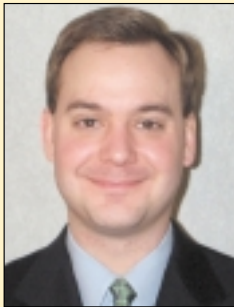


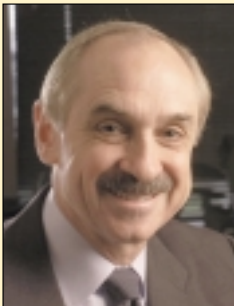
Science  
& Policy  
OPINION

## Risk Management, Health Economics and Outcomes Research: An Intersection? (PART 1 OF A 2-PART SERIES)



By Charles Clark and Bryan Luce, Ph.D., M.B.A.

It is well accepted that all drugs carry some element of risk. When the FDA approves a drug for marketing, it implicitly...sometimes explicitly...concludes that benefits are judged to outweigh perceived or known risks. To date, risk for most drugs is dealt with through several postmarketing activities including provision of use information in the package insert, regulation of promotional activities and claims, provider voluntary reporting and manufacturer mandated reporting of safety concerns. Recent findings concerning COX-2 inhibitors and SSRIs have raised public, political and regulatory antennae related to monitoring and managing risk.



However, as FDA policy on the minimization of risk (see Guidance FDA May 2004) continues to develop, one must keep in mind that risk is dependent upon benefit for FDA, as well as to manufacturers and the public at large. That is, risk acceptability is always relative to benefit. Benefit, of course, is essentially synonymous with the likelihood and magnitude of clinical improvement and, we would argue this can be measured via economic outcomes. When clinical benefit is perceived or demonstrated to be high, higher risk may be tolerated.

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## Enhancing Survival Analysis of Adherence with Time-Dependent Variables

By Steve Blume, M.S.

The adherence of patients to their prescribed medication is critical to successful disease management, and thus to providers, payers, and manufacturers, and ultimately to the patients. Historically, low patient adherence rates across all illnesses and therapeutic areas has stimulated much research to measure adherence and understand the factors involved.<sup>1,2</sup>

One analysis begins with counting the number of patients who are compliant for certain lengths of time (e.g., 30 days, 90 days, one year). The frequency counts can be analyzed by

cross-tabulating them by treatment or other variables and computing chi-square statistics for hypothesis testing.

Another approach known as *survival analysis* has become popular in adherence research. Survival analysis models the probability of discontinuing at a particular time, given continuance until that time (referred to as the *hazard function*). It turns out that the mathematics of this approach yield several advantages over analyzing cross-tabulations: 1) It is more efficient, as each patient's length of adherence is used, not just whether they discontinued within an arbitrary length of time; 2) The available information from patients who are lost to follow-up is retained and incorporated in the estimates of sampling error. For example, the patient who disappears from a claims database after 3 months can still be part of the sample of

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## Electronic Data Capture: A Window on DataFax

By Yasmine Draoui, M.S.

**M**EDTAP ensures fast and accurate electronic data capture with DataFax Software. DataFax is a closed and validated computerized system that MEDTAP acquired in the summer of 2004 to enhance the efficiency of in-house data management. This system allows data to be faxed directly into the database from anywhere in the world using Intelligent Character Recognition (ICR) technology. This data is then reviewed and “cleaned” by a team of at least two staff members. With this system in place, MEDTAP can offer secure data transfer and management that is far more efficient than relying upon printed Case Report Forms (CRFs), which require mail transport. Specific benefits include:

- **Improved Data Accuracy.** To ensure the data’s accuracy, the project team reviews all data read by the software. The project team can correct mistakes literally as soon as they occur, and can ensure that mistakes are not repeated as future participants enroll in the study.
- **More Efficient Data Management.** With queries being sent and responded to on a regular basis, the time for database lock is reduced and analyses can be completed more rapidly.
- **Increased Regulatory Compliance.** MEDTAP has established the necessary processes within DataFax to ensure that studies using this system will comply with all applicable data-management regulations.

This system provides maximum efficiency and the highest quality data for all parties involved. It also offers these additional advantages:

- Dramatically simplified printing requirements (for example, CRFs do not need to be printed on 3-part NCR paper).
- Less administrative work for the site staff, who can now process the CRFs at the time of submission—this in turn can lead to easier site recruitment and more effective data collection on-site.
- Automatic tracking of all CRFs received, with less work required of the project team. Multiple reports can be generated at any time to provide an accurate picture of the current database status and quality.

- The ability to save all CRFs submitted to DataFax as a .PDF document, which can be sent more conveniently to all necessary and authorized personnel at the end of the study.

The DataFax system can accept faxes 24 hours a day, 7 days a week, year-round, resulting in faster, simpler, secure data collection for the many international studies that MEDTAP designs and oversees. With DataFax, MEDTAP can provide rapid and efficient data entry, and better review, quality control, and analysis for all types of research, from small studies to large, complex, multi-site trials.

For more information, contact Yasmine Draoui, MEDTAP’s DataFax Administrator, at 301-986-6776, [Draoui@MEDTAP.com](mailto:Draoui@MEDTAP.com). 

## Applying Multi-Attribute Theory in Developing Health Utility Measures

By Kathy Beusterien, M.P.H.

**F**or some health conditions like amyotrophic lateral sclerosis (ALS), there is substantial variability in the combinations of functional status areas (e.g., swallowing and walking) that decline over the course of disease, thus resulting in a wide range of possible health states that may be observed in the study population at any given time. When developing health utility measures for such conditions, it would be ideal to allow computation of utilities, or preference, weights for all the possible health states. This can be addressed using multi-attribute theory, which is concerned with expressing the utilities of multiple-attribute outcomes as a function of the utilities of each attribute taken singly.

Using a multi-attribute preference approach, MEDTAP developed the ALS Utility Index (ALSUI) for estimating US population-based utilities for the various possible health states observed in ALS. The ALSUI incorporates utilities for different severity levels within the following attributes: Speech and Swallowing; Eating, Dressing, and Bathing; Leg Function; and Respiratory Function. Data were collected through an internet-based survey administered to a random sample of the US population. The study provides a useful tool for classifying ALS patients and determining a general public-based utility score for ALS health states.

The study findings titled “Integrating preferences into health status assessment for amyotrophic lateral sclerosis: the ALS Utility Index” is currently in press in *ALS and Other Motor Neuron Disorders*.

For more information, contact Kathy Beusterien, [Beusterien@MEDTAP.com](mailto:Beusterien@MEDTAP.com). 

## An Intersection?

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Conversely, when benefit is low, little risk will be tolerated. It is also noteworthy that risk and risk management are not without cost. Thus, when the risk-benefit ratio is affected, the cost-benefit ratio will likely also be affected.

### Science & Policy OPINION

This is the first of two articles to be published by *ResearchNEWS* on the topic of the relationship between risk and outcomes. This first article focuses on how the FDA defines and approaches risk management. A follow-up article will explore the intersection of risk management, health economics and outcomes research.

### The FDA and Risk Management

In May, 2004, FDA released long-awaited draft guidance for pharmaceutical product risk management. Over the past five years, FDA has publicly promoted the need for manufacturers to reconsider how they define, minimize and evaluate the risks associated with their products during and after approval. Consistent with FDA's goals under the Prescription Drug User Fee Act (PDUFA III), three draft guidance documents were released for comments: (1) Guidance for Industry: Premarketing Assessment, (2) Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment and (3) Guidance for Industry: Development and Use of Risk Minimization Action Plans. These draft guidance documents provide insight into FDA's current perspective on risk management and its future direction. It should be noted that FDA has already implemented many of the concepts discussed within these guidance documents on a limited scale for unique products.

