

Improving Precision in Clinician Rated Scales

By Catherine Spear and Kathy Beusterien, M.P.H.



Ms. Spear is the President of PharmaStar LLC, a wholly owned subsidiary of UBC, and the Group President of UBC's Training and Education Group. One of PharmaStar's areas of expertise is training investigators and sites on the administration of Clinician Rated Scales, to increase precision by improving the comprehension and application of clinical measures used during the course of a clinical trial.



Ms. Beusterien is a Research Scientist at The MEDTAP Institute. She has 13 years of experience performing outcomes research for a wide array of medical therapies and interventions. Specific areas of interest include questionnaire development, utility measurement, and conjoint analysis.

Clinician Rated Scales are selected as pivotal endpoints in clinical research across a wide range of diseases. However, when the ratings rely on clinical subjectivity, which is often the case, substantial variability in scores across research clinicians (also called raters) can occur. This lack of measurement precision creates challenges in both clinical study design and in trial outcomes. With reduced

precision comes the need for larger sample sizes to achieve sufficient statistical power to detect differences between treatment groups. Additionally, the lack of standardization produces overlap between study groups, reducing the clarity of the potential treatment effect.

These challenges become more complex for large multi-center and multi-national studies involving numerous raters with diverse clinical, research, and cultural backgrounds.

Solution: The potential for ratings discordance with Clinician Rated Scales can be mitigated by well-designed training and certification programs customized to address

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Science & Policy OPINION

Evidence-Based Medicine at the AARP Watchdog Forum

By Bryan R. Luce, Ph.D., MBA

The American Association for Retired Persons (AARP) held a Watchdog Forum in February of 2005 entitled "Effectiveness Research: Fact or Fable for the American Consumer?" The occasion was used to unveil AARP's evidence-based medicine website. The Forum brought together experts in strategy, policy, medicine and evidence-based research from academia, government, and non-governmental organizations for a candid discussion of the "pros and cons of comparative effectiveness research." A key focus of the forum was the use of the Oregon Health & Sciences University's Evidence-Based Policy Center's Drug Effectiveness Review Project (DERP) reports in evidence-based health care decision-making.

Bryan R. Luce, MEDTAP's Founder and Director, Science Policy at United BioSource Corporation (UBC), addressed the group as follows:

"Let me begin my remarks by expressing my appreciation for being invited to address this important forum and also by noting that I and my company, The MEDTAP Institute, which is the scientific outcomes research arm of United BioSource Corporation, conducts health and economics outcomes research for, and consults with, the pharmaceutical industry. We also consult with Federal agencies in the US and abroad and various non-profit organizations. More specifically, I personally am presently consulting with both PhRMA and pharmaceutical manufacturers on the very evidence-based medicine topic we are addressing today.

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Clinician Rated Scales

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protocol design challenges, study population issues, rating instrument subjectivity, cultural biases, language barriers, rater turnover and rater drift. Basic educational principles suggest that raters learn best from programs with the fewest attendees and optimal duration, a challenging and interactive curriculum, meaningful feedback, and reinforcement of essential learning points. Diverse presentation techniques (didactics, videos, interactive workshops) invariably yield more positive outcomes. Obviously, learning is enhanced when raters understand the language in which the training is being offered. Furthermore, instructional materials and assessment techniques need to address both visual and aural senses to sustain engagement and facilitate comprehensive rater evaluation. Refresher training for studies longer than 18 months and data quality monitoring are critical components for maintaining inter-rater reliability. Statistical measures including Kappa and Intra-Class Correlation Coefficient are often used to assess the amount of agreement between raters (inter-rater reliability) and thus “confirm learning”. Ideally, effective rater training and certification programs integrate the above educational principles within the design of a “learn and confirm” curriculum.

