interactive exercises on translation methodology and cognitive interviewing.

level: Basic

Workshop 2

COPING WITH THE VALIDATION REQUIREMENTS OF THE FDA PRO GUIDANCE: SCIENCE AND THE PRACTICAL OUTCOMES RESEARCHER

Instructors: William Lenderking, Michelle Stewart, Pfizer Inc, USA and Elizabeth Merikle, Pfizer Inc, Canada

This workshop will take off from the draft PRO guidance and consider the practical implications and scientific evidence supporting certain aspects of the guidance. In particular, we will focus on validation of patient reported outcome measures in light of the guidance on conceptual frameworks, conceptual models, and endpoint models. We will also consider the scientific evidence for the recommendations around the recall period. Practical, real-world examples/ research dilemmas will be presented for discussion, and we will consider alternative solutions, as well as discussing the solution ultimately chosen. Questions to be considered include the following: What does the literature say about validation requirements for a scale that has been in use for decades but has obvious limitations? What constitutes sufficient validation? If a scale has been validated in a given study population, what are the validation requirements for applying it to a new population, according to both the FDA and the literature? What if your research team wants to administer a questionnaire on a weekly basis, and it has only been previously developed for monthly administration? Are there different aspects of health and functioning which might be optimally measured over different recall periods? Can measures with different recall periods be compared within the same study? Does it make sense to assess functioning on a daily basis, or should daily measurement be more appropriately reserved for symptoms?

level: Basic

Workshop 3

CAPTURING PATIENT-REPORTED OUTCOMES ELECTRONICALLY: FROM E-PRO DESIGN TO IMPLEMENTATION

Instructors: Kellee Howard, Jennifer Pettillo, United BioSource Corporation, USA, Jacqueline Thong, CRF, Inc., USA, Meghan Werner and Nancy Kline Leidy, United BioSource Corporation, USA

With rapid improvements in technology comes the opportunity to increase the efficiency and effectiveness of gathering patient-reported outcomes (PROs) by electronically capturing these data. E-PROs involve a variety of techniques, including personal digital assistants (PDAs), interactive voice response systems (IVRS), and computer touch screens, each offering unique opportunities and challenges. This workshop will address critical issues in e-PROs, including selection of the appropriate technology, instrument development and validation, and the execution of studies involving e-technologies. We will give specific attention to the use of PDAs for gathering quality of life, symptom, and other data during random, daily, or weekly assessments in keeping with the recall needs of the underlying concept being measured.

During the first portion of the workshop, moderators will lead participants in a discussion of the following issues: types of concepts most and least suited to e-data capture, unique features of each format, the development or revision of instruments for use on PDAs, and the type and timing of data to track study progress and contribute to instrument evaluation. Item development, cognitive debriefing, and scoring options for e-PRO using PDAs will be addressed, as will issues related to patient and site training to optimize data quality. Examples from the literature, the field, and experience with the EXACT-PRO Initiative(1) will inform the discussion. During the second portion of the workshop, participants will be involved in a practical application of ePRO-PDA development and will engage in hands-on experience using PDAs pre-programmed with a variety of question formats suitable for e-PRO data capture.

Organization: 50% lecture and discussion, 35% in-class exercise, 15% Q&A

(1) The EXAcacerbations of Chronic pulmonary disease Tool - The EXACT-PRO Initiative brings together industry, clinical, and regulatory (FDA) experts to develop a single PRO measure to evaluate exacerbations of COPD.

level: Basic

Workshop 4

SPECIFYING PATIENT-REPORTED OUTCOME MEASURES FOR CHRONIC DISEASE SELF-MANAGEMENT PROGRAMS : A FRAMEWORK TO ENSURE THE RIGHT OUTCOMES ARE ASSESSED AT THE RIGHT TIME

Instructor: Richard Osborne, The University of Melbourne, Australia

The choice of the right range of measures to capture the intended and unintended effects of interventions can be difficult for researchers and evaluators alike. With the plethora of measures available and the wide range of possible intended impacts of interventions, including immediate and long term effects, a framework to support comprehensive assessment is warranted. This workshop will focus on chronic disease self-management and education programs as a working example of how to specify what needs to be measured and how this can be done. Such programs may have a wide range of

immediate impacts (e.g., education/knowledge), intermediate impacts (e.g., empowerment, life quality) and longer term impacts (e.g., use of health services, reduction of symptoms).