Risk management, as defined by the FDA, is the coupling of risk assessment and risk minimization. The risk management process is iterative, and should equally focus on assessing the overall benefits and risks of the product, developing and implementing systems and methods, or tools as termed by FDA, that most effectively minimize risk while maintaining the benefits of the product, evaluating these tools to ensure effectiveness, and adjusting the selected tools to improve the balance between benefit and risk. Once a product's benefits and risks are properly assessed, the risk management process changes focus from risk identification to program development, implementation and evaluation. To successfully accomplish all of these tasks, FDA has outlined processes and elements of potential programs collectively defined as a Risk Minimization Action Plans or RiskMAPs.

### Risk Minimization Action Plans

RiskMAPs are not expected to be required for all New Drug Applications (NDAs), but FDA will be evaluating the need for RiskMAPs on a case by case basis to determine

whether a RiskMAP is appropriate. Criteria to determine the need for a RiskMAP includes: (1) evaluation and comparison of the rate and severity of the known risks compared to the anticipated benefit, (2) evaluation of the probability that preventive measures can be taken to successfully reduce the known risk, and (3) belief that the product when coupled with a RiskMAP still constitutes net benefit to the public.

### Goals and Objectives

A RiskMAP provides clear goals and objectives, and outlines specific tools necessary to implement and evaluate a solution which will minimize risk while preserving its benefits. Creating a RiskMAP starts with stating goals, and these goals should identify optimal outcomes even if these outcomes may not be achievable. An example of a goal is "no woman who is already pregnant will be prescribed/dispensed drug X and no pregnancies will occur while on drug X". Once goals have been defined, they can be effectively translated into practical, specific and measurable objectives.

### Tools

Proper risk minimization tools can be selected after goals and objectives are clearly defined. These tools usually consist of programs which will more effectively communicate information related to the optimal use of the product, and they may provide information to encourage appropriate prescribing, dispensing, and use of the product. Finally, these tools may require additional procedural steps in the care process to help achieve one or more of the stated objectives where education and communication are not believed to be sufficient.

RiskMAP tools generally fall into one of three categories defined by increasing level of effort and restrictiveness: (1) focused education efforts, (2) systematic reminders to the care group and patient and (3) result-linked product access systems. As can be expected, the selection of the appropriate method to use is based on the severity of the risk and the likelihood that the chosen tool will most effectively minimize the risk while maintaining the highest possible benefit, including maintaining patient access to the medication and minimizing provider burden.

### Focused Education

The intent of focused education is to provide specific information to physicians, pharmacists and patients who have an impact on the proper use of the product. This targeted information must be comprehensible to the audience and should be relevant to the audience's role as a healthcare provider, caregiver or patient. For healthcare providers, these programs may consist of "Dear Doctor or Dear Pharmacist" letters, Continuing Education programs focused on the specific risks, and labeling information

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such as Black Box Warnings. Targeted patient education can be more difficult. Today, the most effective form of targeted education is through Patient Medication Guides.

### Science & Policy OPINION

Similar to labeling, FDA has established guidelines for the format and content of such Guides. Patient Medication Guides provide simple, easy-to-read summaries of the risks associated with the product. For instance, the Medication Guide

for Orphan Medical's Xyrem®, a Schedule III controlled substance with the active ingredient gamma-hydroxybutyrate (GHB), provides a bullet point on the first page of the Guide warning patients that the drug can lead to dependence and can cause coma or death.

### Reminders

Where targeted education is not sufficient, focused reminders may be more effective. Here, the intent is to create steps and processes that continuously remind the care group and patients of the risks and responsibilities associated with the use of the product. These programs may consist of Prescriber Certification or Self-Certification, Patient Informed Consent, and special packaging such as Unit Dose packaging or limited supply/no refill dispensing parameters. None of these steps directly reduces risk; however, they heighten product risk awareness. An example of a reminder is the Patient Informed Consent document that every patient must sign prior to a physician performing Laser-Assisted In Situ Keratomileusis or LASIK surgery explaining that the surgery may result in permanent blindness.

### Result-linked Access (Registries)

In unusual circumstances, focused education and reminders are deemed insufficient by the FDA. For products with particular serious risks, result-linked, or performance linked, access systems may be the only chance for product approval or for maintaining market approval. In most cases, the benefits of these products are unique to specific patient populations, providing significant benefits over other therapy options. A classic example of a result-linked access registry is the program required for Novartis's Clozaril®. In this case, since Clozaril® can cause agranulocytosis, a potentially fatal condition, all physicians prescribing, pharmacies stocking, and all patients receiving the medication must be registered within a database. In addition to being registered, the physician and pharmacist must review the white blood cell count for the patient either weekly or every-other-week, depending on set criteria, to ensure that the count remains normal. If the count drops below specified levels, the patient must be removed from the product. All laboratory values must be reported to the manufacturer for monitoring.

In many cases, these tools can be modified to achieve the proper balance between risk and benefit. For example, as a deviation from the previously described performance linked access system, FDA has approved programs where test results must be monitored by the healthcare provider but the data may reside with the prescriber only. Here, the level of effort necessary for the healthcare provider to participate in the program is minimized by eliminating the need to interact with a centralized database.

### Evaluation

Just as having the proper goals, objectives and tools are critical to the success of the RiskMAP, proper evaluation design is essential

**Today, the most effective form of targeted education is through Patient Medication Guides.**

to confirm that these earlier assumptions and elements are demonstrating the anticipated risk minimization impact. In some cases, proper evaluation design has been overlooked and programs have failed, in the eyes of the FDA, due to the manufacturer's inability to provide scientifically sound and meaningful data to defend the implemented program. Along with other health outcome measures that the manufacturer may find beneficial, the evaluation should answer the following questions: (1) Are tools effective and cost-effective? (2) Are stakeholders satisfied with the results? (3) Can the tools be improved?

In addition to these questions, these programs can provide the manufacturer with an opportunity to layer additional outcomes objectives into the program for a marginal cost, which one can argue may be more than compensated by the larger expected benefit of capturing market useful evidence of value. In the upcoming issues of *ResearchNEWS*, we will explore the impact of risk management on the product's ROI, product pricing, and the costs, both direct and indirect, associated with the development and implementation of these programs.

*Chad Clark has more than five years of experience with UBC-Late Stage providing the highest level of quality and competence for the management of Risk Management and Registry solutions.*

### References

Guidance for Industry Premarketing Assessment  
<http://www.fda.gov/cder/guidance/5765dft.htm>

Guidance for Industry Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment  
<http://www.fda.gov/cder/guidance/5767dft.htm>

Guidance for Industry: Development and Use of Risk Minimization Action Plans  
<http://www.fda.gov/cder/guidance/5766dft.htm>

For more information, contact Charles Clark, [cclark@unitedbiosource.com](mailto:cclark@unitedbiosource.com) or Bryan Luce, [Luce@MEDTAP.com](mailto:Luce@MEDTAP.com). 

## Will Pharmacoeconomics Have a Role in Implementing the Medicare Part D Drug Benefit?

By Diane L. Simison, Ph.D.

**A**s part of preparing for the implementation of the Medicare drug benefit in 2006, the Center for Medicare and Medicaid Services (CMS) periodically issues guidelines on how the implementation of the new drug benefit will work. Medicare Part D of Title XVIII of the Social Security Act was provided for by Title I of the Medicare Modernization Act passed into Federal law in late 2003, and is to be implemented in 2006. Although of keen interest to pharmaceutical firms, the purpose of these guidelines is to help managed care organizations and pharmacy benefit management companies to decide how and whether to participate in the program and how to plan for its implementation. These potential Medicare contractors, who are under contract to CMS to implement the benefit, will need to have transparent processes and procedures for making coverage decisions for new drugs.

One guideline, titled, "Medicare Modernization Act Guidelines – Formularies: CMS Strategy for Affordable Access to Comprehensive Drug Coverage", was issued on December 3, 2004 and is available on the Prescription Drug Plan (PDP) page of the CMS website ([www.cms.gov/pdps/Formularies:CMSStrategyforAffordableAccessToDrugsCoveredunderMMA](http://www.cms.gov/pdps/Formularies:CMSStrategyforAffordableAccessToDrugsCoveredunderMMA)). It is worth a look by health economists because it describes the ways that CMS will review Medicare prescription drug plans to assure that beneficiaries "receive clinically appropriate medications at the lowest possible costs".