Critical Factors Addressed in Successful Training and Certification Programs:

- **Clinical Experience Variation:** Typically, there are no consistent standards or requirements by which clinicians are selected to rate in clinical trials. Raters can be physicians, nurses, or study coordinators. Rater training prior to Investigator Meetings (IM) may include medical school and/or post-graduate training or simply hands-on clinical research experience. In a group of 13 Central Nervous System (CNS) studies, 25% of raters attending the IMs had no previous experience with the primary efficacy variable being used in the study.¹ Furthermore, pre-study rater surveys collated from the training programs revealed that more than 25% of raters had less than two years of clinical experience in the study indication. *Rater certification programs need to establish minimum standards for educational background and minimum years of clinical experience.*
- **Research Experience Variation:** Clinicians may lack research experience despite years of clinical experience. Ratings accuracy depends on effective training in conducting a research interview.² In contrast to the therapeutic intentions of a clinical interview, the objective of a research interview is to obtain reliable, quantitative data. Well-trained raters adopt a neutral interview style to minimize placebo response. Intentional or inadvertent supportive gestures by inexperienced raters who want to “help” the patient may generate higher placebo responses. Clinicians with less research experience may blur the boundaries between their clinical understanding of the illness and the more stringent scoring criteria

used in rating scales (e.g., adherence to operational anchors). Alternatively, some “experienced” clinicians simply ignore the anchors altogether despite protocol requirements. Clearly, clinical and/or research experience do not always correlate with ratings experience. *Rater certification programs should establish minimum years of ratings experience and develop interactive programs that teach and assess both scoring and interviewing competency.*

- **Inter-Cultural Differences:** Inter-cultural differences can substantially affect ratings. Analyses of multinational certification programs have revealed that well trained raters may score the same patient differently based upon their cultural or social perspectives. In one program, English speaking raters from three countries using the Young Mania Rating Scale (YMRS) for acute mania were assessed using videotaped interviews.³ Total YMRS scores differed significantly among raters from India, the UK, and the US.⁴

Cultural interpretations and differences need to be recognized and training materials need to be “culturally-neutral” as raters will not easily change their practices and/or beliefs.

Ratings accuracy depends on effective training in conducting a research interview.

- **Rater Turnover:**

Inter-rater reliability sessions conducted at or prior to IMs are designed to standardize administration of ratings instruments and clarify scoring conventions. However, often raters, many of who lack clinical and/or research experience, do not attend IM training sessions.⁵ The addition of new sites and site turnover in studies with long and/or delayed enrollment further challenges the standardization of measurement precision for *Clinician Rated Scales*. *Rater training and certification programs need to include systematic in-study training and certification processes for raters who do not attend the IM. For longer studies, monitoring and refresher training is a critical component to maintaining inter-rater reliability.*

Case Examples

- **Multi-National Program:** While ultimately, rater training and certification is best accomplished with smaller groups actively engaged in the learning process, large global studies that require multiple country-specific meetings can be successfully delivered. For an international program involving six separate IMs and 446 raters from 16 countries, PharmaStar designed training and certification materials to “neutralize” cultural biases.⁶ *Sub-titled videos, multiple language break-out sessions, and carefully designed didactic materials within a “learn and confirm” curriculum yielded no significant inter-meeting or inter-country differences for the YMRS nor the Clinical Global Impression scale.*

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- In new research to be presented at the upcoming APA 158th Annual Meeting in May and the NCDEU 45th Annual Meeting in June, 2005, more than 2500 ratings representing more than 1000 raters were analyzed from scored, videotaped interviews of the Hamilton Anxiety Scale (Ham-A), Hamilton Depression Scale (Ham-D), Montgomery-Asberg Depression Rating Scale (MADRS), and YMRS across nine different rater qualification programs conducted by PharmaStar. Individual item scores were compared to established acceptable scores and analyzed relative to each rater's previous clinical and scale experience. Inexperienced raters revealed significantly greater scoring variance across the four ratings instruments versus experienced raters. Furthermore, controlling for years of clinical experience, raters with five or more exposures to PharmaStar rater training programs did significantly better than those with only one training session on three of the four instruments. *These findings:* a) demonstrate that rater training experience does matter; b) support the need for more stringent standards for rater eligibility; and c) support mandatory training programs, especially for novice raters.

Relevant Therapeutic Areas

Clinician Rated Scales are selected as pivotal endpoints in clinical research across a wide range of diseases. While CNS disorders are most dependent upon these scales, the prevalence of both psychiatric and non-psychiatric scales in non-mental health diseases is significant. Depression and anxiety, for example, are co-morbidities often linked with multiple diseases, including but not limited to obesity, asthma, sexual dysfunction, pain, menopause, and premenstrual dysphoric disorder. Because these co-morbidities pose a threat to the management of these diseases, the ability to diagnose and treat psychological co-morbidities is critical.