Poor understanding and poor specification of the objective of an intervention leads to poor outcome measurement. Without a clear idea of what you are measuring, how can you measure it accurately? Consider social comparison, learning, changes in self image and the resulting change in perception (or response shift) which may attenuate participant s perceptions of disease severity.

The workshop will include insights derived from the heiQ (Health Education Impact Questionnaire), the National Quality and Monitoring System for chronic disease health education and self-management programs now applied in 250+ organizations across disease groups and intervention types.

In a high energy, fast moving and participatory workshop setting, attendees are encouraged to bring their current chronic disease program to the workshop for work-shopping so that the intended impact of their program can be clarified and a range of pertinent patient reported outcomes can be specified.

level: Basic

Workshop 5

APPLICATIONS OF ITEM RESPONSE THEORY MODELING FOR IMPROVING HEALTH OUTCOMES MEASUREMENT - Part I

Instructors: Bryce Reeve, National Cancer Institute, USA and Chih-Hung Chang, Northwestern University, USA

There is a great need in health outcomes research to develop instruments or assessment tools that can accurately measure a person's health status with minimal response burden. This need for psychometrically sound and clinically meaningful measures calls for better analytical tools beyond the methods available from traditional measurement theory. Applications of item response theory (IRT) modeling have increased considerably because of its utility for instrument development and evaluation, assessment of measurement equivalence, instrument linking, item banking, and computerized adaptive testing. IRT models the relationship, in probabilistic terms, between a person's response to a survey question and their standing on a health construct (e.g., fatigue or depression) being measured. This information allows instrument developers to create reliable and efficient quality of life measures tailored for an individual or group or specific applications. This introductory workshop will discuss the basics of IRT models and applications of these models to improve health outcomes measurement. Illustrations from empirical data will be used throughout the presentation that focuses on measuring key health-related quality of life domains in different disease populations.

level: Basic

Workshop 6

ANALYSIS OF LONGITUDINAL STUDIES OF HRQOL STUDIES

Instructor: Diane Fairclough, University of Colorado Health Sciences Center, USA

This course will provide an introduction to the analysis of longitudinal studies in which missing data can be considered ignorable or missing at random (MAR). We will describe strategies for distinguishing between repeated measures models and growth curve models. Examples will be given for building and testing hypotheses for both simple and complex models including strategies for inclusion of time-varying covariates and interaction. We will discuss the use of polynomial and piecewise linear models as well as covariance structures and their interpretation. Then we will discuss

models where missingness is assumed to be MAR conditional on auxiliary information. Finally we will discuss the concepts of moderation and mediation, and how to construct the appropriate models and tests. Handouts will include all slides. The workshop will include discussion (20% of time).

After completing this workshop, participants will be able to:

1. Choose between a repeated measures and growth curve model for the analysis of longitudinal data
2. Build models and construct hypothesis tests for both simple and complex models
3. Perform sensitivity analysis which incorporate ancillary information into the longitudinal models
4. Distinguish the concepts of moderation and mediations, set up the appropriate models for these concepts.

Participants should have experience with regression analysis.

level: Advanced

Workshop 7

ADVANCED PSYCHOMETRIC METHODS, PART 1: USE OF EXPLORATORY AND CONFIRMATORY FACTOR ANALYSES IN PRO INSTRUMENT DEVELOPMENT AND EVALUATION

Instructors: Dennis Revicki and Donald Stull, United BioSource Corporation, USA

The development and psychometric evaluation of PRO instruments requires the application of a number of different techniques, including exploratory and confirmatory factor analysis (FA). We will provide a brief overview of psychometric analyses and then focus on the application of exploratory and confirmatory factor analysis for understanding of new measures and use of Structural Equation Modeling (SEM) for testing construct validity. Exploratory and confirmatory FA can be used to examine the relationships among items with a PRO measure or among different domains or multiple PRO measures. These techniques are useful for understanding the internal structure of PRO instruments and for understanding construct validity. This workshop will describe the main methods of FA and illustrate these methods with examples from the instrument development literature. SEM is a powerful analytic technique that combines FA and path analysis in a simultaneous, confirmatory approach. Using SEM, the researcher can specify and evaluate hypothesized relationships between observed and latent (unobserved) constructs as well as relationships among the latent variables. SEM can also estimate the reliability and validity of measurement models while explicitly modeling measurement error. A researcher constructs a structural model which specifies relationships among the latent variables to examine construct and criterion-related validity. If the observed covariances are consistent with the model-implied covariances, the researcher has evidence supporting the construct validity of the PRO measure. This workshop will demonstrate the main methods, testing assumptions and criteria, and provide examples to illustrate the methods of SEM.