CMS will require that a pharmacy & therapeutics (P&T) committee be established and used in accordance with nationally recognized P&T guidelines, that is, either the American Society of Health System Pharmacists (ASHP) Statement of the Pharmacy and Therapeutics Committee (1992), or by the Academy of Managed Care Pharmacy (AMCP) Principles of a Sound Drug Formulary System (October 2000). For formulary management, the CMS Formulary Guideline lists the following: "Formulary management decisions must be based on scientific evidence, and may also be based on pharmacoeconomic considerations that achieve appropriate, safe and cost-effective drug therapy." Further, "Clinical decisions by the P&T committee should be based on scientific evidence and standards of practice, including peer-reviewed medical literature, well-established clinical practice guidelines and pharmacoeconomic studies, as well as other sources of appropriate information" (pg. 6 of 11).

We can deduce from this CMS Formulary Guideline that pharmacoeconomic studies may (note: not must) be considered as part of the formulary decision process. The Guideline contents suggest that for Part D plans, the transparent, evidence-based coverage that so many economists

and reimbursement professionals have been writing about may soon become mainstream. The Guideline also suggests that implementing the Part D (see first paragraph) benefit will involve many of the practices in place today as well as future evidence-based research by MCOs which use pharmacoeconomic data as part of the decision making process.

Therefore, we advise manufacturers to assume that the full complement of pharmacoeconomic data will be an important part of a dossier submission for Medicare reimbursement. We refer, of course, to cost of illness studies, claims database analyses, economic evaluation of clinical trials (as appropriate) as well as cost-effectiveness and budget impact models. Even if not required by plans, it appears to us that pharmacoeconomic evidence will likely be both acceptable and accepted by plans. In either case, this will provide manufacturers with the opportunity to present their products in terms of their value. From the plans' point of view, such evidence will help them determine the value for money they will be asked to expend as well as the estimated budget impact under various scenarios.

CMS will soon issue the final rule for implementing the Part D drug benefit, and this rule will probably be available on the CMS website by the time this newsletter is in print.

For more information, contact Diane Simison, [Simison@MEDTAP.com](mailto:Simison@MEDTAP.com). 

## Advancing Patient Reported Outcome Measurement and Research

By Dennis Revicki, Ph.D.

**T**he National Institutes of Health in September awarded the Patient Reported Outcome Measurement and Information Service (PROMIS) statistical coordinating center (SCC) project to David Cella and researchers at Northwestern University. The SCC also includes Dennis Revicki, Karin Coyne, Karen Gold and Chris Thompson in the Center for Health Outcomes Research, MEDTAP International; Ron Hays and Steve Reise from the University of California-Los Angeles; and researchers at WESTAT. The SCC will coordinate PROMIS-related activities, and its investigators will work closely with NIH researchers and an advisory panel to guide the research agenda. In addition, the PROMIS initiative has funded six primary research centers at the University of Washington, Seattle, Stanford University, the University of North Carolina, Duke University, University of Pittsburgh,

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NEWS  
Briefs

## MEDTAP Staff Part of Georgetown University Medical Center's New Georgetown Center for Trauma and the Community

By Lori Frank, Ph.D.

**T**he Georgetown Center for Trauma and the Community is newly funded by the National Institute of Mental Health (NIMH) and is directed by Bonnie L. Green, PhD, Georgetown Department of Psychiatry. Associate directors are Dennis Revicki, PhD, of MEDTAP International, along with Mary Ann Dutton, PhD, (Georgetown Psychiatry) and Sharon Ramey, PhD (Georgetown College of Nursing and Health Studies).

The Center is inter-disciplinary and its primary focus is on developing and testing the effectiveness of innovative and sustainable mental health-related interventions for low-income women who have experienced trauma, and their families. Center personnel conduct research to advance culturally appropriate and innovative methods, and research designs for trauma intervention. The Center provides coordinated research training and mentoring, and maintains ongoing community partnerships to inform its direction and to implement collaborative research activities.

The center has over \$2.7 million in funding for the first five years. A unique feature of the Center is its link to primary health care systems that serve low-income and minority clients in the Washington, DC area. Establishing ongoing partnerships between academic researchers and community providers is a central Center goal. The community partners who are participating in the Center's activities include Unity Health Care, Inc. in Washington DC, and from two surrounding Maryland counties, the Primary Care Coalition in Montgomery County, and the Prince George's County Health Department (Maternal and Child Health).

Dennis Revicki co-chairs the Methods Core Group, with a task of developing and providing consultation on state-of-the-art research design, methods, statistics, and outcomes measures. The Methods Core will provide input on the first set of planned Center research studies.

Lori Frank, PhD, is Chair of the Mental Health Outcomes team, tasked with the development, adaptation, and translation of culturally sensitive mental health and trauma outcomes measures. Key research topics for this team include the definition of clinically meaningful outcomes, item reduction and burden minimization for data collection, and the feasibility of various modes of instrument administration (e.g., PDAs, telephone) for this population.

## MEDTAP Welcomes New Staff

**Steven Blume, M.S. is a Senior Project Manager** in the Center for Health Economics at MEDTAP in Bethesda, MD. His responsibilities include economic evaluation, Markov modeling, retrospective database analyses, and statistical analysis. Prior to joining MEDTAP, Mr. Blume was a researcher for the Center on Drugs & Public Policy at the University of Maryland School of Pharmacy. He researched the cardiovascular risk of COX-2 inhibitors and the costs and adherence to therapy of overactive bladder patients, in both cases using Medicaid claims. The work has resulted in articles for *Health Affairs*, *Archives of Internal Medicine*, *Pain Medicine*, and *Formulary*. Mr. Blume received a M.S. in Engineering-Economic Systems from Stanford University, and an M.S. from Northwestern.

**Peter Dale, M.Sc. is a Senior Research Assistant** in the London office of MEDTAP. Mr. Dale has experience in both economic modeling and systematic reviews. Most recently he was involved in building a decision analytical model, using TreeAge DATA, to determine the cost effectiveness of In Vitro Fertilization (IVF) in Italy. Other projects include a systematic review on IVF and a cost effectiveness analysis of a nasal spray for acute migraine in the UK. He has also conducted market analyses in the biotechnology and medical devices sectors. Mr. Dale holds a Master of Science in Health Management with a specialization in health economics from Imperial College of Science, Medicine and Technology, UK.

**Julia Dixon, B.S. is a Research Assistant** with MEDTAP in Bethesda, MD. Her responsibilities include conducting literature and web searches, developing tables and spreadsheets, data collection and organization, and assisting in the review, preparation and editing of reports and manuscripts. Ms. Dixon recently received her Bachelor's of Science degree in neuroscience from the College of William and Mary.

**Scott Doyle, B.A. is a Research Assistant** in MEDTAP's London office. He is currently undertaking his Masters of Science in Health Psychology at the University of Westminster in London. Mr. Doyle has extensive expertise in the etiology and treatment of obesity and weight disorders, as well as clinical experience in dealing with vulnerable populations, including children and mental health patients. Scott conducts interviews and debriefings

In addition, the Mental Health Outcomes Team will keep a repository of mental health measures that have been used in diverse populations and have been translated and/or culturally validated.

Lori Frank is also collaborating on the first Center study (PI, Joyce Chung, MD): Establishing Ethnographic Grounding of Interventions for Trauma-Related Problems. Data collection for this study has already begun. The

of participants in quantitative and qualitative studies, with particular emphasis on health-related quality of life.