Summary

The importance of obtaining consistent, accurate ratings in clinical trials has made rater training and certification programs an essential part of the drug development process. Beyond the specificity and sensitivity of the rating instrument, the broad diversity of rater education, clinical and research experience, cultural biases combined with the issues of rater turnover and drift may introduce variances that obscure drug effects.

Appropriate and effective rater training and certification programs designed to improve the accuracy of Clinician Rated Scales need to: a) address the educational needs of the less experienced raters; b) challenge the most experienced researchers to re-examine their administration techniques and scoring conventions; c) acknowledge rater differences in education, experience, and cultural beliefs; and d) address study design issues.

Ultimately, successful programs can enhance inter-rater reliability across clinically subjective rating scales, translating into successful study design and effective study

implementation. The quality data that effective training promotes, in turn, saves significant financial resources, minimizes the need to repeat trials and accelerates product approval.

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Naturalistic Studies — Effectiveness Isn't Just for Health Economists Anymore

By Lori Frank, Ph.D. and Mary Kay Margolis, M.H.A., M.P.H.

The Food, Drug, and Cosmetic Act, enacted in 1938, required safety of new drugs to be established before marketing. As complexity of pharmaceuticals and biologics has increased, safety concerns have increased. This, in conjunction with accelerated drug review by the FDA in the US, led to recognition of the need for "post-marketing" surveillance, focusing mostly on safety. Lacking from this post-marketing regulatory imperative is a push for collection of data on effectiveness and broader outcomes relevant to the patient and clinician.

Efficacy, as established through randomized controlled clinical trials (RCTs), is viewed as hard evidence and is at the top of evidence standard hierarchies—for example, the Cochrane Collaboration systematic literature reviews. The hierarchy is an explicit endorsement of efficacy data from RCTs as the gold standard for clinical information.

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Naturalistic Studies

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The limits of the concept of efficacy as determined in RCTs are widely known. Chief among them is the limited generalizability of results, sacrificed to high internal validity. For example, the artificiality of many RCT designs means medication adherence rates are unusually high—nearly perfect conditions for evaluating efficacy, but extremely limiting for information on likely effectiveness when adherence rates decline in the real world. Also, concomitant treatments that occur in the real world are usually strictly circumscribed within the RCT. The costs of RCTs are enormous and number of patients is limited; for low frequency events, these sample sizes are often not sufficient for signal detection. Naturalistic studies offer the possibility to collect data from a sufficiently large sample to permit less ambiguous detection of safety concerns, and by design, provide data on effectiveness—defined here as efficacy in actual real-world use.

Obviously, regulatory imperatives keep an emphasis on efficacy data. But why are naturalistic effectiveness studies so poorly understood by clinicians and policy makers? And why aren't more effectiveness studies conducted? Among the answers are the costs and risks involved in collection of effectiveness data in naturalistic settings. However proactive collection of naturalistic data is often desirable.

Below we briefly describe some of the information that naturalistic effectiveness studies can provide, to underscore their value. Recognition of the value of non-RCTs is important for several reasons. In general, more information is a good thing. Depending on the specific design, naturalistic studies offer a thorough understanding of the types of patients using the medication, their sociocultural context, barriers to proper use, and potential limitations to adherence, as well as an opportunity to identify safety issues that emerge with widespread, real-world use. Comprehensive understanding of factors related to appropriate adoption and use of new medications enhances the public health goals of society.

Manufacturers also stand to gain from well-designed and executed naturalistic studies. First is the obvious benefit of proactive information collected on safety. While the current system in the US does not always require the manufacturer to bear the cost burden of safety surveillance post-launch, responsible marketing of a product suggests it is wise to collect these data. With relatively minimal extra effort, substantial information on a disorder and its treatments can be gained, a benefit for both the manufacturer and society at large. Finally, a wide range of outcomes can be evaluated in the naturalistic setting, many of which can immediately enhance patient care and patient well-being. Barriers to acceptance or adherence of a treatment, the influence of concomitant pharmacological and non-

pharmacological treatments, educational needs for complicated regimens, and patient satisfaction can all be obtained in naturalistic settings, and knowledge of these variables can make meaningful improvements in patient care possible.