level: Advanced

Workshop 8

INTERPRETING UTILITY (PREFERENCE-BASED) MEASURES OF HEALTH-RELATED QUALITY OF LIFE

Instructors: David Feeny, Kaiser Permanente, Northwest Region, USA, George Torrance, i3 Innovus, Canada, William Furlong and John Horsman, McMaster University, Canada

The Workshop will be at an advanced level, focusing on the interpretation of utility scores from direct and multi-attribute (indirect) approaches to measurement. The direct approaches will include the visual

analogue scale (Feeling Thermometer), time tradeoff, and standard gamble. Major multi-attribute utility measures will include the EQ-5D, Health Utilities Index (HUI), and Short-Form 6D. In addition, recent work on disease-specific utility instruments will be presented. The Workshop will include hands-on experience in the direct assessment of utility scores, completing questionnaires from several systems, and analyzing and interpreting the results. The interpretation of scores will be considered in the context of comparing groups at a point in time as well as comparing within-person change over time. Applications will be drawn from diverse settings including osteoarthritis of the knee, multiple sclerosis, total hip arthroplasty, and acute lymphoblastic leukemia. Evidence on clinically important differences will be discussed. Attendees should, at a minimum, have a basic knowledge of the conceptual foundations and practical approaches of the utility approach to assessing health-related quality of life.

level: Advanced

Afternoon Workshops (9-16)

1:30 - 4:30 pm

Workshop 9

METHODS FOR DEVELOPING PREFERENCE-BASED MEASURES OF HEALTH

Instructors: John Brazier, Tracy Young and Katherine Stevens, The University of Sheffield, UK

Recent years has seen increasing reliance on a few generic preference-based measures of health (e.g. EQ-5D, HUI3, QWB or SF-6D) for calculating Quality Adjusted Life Years (QALYs) for economic evaluation. However, generics measures may not be used in key clinical studies. This may be due to a desire to reduce patient burden or a view that generic instruments are not valid for the condition or responsive to the effects of treatment. For these reasons there is interest in developing new preference-based measures of health. This workshop focuses on the development of the health state classification of a preference-based measure rather than the other stages of valuing a sample of states and modelling the health state values. The workshop offers a practical introduction to the use of qualitative and psychometric methods in the development and refinement of health state classifications. It will also examine the policy implications of using different descriptive systems to derive preference-based measures. It assumes a basic knowledge HRQoL measurement and QALYs.

There will be four brief presentations:

1. An introduction: rationale and overview
2. The use of qualitative methods to develop a health state classification
3. The use of psychometric methods (including Rasch analysis) to develop a health state classification amenable to valuation
4. Policy implications of using different descriptive systems to estimate preference-based measures of health.

These presentations will use practical examples throughout. Organisation of workshop: 60% will be composed of these four brief presentations on each of these topics, 40% for discussion of the presentations and general Q&A. Recommended reading: Brazier J, Roberts J (2006) Methods for developing preference-based measures of Health. In (ed) Jones A. The Elgar Companion to Health Economics. Edward Elgar, Cheltenham UK.

level: Basic

Workshop 10

ADVANCEMENTS IN THE THEORY AND PRACTICAL APPLICATION OF RESPONSE SHIFT (RS)

Instructors: Lena Ring, Uppsala University, Sweden, Sara Ahmed, McGill University, Canada, Carolyn Schwartz, Delta Quest Foundation, USA, Mirjam Sprangers, Academic Medical Center/University of Amsterdam, The Netherlands and Richard Osborne, University of Melbourne, Australia

This workshop will have a balance between the theoretical underpinnings of RS, the alternative methods of revealing the presence of RS, and the practical applications in the research setting. Special attention will be paid to how RS might confound measurement or be a key indicator of an intervention effect.