**Beth A. Hahn, Ph.D. is Managing Director** with MEDTAP's Center for Pricing & Reimbursement in Arlington, VA. Dr. Hahn received her Ph.D. from the University of Illinois. Her expertise is in health outcomes research, reimbursement strategy, and tactical implementation across all segments of managed care for the pharmaceutical industry. Dr. Hahn's experience in the health care arena includes 10 years with GlaxoSmithKline where she held a variety of positions in both the commercial and R&D organizations. Her work with the commercial organization included developing and implementing reimbursement strategies with brand marketing, field sales, and managed care groups. Her work within R&D included designing and conducting health outcomes studies within the clinical trials program, development of reimbursement dossiers, and directing the development of health economic models. She has conducted research in a broad range of therapeutic areas including neurology, psychiatry, and gastroenterology.

**Judy Maltz is a Field Program Associate** with MEDTAP's Center for Pricing & Reimbursement in Arlington, VA. Ms. Maltz brings over 18 years of experience in the healthcare reimbursement arena. Prior to joining MEDTAP, Ms. Maltz was the Reimbursement Operations Supervisor for McKesson Health Solutions. She facilitated the design and use of a payer database, automated referral processes, and internal and client reports, working directly with the IT team. She managed the daily operations of McKesson's Payer Policy Unit in addition to several reimbursement support programs supporting a wide array of therapeutic areas, including oncology, HIV/AIDS, CNS, and mental health.

**Beenish Nafees, M.Sc. is a Senior Research Assistant** in MEDTAP's London office. She obtained her Master's in Forensic Psychology at the University of Surrey, Guildford in 2002. Prior to joining MEDTAP, Beenish worked for the National Health Service at the Institute of Psychiatry, London, investigating pathways into forensic care. She interviewed mentally ill patients at health care wings in prisons, medium secure units, and psychiatric intensive care units. Her areas of expertise are mental health, psychiatric disorders, and effects of social factors, e.g., culture, discrimination on mental health. Beenish has a publication in *Child*

*Care Health Development*, and is a visiting Research Associate at the Institute of Psychiatry, London.

**Laurie Roberts, M.P.H. is a Project Manager** with MEDTAP in Bethesda, MD. Ms. Roberts' responsibilities include the design, management, and analysis of health-related quality of life and other patient-reported outcomes projects. Prior to joining MEDTAP, Ms. Roberts coordinated Phase III and IV pacemaker and defibrillator clinical trials at Brigham and Women's Hospital in Boston and worked as a project manager at WorldCare Clinical, an imaging core laboratory for oncology clinical trials. She also managed the Anti-Epileptic Drug Pregnancy Registry at Massachusetts General Hospital, a pharmaceutical sponsored registry which seeks to determine if various anti-epileptic drugs taken during pregnancy are associated with increased risk of major malformations at birth. Ms. Roberts received her Master of Public Health degree with a concentration in chronic disease epidemiology from the Yale School of Epidemiology and Public Health.

**Maria Nicole Stoeckl, B.A., M.P.H. is an Associate Project Manager** with MEDTAP in Bethesda, MD. Prior to joining MEDTAP, Ms. Stoeckl worked as a Cardiology Project Manager at Boston University Medical Center, managing large NIH-funded Phase II clinical research projects, testing endothelial function by non-invasive brachial artery ultrasound. Her recent work has been accepted for publication in *New England Society for Vascular Surgery* and *The American Journal of Cardiology*. Ms. Stoeckl is completing her Master's degree in public health, with a concentration in social and behavioral sciences, from Boston University School of Public Health.

**Dorina Theodoratou, M.Sc. is a Research Assistant** in MEDTAP's London office. Ms. Theodoratou holds a degree in economics from the University of Kent, Canterbury, UK, as well as a Master of Science in Health Management (specialization in health economics and pharmaceuticals & biotechnology) from Imperial College of Science, Medicine and Technology, UK. Ms. Theodoratou has experience in economic modeling and market research. Relevant projects that she has worked on include a cost-effectiveness analysis of a nasal spray for migraine attacks, an econometric analysis of medical practitioners' earnings functions in the UK during the 1990's, and a market analysis of the European ophthalmic device sector. 🌐

process involves in-depth qualitative interviews with community providers and patients to describe the current organization of primary care for the population of interest. Future studies will include the development and testing of relevant interventions, and the evaluation of strategies to enhance recruitment and retention of subjects.

MEDTAP's involvement in the Center builds on the past work of its research scientists. Dennis Revicki and Lori

Frank have been involved in collaborative work with the Georgetown Department of Psychiatry for the past seven years, examining outcomes of depression treatment for low-income women. The main findings from this work appear in Miranda et al. 1993, with cost effectiveness of the mental health interventions evaluated and reported in Revicki et al. (submitted for publication).

For further information about the Center, feel free to contact Lori Frank at (301) 986-6762, Frank@MEDTAP.com. 🌐

## The Value of the Cost-Effectiveness Threshold

By Ágnes Benedict, B.Sc., M. Sc., John Hutton, B.Sc.Econ., B.Phil.

One of the questions which health economists try to answer is, “are health technologies worth using?” Some also address the question, “how much are technologies worth?” The conventional view has been that such questions of value can only be addressed by cost-benefit analysis (CBA) rather than cost-effectiveness analysis (CEA). However, in practice, health care decision-makers place an implicit value on health benefits each time they use cost-effectiveness data in allocating resources.

The point at which the marginal benefits are considered to be of equal value to the marginal resources used in their realization has become generally known as the cost-effectiveness threshold. If we knew the value of the cost-effectiveness threshold, answering questions of value would be much easier. Decision-makers in health care, and health economists in academia and in pharmaceutical companies, would all like to have a number, and certain numbers are cited regularly. Whether a single true value does (or can) exist is not at all clear.

Theoretically, the threshold value can be derived and utilized in two ways. For both processes, we need to assume that we have complete information to compile an accurate ranking (league table) of all treatments by incremental cost-effectiveness ratio (ICER), using the same effectiveness measure—usually the quality adjusted life-year (QALY). From this point, two different decision rules can be used to maximize health effects subject to a constraint. In one, the constraint is in the form of a fixed health budget which is externally determined to reflect society’s willingness to pay for health care. The budget is allocated by implementing programs, starting with the one with the lowest ICER, until the health care budget is exhausted. The ICER of the last program (i.e., the marginal cost of the least effective treatment adopted) is the shadow price of the budget constraint. If the budget truly reflects social preferences, this is also the marginal value of a unit of health benefit, i.e., a QALY.

In the second approach, the constraint is given in the form of a “fixed price,” reflecting an externally determined social value for a unit of health benefit. Society is unwilling to pay for programs which produce health benefits at a higher price in terms of resources consumed. This willingness to pay can be estimated in terms of a target ICER, usually a cost per QALY. Using the same league table, all interventions with a more favorable ICER will be implemented, which in turn determines what the health care budget should be.

Outside of the theoretical literature, however, this distinction between the threshold perceived as a societal value of willingness to pay for a QALY and as the shadow price of

the health care budget is not clear. Although threshold values are widely quoted for many countries, their origins and methods of derivation are obscure. Most seem to be based on arbitrary assumptions about the value of a QALY, derived from past funding decisions or perceptions of social willingness to pay for health care. The main problem is that these decisions and perceptions have been developed in the absence of consistent data on the cost-effectiveness of most interventions; to date, there is no comprehensive and consistent league table.

Several other factors also complicate cost-effectiveness evaluations. First, the selection of health technologies for CEA is subject to bias. Payers tend to target technologies which they do not expect to be cost-effective, while sponsors usually publish results which are favorable. Furthermore, many interventions that clinicians assume to be indispensable go unevaluated. Because cost-effectiveness changes over time (Remak & Hutton 2003), many studies are dated. Reviews have shown the variable quality of studies (Neumann et al. 2000, Briggs & Gray 1999).

Despite these difficulties, the potential value of a threshold to decision-makers has been recognized. Interestingly, there has been a tendency to adopt figures derived elsewhere without considering their theoretical and empirical validity, or their transferability. In a circular process, repeated citation seems to confer legitimacy. The most frequently quoted figures are those of Laupacis et al., (Can \$20-100,000, at 1992 prices) which have been adopted elsewhere, often without currency conversion or any inflation adjustment.