Implementation: The Devil is in the Details

Naturalistic studies can be complicated to implement. Often settings for data collection are far removed from academic medical centers and experienced clinical trial sites. This is desirable from the standpoint of generalizability and reproducing true conditions of use with the highest fidelity, but training clinical staff to accurately complete the steps required for the research study is no small undertaking.

In some cases, the organization of the study sponsor can add complexity. The formal clinical trial program for a compound is typically managed by a different functional unit within pharmaceutical companies than Phase IV or naturalistic studies. When these units collaborate on design and implementation of a naturalistic study the culture clash can be palpable. Careful collection of clinical data points and AEs, crucial to the clinical trial program, may not be possible and may in fact be undesirable in a naturalistic study. The push to maximize measurement—to obtain all relevant information possible—must be carefully weighed against the pragmatism required in real-world settings. Patients in a clinical trial know they are subjects of research. In a naturalistic study, while individual consent to participate is required, minimizing the intrusiveness of measurement is extremely important. Participants should not feel like "specimens" under study, particularly given the tendency of phenomena of interest to morph under such a spotlight. Minimizing subject and clinical staff burden is paramount for successful naturalistic studies.

As with any research program, tradeoffs of naturalistic studies in terms of costs, risks, and the potential value of information obtained require careful consideration. Technology advances can tip the balance though. For example, web-based data collection simplifies the data collection process for clinical practices that otherwise could not afford the staff time to participate, and the ease of electronic methods of data collection can make the burden on the patient appropriately low.

Clinical practice is complex and varied. Retrospective claims review and review of prescribing patterns can provide some information relevant to health concerns and their treatment. For many treatments, achieving broader goals of capturing the realities of medication use in a highly complex and varied context, and obtaining the information necessary to improve care, requires prospective, naturalistic studies.

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AARP Watchdog Forum

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However, today I am speaking for myself alone.

Since I have only five minutes, I will get directly to my main points.

First, I commend the AARP for embracing the evidence-based medicine concept to assist its members in making informed decisions about pharmaceuticals. Seniors are major consumers of drugs, they are often vulnerable from a health and cost standpoint, and they are now, and will be, financially liable to a great extent for the choices they make.

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Second, I commend Governor Kitzhaber and his Drug Effectiveness Review Project team, including especially Mr. Gibson and Dr. Santos, for bringing evidence-based medicine to the policy forefront across this country. Their effort could not be more timely given the Medicare Modernization Act and the various health, economic and technological forces in operation today.

Notwithstanding the high quality of work that goes into DERP reports, I caution the AARP and other consuming organizations about adopting these reports as presently constituted, and I challenge the Oregon Evidence Based Policy Center, as well as my colleagues here today, to broaden and strengthen these reports.

Here is my reasoning for these recommendations.

First, DERP's evidence-based reports only review, synthesize and report on randomized-controlled trial evidence to estimate comparative efficacy. Evidence of a drug's efficacy as shown in randomized-controlled trials (RCTs) is not the same as evidence of effectiveness in the real world. Thus, the evidence contained in DERP reports is not the whole story and generally not the best estimate of a drug's relative effectiveness. This fact is well known and well accepted in academic, policy and clinical circles.

Secondly, unlike DERP, numerous high profile health care organizations in the US and around the world have adopted formal evidence-based medicine processes which do, in fact, embrace the broader concept of comparative effectiveness. These include the Centers for Medicare & Medicaid Services' (CMS's) Medicare Coverage Advisory Committee (MCAC), the Academy of Managed Care Pharmacy's (AMCP's) Format for Formulary Submission, Blue Cross Blue Shield's Technology Evaluation Center (TEC), the Agency for Healthcare Research & Quality's (AHRQ's) Evidence-based Practice Centers (EPCs) (including the Oregon Health & Science University's own EPC which, ironically, generates the DERP reports), Harvard's Center for Risk Analysis; and arguably the most eminent EBM organization in the world today, the UK's National Institute for Clinical Excellence (NICE). So there are many models which DERP can emulate to produce more valid comparative effectiveness data.