A variety of techniques are available to identify RS, these include open interviews, structured interviews using the then test, pen and paper questionnaires and through statistical procedures. The pros and cons of these will be outlined, drawing heavily on workshop participant's current experiences and future research needs. Case studies will be used throughout the workshop to help participants walk through the thinking process patients go through when responding to health status questionnaires and to understand how response shift may come into play.

The following will be introduced throughout the workshop:

Introduction to Response Shift

- i. A 'potted' history of RS
- ii. Current definitions of the phenomenon
- iii. Why is RS the 'dirty laundry' of measurement?

Part B:

The practical application and utilization of RS across research settings

- i. When might RS be a measurement confounder?
- ii. When might RS be an intended outcome?
- iii. Mechanisms for identifying and quantifying RS across settings
- iv. Examples of where RS has moved from theory to practice.
- v. The role of response shift in the clinical setting

level: Basic

Workshop 11

MIGRATING PAPER PATIENT REPORTED OUTCOMES (PRO) TO ELECTRONIC PATIENT REPORTED OUTCOMES (EPRO) IN THE CONTEXT OF THE FDA'S PRO GUIDANCE

Instructors: James Pierce, ClinPhone, USA

Patient-reported outcome (PRO) assessments play important roles in many clinical trials. The FDA has issued a draft PRO Guidance intended to describe how PRO instruments will be evaluated in terms of their appropriateness and adequacy as efficacy endpoints in clinical trials. In addition, the draft Guidance states that modified PRO instruments will be reviewed by the agency to determine if the changes have been adequately justified and whether sufficient evidence exists that the changes have not introduced response bias. Most PRO instruments have been developed for paper administration, but there is increasing recognition of the many advantages of electronic data capture (i.e., ePRO).

Therefore, administering an initially paper-based PRO instrument on an electronic platform is considered an instrument modification, which must be justified by the sponsor. The goal of this session is to review the scientific and practical implications of migrating PRO instruments to ePROs in light of the draft Guidance. Our speakers spotlight typical ePRO migration scenarios and offer suggestions on how to meet the scientific and regulatory expectations of each. Dr. Stephen Coons will present preliminary recommendations from an academic-industry-FDA ePRO Consensus Development Working Group that considered the state of the science regarding PRO migration and validation issues. An FDA speaker will be invited to provide further detail from the Guidance with respect to regulatory expectations regarding the re-validation process. The speakers will consider the practical, psychometric, statistical, and regulatory issues involved in migrating PRO instruments developed and validated on paper to electronic platforms.

level: Basic

Workshop 12

DECISION MAKING AND QUALITY OF LIFE

Instructors: Penny Pierce, Patricia Hershberger, Anne Thomas, Cynthia Arslanian-Engoren, University of Michigan, USA

Decision making is a complex and dynamic human endeavor made evermore difficult when facing a potentially life-threatening illness for which one must choose from among an array of unfamiliar options. Sometimes a decision leads to a good outcome and other times an unwanted and untoward outcome creates havoc and disrupts one's psychological equilibrium in pervasive ways. The linkage between decision behavior and the outcomes of one's decisions ultimately defines those features we call quality of life. Yet this relationship between decision making and quality of life is a relatively unexplored area of investigation. This workshop will give an overview of the state of the science in patient decision making identifying the critical features instrumental in influencing the appraisal of quality of life. Specifically, the workshop will present a discussion of potential pre-decision hazards (e.g., satisficing), the elicitation of preferences and values, relevant psychological processes (e.g., affective forecasting), and executive cognitive functions that influence decision outcomes, which in turn, play an important role in the features holistically characterized as quality of life. An emphasis will be placed on identifying relevant measures and methods used to capture these sometimes elusive human experiences that are involved in making decisions which may inextricably change the course of one's life as well as the personal appraisal of one's quality of life. The importance of understanding the decision making process lies in targeting areas where structured interventions could be tailored to improve health care decisions thereby enhancing the likelihood of post-decision satisfaction, psychological well being and a desirable quality of life.

level: Basic

Workshop 13

PROGNOSTIC ASSESSMENT OF BASELINE HRQOL IN ONCOLOGY

Instructor: Murielle Mauer, PhD, Data Center, EORTC, Belgium

Prognostic factor analyses are used in oncology to identify variables that are independent predictors of outcome. Since the advent of methods for measuring health-related quality of life, several studies have been published in which QoL variables have been identified as important prognostic factors in addition

to clinical factors. This finding has considerable importance, particularly in advanced disease where treatment is generally palliative and the aim is to optimize QoL.