Outside of health economics, the value of statistical life (VSL) literature has provided possible threshold values based on sounder foundations. Revealed preference studies, contingent valuation studies (stated preferences),

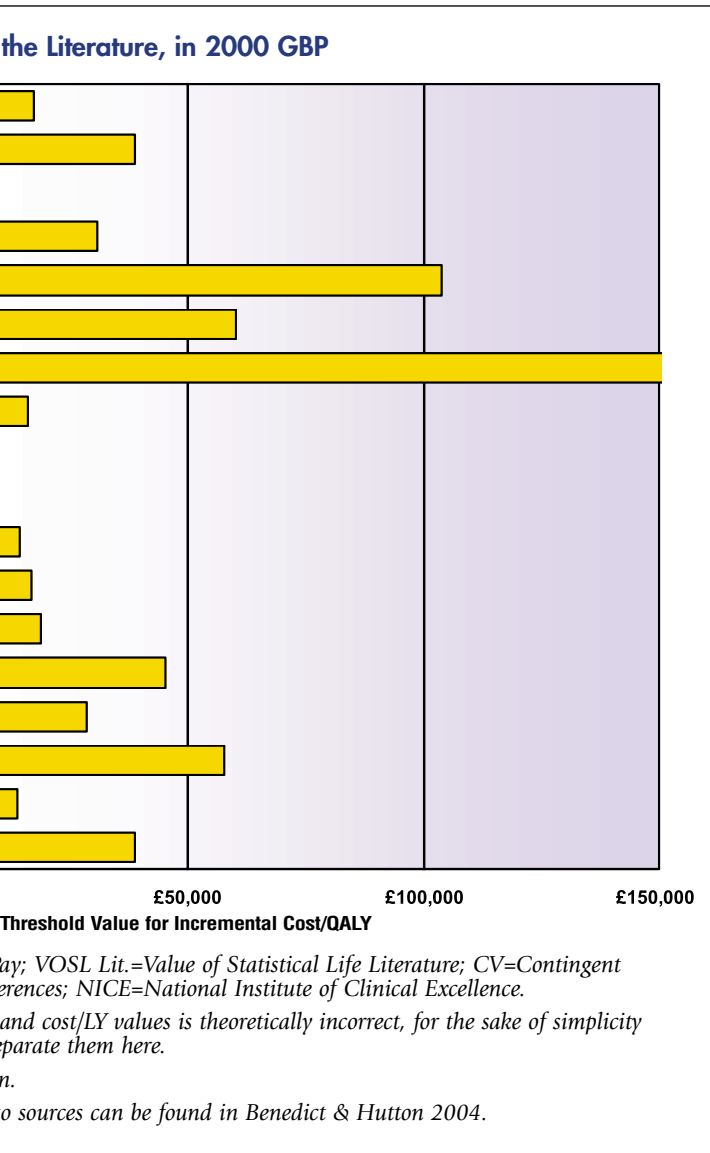
### Threshold Values from

Category	Source	Value (€0)
EXPERTS	Williams (UK)	£20,000
	Newhouse (UK and US)	£20,000
WTP	Gyrd-Hansen (Denmark)	£20,000
VOSL LITERATURE	Loomes (UK)	£20,000
	Hirth (US): CV	£20,000
	Hirth (US): RP - safety	£20,000
	Hirth (US): RP - job market	£20,000
	Hirth (US): Human capital	£20,000
CURRENT THRESHOLDS	Pritchard (NZ)	£20,000
	Netherlands*	£20,000
	Spain*	£20,000
	George (Aus)	£20,000
	Cromwell (Aus)	£20,000
	Cutler (US)	£20,000
	NICE (UK)	£20,000
PAST IMPLICIT DECISIONS	Kaplan-Bush (US)	£20,000
	Stevens (UK)	£20,000
	Laupacis (Can)	£20,000

Note: WTP=Willingness to Pay; RP=Revealed Preference. Although pooling cost/QALY of presentation, we did not see \*From private communication. Sources: Detailed references to

and past explicit decision making (e.g., installing road safety measures) have produced values for a statistical life saved which, under certain assumptions, can be converted to the value of a statistical life year saved (Viscusi 1993).

The values we found (Benedict & Hutton 2004), plotted in the chart below, vary between countries, as would be expected given economic and social differences. It is



interesting to see that most of the values from VOSL are much greater than the current arbitrary thresholds and those which have been suggested by health economists.

There are two important conclusions for researchers analyzing and evaluating the cost-effectiveness of health technologies. First, more research is needed on the definition and measurement of the threshold. Clearly, the

threshold depends on a nation's ability to pay for health care, but it also depends on society's willingness to pay for health care in place of other goods and services. Second, the concept has consequences for the methods of CEA; a societal threshold value would be consistent with a societal evaluative perspective, which is not the current requirement for economic evaluation in many countries.

Finally, conclusions that state a given technology "is very cost-effective" need to be treated with caution, since the threshold value and decision context are uncertain. Cost-effectiveness acceptability curves are a more suitable way to present the results of CEA studies because they represent, at each possible threshold level, the probability that a technology is cost-effective. The decision-maker can see the decision consequences of an arbitrary application of unsupported threshold values.

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For more information, contact Ágnes Benedict, [Benedict@MEDTAP.com](mailto:Benedict@MEDTAP.com) or John Hutton, [Hutton@MEDTAP.com](mailto:Hutton@MEDTAP.com). 

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Editorial  
OPINION

## Value of Research: The Quest is Its Own Reward

By Audra Boscoe, M.P.H.

**D**id you ever have the frustrating experience as a child at the beach of thinking you really could dig your way to China? The exercise was particularly maddening if you started to dig in the loose sand far from the water. No matter how fast and furiously you dug, the sand filled your hole just as quickly as you could remove it.

In this sense, those of us in research spend every day at the beach – some further from the water than others. The volume of information available to us far exceeds our capacity to absorb it. In other words, no matter how much we dig, there will always be more sand to fill the hole. How often do you explore a topic that is new to you, only to discover related issues and complexities that you never could have predicted? The more you learn, the more you realize how much you don't know.

Gathering and sifting information in pursuit of knowledge can be tedious and sometimes frustrating, but at the same time, it is one of few activities where the process is as fascinating and enlightening as the ends which we seek. As scientific researchers in pursuit of knowledge and truth, we act in good faith and usually find the means of achieving the ends to be as rewarding as the ends themselves.

Some people are experts at one thing, while others know a little bit about everything. Although some would like to

be experts at everything, truth be told, most of us fall into the category of "knowing a lot about something and a little bit about many things." No person can know all that there is to know about every subject, but collectively we have amassed an immense amount of scholarship, skills, and resources. No matter what our individual field of expertise, industry, or job title, we are all researchers and economists. We have all sought information, and we have all made decisions intended to maximize our utility based on the best information available to us.

Taking advantage of the acquired knowledge, proficiencies, and wisdom of those around us can significantly cut down on the volume of information we have to sift through. It is an intriguing irony that something as infinite as time is something that we all seem to have so little of. Therefore, it is critical that we make the most of the resources available to us since the timeliness of information is almost as important as the information itself. Given the short space of time we have to gather knowledge for specific purposes, it is unfortunate that we often forget to take advantage of our own colleagues' expertise.

None of us has made it to China yet, and we now know not to expect to. We also know that we will never have all the answers to our questions, but the quest for information is not an exercise in futility. The knowledge we acquire in the process is extremely valuable, and priceless when it informs sound decision making. Good research isn't always about digging down or looking forward...sometimes good research is about looking around us. 🌐

## Feasibility and Barriers for a National Item Bank: If We Build It, Will They Come?

By Dennis A. Revicki, Ph.D.