My third point addresses cost-effectiveness. The DERP reports explicitly exclude economic consequences. This makes some sense since they address efficacy not effectiveness. Cost efficacy is a meaningless concept. However, DERP's clients, including 13 Medicaid agencies, Consumers Union and I expect AARP, do care about costs and use DERP reports as a basis to obtain best value for money in their drug decisions. DERP reports are not adequate as a foundation for cost-effectiveness. For instance, Consumers' Union's "BestBuyDrugs" is highly misleading to consumers since it not only reports the relative efficacy rather than the relative effectiveness of drugs of drugs but it also couples efficacy with a simplistic notion of cost.

My fourth point will be more esoteric to many of you, but it is important. DERP is attempting to synthesize evidence for informed real world decision-making. But it uses the wrong statistical technique. DERP uses classical frequentist biostatistics when it should be using Bayesian statistics. Ironically again, the very analysts at OHSU who produce the DERP reports are Bayesian analysts.

So I conclude my brief remarks with the following:

The evidence base from DERP reports as presently constituted is necessary but not sufficient for informed decision-making to take place. To complete the evidence synthesis process, DERP reports need to use the appropriate statistical technique and to embrace real-world evidence and other information as other organizations and their own analysts do routinely. The result will be more valid, more useful and better accepted evidence for informed decision-making to take place. But, you should expect that the resulting evidence of comparative effectiveness will not be as straightforward as it appears to be now. However, as Mishan noted more than thirty years ago, "...an imprecise estimate of the right concept is superior to a precise estimate of a wrong concept." More recently, my friend and colleague, J. Leighton Read, articulated the same concept in a more entertaining way when he stated: "It is better to be approximately right than precisely wrong."

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Interplay Between Reimbursement and Pharmacoeconomics

By Beth Hahn, Ph.D.

What does pharmacoeconomics have to do with reimbursement? Depending on the audience, the answer has historically been nothing or everything. European, Canadian, and Australian regulatory authorities have firmly linked pharmacoeconomic outcomes with reimbursement; however, the US has been slow to base reimbursement decisions on pharmacoeconomics, creating a division between academic theory and practical management in managed care organizations and PBMs.

The reasons given are standard in the managed care industry. They include the following: the pharmacoeconomic data produced within clinical trials do not remotely resemble real-life clinical practice or typical patient drug utilization, the data don't adequately match the MCO decision-maker's population, and the differences shown are difficult to interpret in terms of impact on a formulary budget. Less frequently listed, but very real factors, are the role of rebates in formulary positioning and the limited control of many MCOs in preventing access to and reimbursement for drugs in benefit structures that are open.

Rebates, or the discounts paid by a pharmaceutical manufacturer to the MCO after proof of utilization, are a revenue line in many MCOs and requires a contractual arrangement that can be extremely complicated depending on the structure and whether a manufacturer's portfolio is involved or the contract deals exclusively with one drug. Even when limited to a single drug, many contracts are based on performance in terms of achieving a set dollar goal, number of units sold, or market share for the drug class. Substantial resources from both the manufacturer and MCO are required to support the contract negotiations as well as contract enforcement with rewards for both parties if the drug is used at the level specified by the contract.

With regard to control of access to drugs, MCOs offer an array of benefit structures which are generally purchased by employers who dictate coverage and cost sharing for their employees. Increasingly, employers have favored 3-Tier benefit structures with varied copay levels depending on whether the employee received a generic, a preferred brand on formulary, or a non-formulary brand. In many benefit plans, all drugs are reimbursed and access is limited only by the physician's willingness to write the prescription and the employee's willingness to pay the copay. There is no prohibition based on cost-effectiveness or quality of life outcomes. Rather, that data may have helped position the drug in a 2nd-tier position with the lowest copay for a

branded drug, but it would not prevent access to other drugs.

Despite the prominence of rebates and benefit structures with open access, there are signs that pharmacoeconomic data may soon play a larger role in reimbursement in the US as drug approval and reimbursement become more closely linked due to increasing cost pressures on public and private payers. The secretary of the US Department of Health and Human Services has named a closer collaboration between the FDA and CMS as one of five task force initiatives. The agencies have agreed to collaborate in parallel review processes for new drug applications at the request of the applicant to speed marketing approval and reimbursement. Moreover, within the Medicare Modernization Act legislation, Section 1013 authorizes research, demonstrations, and evaluations to improve the quality, effectiveness and efficiency of Medicare, Medicaid and the State Children's Health Insurance Program.