However, due to the specific nature of QoL data, classical analysis techniques are not always appropriate and might lead to parameter estimates of incorrect magnitude, incorrect sign etc. This workshop aims to give an overview of the issues related to the assessment of the prognostic value of baseline QoL in oncology trials and to propose some practical recommendations to circumvent these problems. Examples will be drawn from application of the discussed techniques on an existing data set.

Workshop outline:

1. Introduction
 - a. Definitions: prognostic/predictive/risk groups
 - b. Prognostic models
 - c. Classic methodology
2. QoL specific issues
 - a. Multiplicity
 - b. Multi-collinearity
 - c. Missing data
3. Analysis plan
 - a. Variable selection
 - b. Building the model
 - c. Checking the model
4. Validation
 - a. Internal validation
 - b. External validation
 - c. Bootstrap
 - i. Variable selection
 - ii. Model stability

level: Basic

Workshop 14

APPLICATIONS OF ITEM RESPONSE THEORY MODELING FOR IMPROVING HEALTH OUTCOMES MEASUREMENT - Part II

Instructors: Chih-Hung Chang, Northwestern University, USA and Bryce Reeve, National Cancer Institute, USA

There is a great need in health outcomes research to develop instruments or assessment tools that can accurately measure a person's health status with minimal response burden. This need for psychometrically sound and clinically meaningful measures calls for better analytical tools beyond the methods available from traditional measurement theory. Applications of item response theory (IRT) modeling have increased considerably because of its utility for instrument development and evaluation, assessment of measurement equivalence, instrument linking, item banking, and computerized adaptive testing. IRT models the relationship, in probabilistic terms, between a person's response to a survey question and their standing on a health construct (e.g., fatigue or depression) being measured. This information allows instrument developers to create reliable and efficient quality of life measures tailored for an individual or group or specific applications. This introductory workshop will discuss

the basics of IRT models and applications of these models to improve health outcomes measurement. Illustrations from empirical data will be used throughout the presentation that focuses on measuring key health-related quality of life domains in different disease populations.

level: Advanced

Workshop 15

EVALUATING CHANGE IN HEALTH-RELATED QUALITY OF LIFE MEASURES

Instructor: Kathleen Wyrwich, Saint Louis University, USA

Although numerous measures have been developed for the evaluation of health related quality of life (HRQoL), strategies for identifying meaningful change in these measures have not kept pace with instrument development. As a result, clinical trial researchers, quality assurance assessment teams, practicing clinicians, and patients are without established standards to evaluate change in HRQoL measures. This course will review, critique and compare the methods that have been applied to establish HRQoL change standards, which include anchor- and distribution-based techniques. Practical approaches to improving and advancing HRQoL change evaluations that enhance the interpretation of change, as well as a review of controversies that have developed will be provided. In addition, the course will explore future qualitative and quantitative challenges in this area of HRQoL research, and current regulatory guidelines for demonstrating important change in patient-reported outcomes.

level: Advanced

Workshop 16

ADVANCED PSYCHOMETRIC METHODS, PART 2: EXECUTING AND INTERPRETING EXPLORATORY AND CONFIRMATORY FACTOR ANALYSES IN PRO INSTRUMENT DEVELOPMENT AND EVALUATION

Instructors: Donald Stull and Margaret Vernon, United BioSource Corporation, USA

This half-day workshop will build on Advanced Psychometric Methods, Part 1 by presenting results from examples of exploratory and confirmatory factor analyses; executing live, interactive analyses; and interpreting results of output, particularly for confirmatory factor analyses and structural equation models. We will work through examples of analyses by presenting hypothesized models, discussing key analytic criteria (e.g., sample size, factor loading size, extraction, rotation, key parameter estimates, cross-loadings and correlated errors, model specification and identification, fit indices, indications of model misfit), and how to interpret output. Annotated examples will be presented from output from selected software (e.g., SAS, Stata, EQS, and Mplus), but the issues are relevant regardless of the users software.

level: Advanced