### Introduction

**T**he development and application of item response theory (IRT) and computer adaptive testing (CAT) methods to health status outcomes have the potential to provide efficient collection of better quality, more precise self-reported data from patients participating in clinical trials, clinical observational studies, and in population surveys both nationally and in managed care organizations (McHorney 1997; Revicki & Cella 1997). CAT allows the more efficient data collection and enables the application of IRT-based assessment. Although IRT and CAT methods are currently under evaluation in a number of different disease areas and for assessing different domains of patient-reported outcomes (PROs), they have not been widely applied in clinical or health services research. The techniques of IRT, item banking, and CAT provide an innovative solution to the challenges of assessing health status in subjects with varying problems across different health domains.

It is now technically feasible and possible to develop a national item bank for the implementation of IRT-based, tailored testing; but much work remains to bring these ideas into practical application (McHorney 2002; Bode et al. 2003). Even if sufficient financial support was available for a national item bank, including software for administering and scoring, it is uncertain if instrument developers, clinicians and clinical researchers, the pharmaceutical and health care industries, and regulatory agencies would fully accept this measurement approach.

### Feasibility and Acceptance of a National Item Bank

#### ■ Instrument Developers

Instrument developers may have a vested interest in maintaining the integrity of the existing generic- and disease-specific measures that they have developed over time that include static, fixed item sets for all respondents. For some, academic reputations have been built upon developing and evaluating health-related measures. Although several instrument developers are working at developing item banks, IRT models and CATs based on their assembled items from various health status instruments, it is uncertain how ownership of these new IRT-based measures will be handled.

Some developers market and license these health measures and receive a revenue stream from their instruments. What is the incentive for instrument developers to contribute their copyrighted items to the larger national item bank? In addition, if a national item bank is available and researchers

actively use this bank and related CAT methods, there is no real need for “brand name” instruments. There may be considerable resistance to cooperating in any national measurement effort and those researchers who do collaborate in the development and evaluation of the national item bank may find themselves in a monopoly position.

There is no easy way to address this potential barrier, since there are important academic (i.e., promotion, tenure) and financial stakes at risk. Possible solutions include involving a broad range of researchers in the development and psychometric evaluation process, since there will need to be extensive field studies required to build, test and maintain the bank. Second, a modest royalty (0.25 to 1 cent) might be offered to instrument developers associated with each time one of their items is used in a study. However, this would require some independent entity to manage the national item bank and some sort of new financial model for deriving revenues.

#### ■ Clinical Researchers

Although many may recognize that an approach is needed for measuring health status across the relevant continuum of functioning and well-being for longitudinal, chronic disease studies

where subjects may deteriorate at different rates over time, they may not accept IRT-based tailored tests as the best approach. A static health status instrument may not be able to capture these effects for long-term studies.

It is uncertain

whether clinical researchers will accept and include the IRT-based measures in studies. First, significant barriers are associated with their understanding and unfamiliarity with the IRT/CAT method, and continued skepticism from some clinicians about PROs, in general, may limit acceptance. Second, application of CAT will require computer-administered instruments, and there may be practical feasibility or budget issues associated with applications in studies. One significant barrier is that desktop or laptop computers may not be very practical in the clinical context. This problem may be addressed by deriving “static” IRT-based instruments using the item bank, tailored to the relevant patient population and study, or through the use of handheld computers for administering health status instruments.

#### ■ Food and Drug Administration

The Food and Drug Administration (FDA) and other regulatory agencies have recently accepted the importance

**It is now technically feasible and possible to develop a national item bank for the implementation of IRT-based, tailored testing.**

of PROs for understanding effectiveness of treatments from the patient's perspective. Although there has been increased understanding about PRO measures and methods (Burke 2001; Revicki, in press), regulatory agencies have few staff members who really understand psychometrics, and none who understand IRT and CAT. Currently, the FDA focuses on static, disease-specific health status and other PRO measures, and requests information on instrument development, face and content validity, and measurement characteristics (i.e., reliability, validity, responsiveness) as part of the documentation package underlying labeling or promotional claims for PRO benefits for all products. It may be difficult for FDA staff to understand and accept measures where the item content is different across individual study subjects and that may vary in item content within subjects over the duration of the study. There may be some cognitive discontinuity in adjusting from a situation where the focus is on static instruments to one where outcomes researchers endorse no set instrument but banks of items designed to measure different domains. There are also challenges in meeting documentation requirements when measures are collected through electronic data capture. These technical challenges are likely to be more surmountable than the cognitive ones.

#### ■ Pharmaceutical Industry

To a great extent, the FDA drives the actions of the pharmaceutical industry. Few pharmaceutical companies will select PRO measures that will not be acceptable to the FDA. There may be reluctance for industry researchers to take a chance that the regulatory agencies will accept CAT and IRT based assessments for evaluating the patient-related effectiveness of new products. There will need to be continued dialogue and exchange between health outcomes research, psychometricians, the FDA and industry researchers to determine the best and most scientifically acceptable way to incorporate IRT based measures and CAT into clinical trial programs. The start may be with more tailored tests for different patient populations and applications that are more consistent with static measures used currently. Regulatory agencies are interested in PRO measures that provide assessment of the effectiveness of new treatments and, based on the current situation require evidence supporting content validity, good psychometric characteristics and guidance on interpretation of results. To the extent that industry can provide this documentation, the CAT-based measures may prove acceptable for drug evaluations, but the additional expense associated with application of CAT in clinical trials must result in some positive trade-off in the increased probability for demonstrating effectiveness of the new treatment.

### Financial Considerations in Developing and Maintaining a National Item Bank

There are significant challenges associated with financial support for a national item bank, and some type of

publicly and privately funded entity may be the best solution. The most important aspects of this entity will be to balance providing ready access, IRT findings, and any developed software for administering CAT, having enough revenues to remain viable and continue to update and maintain the item bank. However, without the cooperation and support of Federal agencies, clinical researchers, instrument developers, the pharmaceutical industry and managed care organizations, it is unlikely to survive. Several financial models exist, such as charging modest user fees for use of item bank measures and software and/or royalties. A useful model to consider is that of the Educational Testing Service in developing and supplying college entrance examinations, professional competency tests and other achievement tests. However, demand for this type of service for PRO assessment is uncertain.

### Summary and Conclusions

If we (or they) build it, will they come? There are considerable challenges associated with building and maintaining a national item bank and it is uncertain whether there is sufficient interest among key stakeholders for IRT-based and CAT measures. The most convincing activity is demonstrating that the approach is feasible, psychometrically sound and useful in a specific application. Demonstrated success opens up the possibility of more widespread acceptability and application. As part of the development effort, there needs to be continued meetings and discussion with psychometricians, instrument developers, clinical researchers, the FDA, pharmaceutical industry researchers, and managed care organizations about the advantages and disadvantages of a national item bank. These discussions may be as important as the investment in the actual development of a national item bank and CAT software.

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For more information, contact Dennis Revicki,  
Revicki@MEDTAP.com. 

## Time-Dependent Variables

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patients for the first 3 months (*censored* at 3 months) instead of being dropped altogether; and 3) Analyzing the effects of treatments and adjusting for covariates is more straightforward and susceptible to statistical analysis.

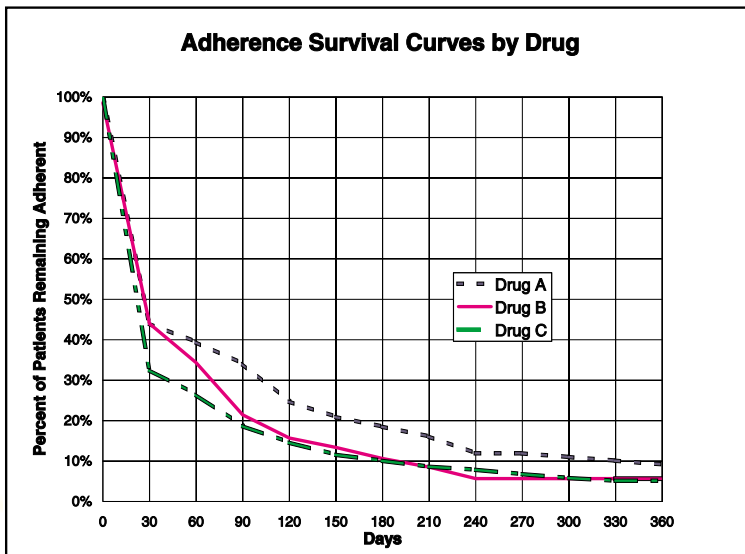


Figure 1

A survival model commonly seen in the medication compliance literature, the *Cox proportional hazards regression*, does, however, have a disadvantage compared to the frequency count approach. It assumes that the relative hazard, or *hazard ratio*, between two treatments is the same throughout the study period. The hazards might change with time, but their relationship to each other does not.