Private industry has also responded with initiatives to derive more value for health care dollars and to curb the rate of increase. Well known examples include Pitney Bowes' elimination of tiered formulary structures to encourage compliance for asthma, diabetes, and hypertension in exchange for overall decreases in health care costs, and Pfizer's Healthy State program in Florida Medicaid to deliver patient-focused care and medical cost savings.

Yet another example of increased exposure for pharmacoeconomics by reimbursement decision-makers has been the development of AMCP dossiers. The use of AMCP dossiers remains mixed in managed care, but pharmacy directors are well aware of their existence and contents. As more manufacturers strive to deliver complete dossiers that include information on the pharmacoeconomics of the drug, the value of these documents will only increase.

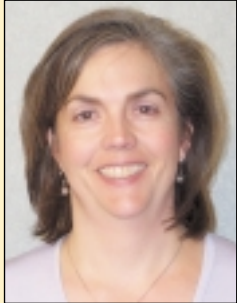
Regardless of whether the arena is public, private, or a collaboration between the two, all of these initiatives employ pharmacoeconomic tools for data collection and analysis to determine the value of health care services. Pharmacoeconomic methods of predictive modeling, instrument development for assessing interventions, and retrospective analysis of large data sets are central to these initiatives. An accurate picture of health care in exchange for cost cannot be delivered without these tools, as clinical safety and efficacy are not expansive enough to provide a rationale for reimbursement in a competitive market with limited resources. Although mandatory pharmacoeconomic data to achieve reimbursement is not likely in the immediate future, a firmer bond is forming between pharmacoeconomics and reimbursement in the US with growing momentum from public and private payers that will be uniquely American in its approach.

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NEWS
Briefs

Lynn Okamoto Announced as New Director of MEDTAP's Center for US Health Economics & Policy

The MEDTAP Institute at UBC is pleased to announce that Lynn J. Okamoto, Pharm.D. has accepted the position of Director of the Center for US Health Economics & Policy. Dr. Okamoto's extensive experience in global management, and her advanced leadership skills and command of strategic planning and implementation are an invaluable asset to MEDTAP. In this position, Dr. Okamoto will be leading the health economic and policy efforts in the US, as well as interfacing with MEDTAP's European operations on global issues.



Dr. Okamoto has well over a decade of experience conducting health outcomes and pharmaco-economic research and has held senior-level positions at NDC Health and Glaxo Wellcome. Her expertise spans a range of therapeutic areas, including respiratory diseases, cardiology, infectious disease, and digestive disorders. She has also managed the marketing strategy of several major pharmaceutical products and assisted in developing domestic and international pharmacoeconomic research strategy for respiratory products.

During her tenure at Glaxo Wellcome, Dr. Okamoto took an active role in pharmacoeconomic research at many levels, including decision modeling, strategic health outcomes research in support of new products, and regulatory strategy. Bringing this expertise to NDC Health, she created and directed the company's Outcomes Research department. She went on to strengthen the Research and Consulting division by acquiring and integrating new data sources, and by creating and implementing sales strategies to capitalize on integrated patient-level data.

In her most recent position at NDC, Dr. Okamoto served as Vice President and General Manager of the Intelligent Health Repository, the company's newest business unit that developed the integrated medical/pharmacy patient-linked claims repository, which led to the development of new products and services for customers across all healthcare markets.

Dr. Okamoto received her Doctor of Pharmacy from the University of Michigan, and her work in pharmacoeconomics has led to publications in healthcare journals, including *Clinical Therapeutics*, the *Journal of Asthma*, *Pharmacotherapy*, the *American Journal of Managed Care*, and the *Annals of Allergy, Asthma & Immunology*. Her research covers a wide variety of therapeutic areas and perspectives, from cost-of-illness analyses in respiratory care and influenza management, to quality-of-life studies in asthma. Dr. Okamoto's research has been exhibited internationally at conferences such as the International Society of Pharmacoeconomic and Outcomes Research Annual European Conference and the European Respiratory Society Annual Congress.

"I am excited about being a part of the The MEDTAP Institute and the UBC organization" says Dr. Okamoto. "I look forward to being a part of MEDTAP's tradition of excellence in scientific and strategic health economic services and UBC's commitment to providing evidence-based solutions to meet our customers' needs."

MEDTAP's Center for US Health Economics & Policy applies scientific principles in identifying and analyzing economic data for presentations to health care decision makers, including services such as: cost-effectiveness and burden of illness studies, economic dossiers, clinical trial support, economic modeling, and strategic and scientific consulting.

To contact Dr. Okamoto, please email lynn.okamoto@unitedbiosource.com. 

Luce Invited to Serve on Medicare Coverage Advisory Committee

Bryan R. Luce, Ph.D., MBA, MEDTAP's Founder, has been invited to serve as a member of the Medicare Coverage Advisory Committee (MCAC) for a term of two years, beginning in the summer of 2005. The MCAC advises the Centers for Medicare & Medicaid Services (CMS) on whether specific medical items and services are reasonable and necessary under Medicare law. It performs this task via a careful review and discussion of specific clinical and scientific issues in an open and public forum.

"I am honored to be chosen to serve on the MCAC," commented Dr. Luce. "As the emphasis on evidence-based medicine continues to grow, especially in light of the Medicare Modernization Act, CMS is under greater pressure to make informed, rationale and supportable coverage decisions. The MCAC plays an important role in that process."

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MEDTAP Welcomes New Research Scientist

Donald E. Stull, Jr., Ph.D. has joined the Center for Outcomes Research at The MEDTAP Institute at UBC as a Research Scientist. In this capacity, Dr. Stull's responsibilities include the design and management of research studies focused on patient reported outcomes, including instrument development and validation. Dr. Stull has over twenty-five years of health outcomes and health services research experience including studies of the measurement of physical and mental health; the validity of patient-reported health; and studies of health outcomes, such as mortality, hospitalization, and physician visits. His extensive experience in the measurement of key health-related constructs and analysis of longitudinal data provide an exceptional addition to the Center for Outcomes Research.

Dr. Stull's areas of interest include health services research; research methods (quantitative and qualitative); families and health; cardiovascular disease; long-term care; and gerontology. His work has led to articles in publications such as *Journals of Gerontology: Psychology Sciences*, *Journals of Gerontology: Social Sciences*, *Heart and Lung*, *Research in Nursing and Health*, *Journal of Applied Gerontology*, *Journal of Clinical Geropsychology*, *Encyclopedia of Home Care for the Elderly*, *The Gerontologist*, and *Research on Aging*. In addition, he was a co-editor of an award-winning book, *Ethnic Elderly and Long-Term Care*.

Before joining MEDTAP, Dr. Stull held the position of Senior Health Services Researcher at Medstat, and prior to that, he was a Senior Researcher and Associate Professor in the Department of Adult Health Nursing, University of Maryland School of Nursing. Dr. Stull is also an Adjunct Associate Professor at the University of Maryland School of Nursing. In his university positions, he has taught graduate-level courses in Research Design, Qualitative Measurement and Analysis, Advanced Multivariate Statistics, and Structural Equation Modeling. Dr. Stull received his Ph.D. in Sociology, along with his Master's and Bachelors' degrees in Sociology, from the University of Washington.

"I am excited about joining MEDTAP. Their reputation is second-to-none. Joining MEDTAP provides a unique chance to share my experience and skills with clients who need rigorous research to advance the understanding of patient outcomes and quality of life, and shape programs and policies that benefit the health of people around the world. Working with the exceptional researchers at MEDTAP is a wonderful opportunity for me."

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New ISPOR Special Interest Group Established

The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) is establishing a Special Interest Group (SIG) on Value-Based Reimbursement. This SIG will be chaired by Diane L. Simison, Ph.D.

of the Center for Pricing & Reimbursement at The MEDTAP Institute at UBC.

The Mission of the Value-Based Reimbursement SIG will be to:

- Provide a professional forum for ISPOR members on global reimbursement issues and the clinical and economic data needed or required as evidence for third-party reimbursement decisions
- Contribute to communicating this knowledge to the ISPOR members through publications, workshops, and industry meetings
- Contribute to reimbursement research through the marriage of the outcomes and pharmacoeconomics disciplines with the practical decision-making needs of third party payers, and disseminate this information to scientists and payers through the peer-reviewed literature

Work groups being established to achieve the above objectives will focus on the following:

- Evidence and Payer Decision-making
- Global Reimbursement Strategies
- Global Reimbursement Trends
- Reimbursement Literature
- Payer-oriented Evidence Guidelines

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For more information, contact diane.simison@unitedbiosource.com. 