This may not be realistic in a study comparing adherence to different drugs. Those who have studied adherence will find the trends in Figure 1 familiar; it shows the survival curves for adherence to three different drug therapies (for a particular mild to moderate chronic condition). There are many patients that adhere only 30 days, i.e., not refilling their prescription even once, regardless of the drug: 44% for Drugs A and B, and 32% for Drug C. (Here the standard of adherence is continual refills within 15 days of the expected refill date.) After 30 days, differences appear between Drugs A and B, whereas the Drug C curve is now parallel to the Drug A curve, indicating that its users are now discontinuing at about the same rate. The ratios of the hazards are not remaining constant.

One explanation is that those who discontinue early do so for reasons more related to the severity of their condition, their attitudes toward adopting new habits, or their finances, rather than related to the drug. Data on such variables is often unavailable. In any case, a model allowing different

relative hazards before and after the critical 30-day mark would better fit the data.

Fortunately, the Cox regression model for survival analysis can accommodate relative hazards that change with time. We can fit a “piecewise regression” model that assumes only that the relative hazards are constant within consecutive time intervals.<sup>3</sup> Essentially, we further distinguish treatment variables with indicator variables that are dependent on time. To take a simple example with no covariates, suppose we defined a proportional hazards model for comparing Drug X to a comparator as

$$\log \{ h_i(t) / h_0(t) \} = Ax_i,$$

where  $x_i = 1$ , if individual  $i$  is on Drug X, and  $= 0$  if they are not,  $\log h_i(t)$  is the instantaneous hazard of  $i$  discontinuing the treatment, and  $h_0(t)$  is the baseline hazard.

In this context, a piecewise model with two time periods would be

$$\log \{ h_i(t) / h_0(t) \} = A_1x_i + A_2z_i(t)$$

where  $x_i$  remains as before, indicating treatment in either period, and  $z_i(t) = 1$  if  $x_i = 1$  and  $t$  is in the second time period (e.g.,  $t > 30$  days).

In this model, the log-hazard ratio for an individual on Drug X, relative to the comparator, is then  $A_1$  for  $t$  in the first period, and  $A_1 + A_2$ , for  $t$  in the second time period.

The model can be represented easily in SAS or STATA survival analyses, which allow the coding of variables whose value changes with time. Information on the calculation of standard errors and implementation details is available from the author.

In the data illustrated in Figure 1, a proportional hazards model did not find a statistically significant difference between the drugs. But a period model that distinguished time periods before and after 30 days, and including adjustments for age, race, and gender, found statistical significance for the earlier reading of the graph: Drug C is discontinued at a significantly faster rate than A or B in the first 30 days; Drug B is discontinued at a faster rate than A after 30 days; and of the people who have stayed on Drug C for the past 30 days, they do not drop any faster than those on A. Fitting a similar model for gender effects, we found that if males were going to quit, they were more likely than females to quit in the first 30 days. Of the males that make it past 30 days, they were less likely than females to stop.

The piecewise model is a special case of Cox models with time-dependent variables (e.g., incorporating patient vital signs that change with time). There are other models for non-proportional hazards. An *accelerated failure* model with an assumption that the survival times have a *log-logistic* distribution can model hazard ratios that are changing continuously with time, and that change direction at most

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only once. (The commonly used Weibull distribution assumes proportional hazards.) A *stratified proportional hazards* model may be appropriate where it is assumed that hazards are proportional within certain strata of covariates.

The industry is seeking ways to improve the adherence of patients to their medication. High initial drop-off rates are common, and given the ease with which one can incorporate time-dependent variables, the piecewise Cox regression model is a useful tool for better understanding the factors affecting patient adherence.

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<sup>2</sup>Krueger KP, Felkey BG, Berger BA. Improving adherence and persistence: A review and assessment of interventions and description of steps toward a national adherence initiative. *J Am Pharm Assoc* 2003;43:668-678.

<sup>3</sup>Collet D. *Modelling Survival Data in Medical Research*. London: Chapman and Hall/CRC, 1994.

For more information, contact Steve Blume, [Blume@MEDTAP.com](mailto:Blume@MEDTAP.com) 

## Upcoming Presentations

### Plasma Protein Therapeutics Association: International Plasma Protein Conference

MARCH 8-9, 2005 ■ BERLIN, GERMANY

"Economic Evaluation in Reimbursement Decision-Making" John Hutton, B.Sc. Econ., B.Phil. MEDTAP International, Inc., London, UK.

### 15th European Congress of Clinical Microbiology and Infectious Diseases

APRIL 2-5, 2005 ■ COPENHAGEN, DENMARK

"Cost-effectiveness of linezolid versus vancomycin in complicated skin and soft-tissue infection due to suspected methicillin-resistant staphylococcus aureus infection in Germany" Schumann D<sup>1</sup>, De Cock E<sup>2</sup>, Sorensen S<sup>3</sup>, Baker T<sup>3</sup>, Resch A<sup>4</sup>, Hardewig J<sup>4</sup>, Dutttagupta S<sup>5</sup>. <sup>1</sup>Berlin, Germany; <sup>2</sup>MEDTAP, London, UK; <sup>3</sup>MEDTAP, Bethesda, MD, USA; <sup>4</sup>Pfizer GmbH, Karlsruhe, Germany; <sup>5</sup>Pfizer, Inc., New York, NY, USA.

### The Academy of Managed Care Pharmacy (AMCP) 17th Annual Meeting & Showcase

APRIL 20-23, 2005 ■ DENVER, CO, USA

**SATELLITE SYMPOSIUM** (Sponsored by Sanofi-Aventis) Considerations for Managed Care Organizations and Medicaid Agencies Applying for Prescription Drug Plan Status for Medicare Recipients in 2006 "Introduction and Opening Remarks: PDP Application in Medicare Part D" Bryan Luce, Ph.D., M.B.A., MEDTAP International, Inc., Bethesda, MD, USA.

"Translation of health-related quality of life (HRQoL) burden and outcomes to projected annual healthcare expenditures utilizing data from an observational study of chronic low back pain patients treated with transdermal fentanyl system" Kosinski M<sup>1</sup>, Schein JR<sup>2</sup>, Vorsanger GJ<sup>2</sup>, Ascher S<sup>2</sup>, Vallow S<sup>2</sup>, Harte C<sup>2</sup>, Frank L<sup>3</sup>, Shikhar R<sup>3</sup>, Margolis MK<sup>3</sup>, Brennan MJ<sup>4</sup>. <sup>1</sup>Quality Metric, Inc., Lincoln, RI, USA; <sup>2</sup>Janssen Pharmaceutica, Inc., Titusville, NJ, USA;

<sup>3</sup>MEDTAP International, Inc., Bethesda, MD, USA;

<sup>4</sup>University of New South Wales, Sydney, Australia.

### American College of Obstetricians and Gynecologists' 53rd Annual Clinical Meeting

MAY 7-11, 2005 ■ SAN FRANCISCO, CA, USA

"Overactive bladder with urinary incontinence adversely affects women's sexual quality of life" Rogers R<sup>1</sup>, Margolis MK<sup>2</sup>, Bavendam T<sup>3</sup>, Zyczynski T<sup>3</sup>, Coyne K<sup>2</sup>. <sup>1</sup>University of New Mexico, Albuquerque, NM, USA; <sup>2</sup>MEDTAP, Bethesda, MD, USA; <sup>3</sup>Pfizer, Inc., New York, NY, USA.

### European Association of Urology XXth Congress

MAY 16-19, 2005 ■ ISTANBUL, TURKEY

"Overactive bladder with urinary incontinence adversely affects women's sexual quality of life" Rogers R<sup>1</sup>, Margolis MK<sup>2</sup>, Bavendam T<sup>3</sup>, Zyczynski T<sup>3</sup>, Coyne K<sup>2</sup>. <sup>1</sup>University of New Mexico, Albuquerque, NM, USA; <sup>2</sup>MEDTAP, Bethesda, MD, USA; <sup>3</sup>Pfizer, Inc., New York, NY, USA.


### ISPOR 9th Annual Meeting

MAY 16-19, 2005 ■ ARLINGTON, VA, USA

#### SHORT COURSES:

"Bayesian Analysis: Overview"

"Bayesian Analysis: Applications" Bryan Luce, Ph.D., M.B.A., Senior Research Leader and CEO, MEDTAP International Inc., Bethesda, MD, USA.

Christopher S. Hollenbeak, Ph.D., Visiting Scientist, MEDTAP International Inc., Bethesda, MD, USA, Surgery and Health Evaluation Sciences, Penn State College of Medicine, Hershey, PA, USA. 

## Recent Presentations

### Drug Device and Biologic Combination Projects

DECEMBER 14-15, 2004 ■ LONDON, UK

#### KEYNOTE PRESENTATION:

"Demonstrating the Value of Drug Device Combinations for the Patient" Andrew Lloyd, D.Phil., MEDTAP International, Inc., London, UK.

### The American College of Allergy, Asthma & Immunology Annual Scientific Meeting

NOVEMBER 12-17, 2004 ■ BOSTON, MA, USA

"Impact of omalizumab (xolair) on quality-of-life in patients with moderate to severe allergic asthma" Revicki DA<sup>1</sup>, Niebauer K<sup>1</sup>, Fox-Rushby J<sup>2</sup>; <sup>1</sup>MEDTAP International, Inc., Bethesda, MD, USA; <sup>2</sup>MEDTAP International, Inc., London, UK.

### Seventh International Congress on Drug Therapy in HIV Infection

NOVEMBER 11-18, 2004 ■ GLASGOW, UK

"Understanding patient preferences for HIV drugs using adaptive conjoint analysis: feasibility assessment" Beusterien K<sup>1</sup>, Dziekan K<sup>2</sup>, Flood E<sup>1</sup>, Jordan J<sup>3</sup>; <sup>1</sup>MEDTAP International, Inc., Bethesda, MD, USA; <sup>2</sup>GlaxoSmithKline, Middlesex, UK; <sup>3</sup>GlaxoSmithKline, Research Triangle Park, NC, USA.

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## Recent Presentations

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### World Psychiatric Association International Congress

NOVEMBER 10-13, 2004 ■ FLORENCE, ITALY

"Assessment of health state utilities of Attention Deficit/Hyperactivity Disorder in children using parent-based standard gamble scores" Secnik K<sup>1</sup>, Cottrell S<sup>2</sup>, Matza LS<sup>3</sup>, et al. <sup>1</sup>Eli Lilly & Co., Indianapolis, IN, USA; <sup>2</sup>M-TAG Limited, London, UK; <sup>3</sup>MEDTAP International, Inc., Bethesda, MD, USA.

### American Heart Association (AHA) Scientific Sessions 2004

NOVEMBER 7-10, 2004 ■ NEW ORLEANS, LA, USA

"Economics in cardiovascular care: Resource use and costs associated with atrial fibrillation in the US" Coyne K<sup>1</sup>, Grandy S<sup>2</sup>, Paramore LC<sup>1</sup>, Mercader M<sup>3</sup>, Zimetbaum P<sup>4</sup>; <sup>1</sup>MEDTAP International, Inc., Bethesda, MD, USA; <sup>2</sup>AstraZeneca, Wilmington, DE, USA; <sup>3</sup>Marco Mercader, George Washington University, Washington, DC, USA; <sup>4</sup>Harvard Med School, Boston, MA, USA.

### International Society for the Study of Women's Sexual Health (ISSWSH) Annual Meeting

OCTOBER 28-31, 2004 ■ ATLANTA, GA, USA

"The relevance of three sexual function questionnaires to women with overactive bladder and urinary incontinence" Coyne K<sup>1</sup>, Margolis MK<sup>1</sup>, Zyczynski T<sup>2</sup>, Bavendam T<sup>3</sup>, Rogers R<sup>4</sup>; <sup>1</sup>MEDTAP International, Inc., Bethesda, MD, USA; <sup>2</sup>Pfizer Inc., New York, NY, USA; <sup>3</sup>University of Wisconsin Medical School, Madison, WI, USA; <sup>4</sup>Department of Family Medicine, University of Wisconsin Medical School, Madison, WI, USA.

### American College of Chest Physicians 2004 Annual Conference

OCTOBER 26, 2004 ■ SEATTLE, WA, USA

"Measuring Dyspnea via the Breathlessness Diary" Nancy Kline Leidy, Ph.D.; MEDTAP International, Inc., Bethesda, MD, USA.

### American College of Clinical Pharmacology (ACCP) Annual Meeting

OCTOBER 24-27, 2004 ■ DALLAS, TX, USA

"Determination of costs for patients with complicated skin and soft-tissue infections due to suspected or proven methicillin-resistant staphylococcus aureus" Sorensen SV<sup>1</sup>, Hollenbeak CS<sup>1</sup>, Liu LZ<sup>2</sup>, Baker TM<sup>1</sup>, McKinnon P<sup>3</sup>; <sup>1</sup>MEDTAP International, Inc., Bethesda, MD, USA; <sup>2</sup>Pfizer Inc., New York, NY, USA; <sup>3</sup>Detroit Receiving Hospital, Detroit, MI, USA. 🌐

## Advancing PRO Measurement

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and Stony Brook School of Medicine. The five-year PROMIS project is an NIH Roadmap Initiative to develop and evaluate methods for measuring patient-reported pain and fatigue symptoms, physical functioning, emotional well-being and social functioning for application across a range of chronic diseases. PROMIS will develop measures based on item response theory (IRT) analysis, assemble pools of items across the targeted domains, and evaluate and design software for computer adaptive testing. This measurement research and the developed methods will revolutionize how patient outcome data is collected in clinical trials and other studies, and may allow for more sensitive assessment of important patient health-related outcomes. The project will initially focus on developing measures of pain and fatigue symptom outcomes, along with health-related quality of life domains of physical functioning, emotional well-being, and social functioning. The investigators will identify pools of relevant items from existing data bases to cover these outcome domains. Item response theory analyses will be used to examine and calibrate these items, and software for computer adaptive testing will be developed and tested. PROMIS is also intended to support innovative research on psychometrics, IRT analysis, and other advanced measurement and statistical methods. MEDTAP researchers are involved in planning PROMIS activities and in the project's various research-related activities. If successful, PROMIS has the potential to advance health outcomes research methods and measures for clinical studies. Ultimately, the project may provide an improved understanding of the effect of disease and treatment on patient symptoms and health-related quality of life, and improved evaluation of health-related outcomes in studies evaluating pharmaceutical and other health interventions.

For more information, contact Dennis Revicki, [Revicki@MEDTAP.com](mailto:Revicki@MEDTAP.com). 🌐

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**MEDTAP INTERNATIONAL**  
7101 Wisconsin Avenue  
Suite 600  
Bethesda, MD 20814  
Tel: 301-654-9729  
[www.MEDTAP.com](http://www.MEDTAP.com)

**Contact:**  
Greg de Lissovoy, Ph.D.,  
Scientific Editor  
Susan Potter,  
[potter@MEDTAP.com](mailto:potter@MEDTAP.com)

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