International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 9th Annual International Meeting

MAY 15-19, 2005 ▪ WASHINGTON, DC, USA

SHORT COURSES

"Bayesian Analysis: Overview" Bryan R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.

"Bayesian Analysis: Applications" Bryan R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.

ISSUE PANEL — HEALTH POLICY/HEALTH CARE REIMBURSEMENT/COVERAGE ISSUES

"Should Manufacturers Consult with CMS Staff on the Phase III Study Design, as CMS is Now Requesting?"

MODERATOR: Diane Simison, Ph.D., **PANELIST:** Beth A. Hahn, Ph.D., The MEDTAP Institute at UBC, Arlington, VA, USA.

"Will CMS Begin to Use Economic Data to Evaluate New Technologies for Medicare Coverage?" Simison D¹, King-Shaw R². ¹The MEDTAP Institute at UBC, Arlington, VA, USA; ²The Solutions Institute, Bethesda, MD, USA.

POSTER PRESENTATIONS

"A Review of the Economic Burden of ADHD" Matza L, Prasad M, Paramore C, The MEDTAP Institute at UBC, Bethesda, MD, USA.

"Race and Gender Cost Differences Associated with Comorbid Atrial Fibrillation in the Hospital Setting" Coyne KS¹, Paramore CL¹, Grandy S², Mercader M³, Reynolds M⁴, Zimetbaum P⁴. ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²AstraZeneca LP, Wilmington, DE, USA; ³George Washington Univ., Washington, DC, USA; ⁴Beth Israel Deaconess Medical Center, Harvard Medical School, Boston MA, USA.

"Validation Study of the Osteoporosis Patient Satisfaction Questionnaire (OPSAT-Q)" Flood E¹, Beusterien K¹, Baran R², Shikiar R³, Cella D⁴. ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²Roche Laboratories Inc., Nutley, NJ, USA; ³The MEDTAP Institute at UBC, Seattle, WA, USA; ⁴Evanston Northwestern Healthcare, Evanston, IL, USA.

"Willingness to Pay for Intranasal Corticosteroid Therapy: The Importance of Sensory Attributes" Kleinman L¹, Shah SR², Mahadevia PJ³, O'Dowd L⁴, Leibman C⁴. ¹The MEDTAP Institute at UBC, Seattle, WA, USA; ²Collegeville Professional Center, Collegeville, PA, USA; ³AMGEN, Inc, Washington, DC, USA; ⁴AstraZeneca LP, Wilmington, DE, USA.

"Reliability and Validity of the Readiness for Discharge Questionnaire in Schizophrenia" Ruetsch C¹, Rupnow MF², Revicki DA¹, Kosik-Gonzalez C², Greenspan A², Gharabawi G². ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²Janssen Pharmaceutica Inc., Titusville, NJ, USA.

"Retrospective Analysis of Drug Utilization Patterns in Cancer and Non-Cancer Patients Treated with Transdermal Buprenorphine and Transdermal Fentanyl" Poulsen Nautrup B¹, Nuijten M². ¹Gruenthal GmbH, Aachen, Germany; ²The MEDTAP Institute at UBC, Jisp, Netherlands.

"Establishing the Content Validity of the Urinary Sensation Scale (USS)" Brewster-Jordan JL¹, Guan Z², Green HL¹, Jumadilova Z², Coyne KS¹. ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²Pfizer, Inc., New York, NY, USA.

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Linking Evidence to Product Value Statements

By Clark Paramore, M.S.P.H., Gregory de Lissovoy, Ph.D., M.P.H. and Audra Boscoe, M.P.H.

Including a health economics and outcomes research (HEOR) component in major drug or medical device development projects such as pivotal trials has become almost a routine practice. Manufacturers recognize that achieving optimal coverage and reimbursement, as well as rapid adoption, increasingly necessitates a launch support program that is firmly grounded in “evidence-based medicine”.

Achieving maximum return on the HEOR investment requires careful planning that begins with the ultimate objective: building credible evidence of value and communicating this information to key stakeholders. The first task is to identify stakeholders, the organizations and individuals that shape market access and product uptake. These include regulatory authorities, international opinion leaders, primary or specialty physicians, insurance carriers or national health plans, employers and consumers. The level of influence of particular stakeholders may vary depending on the disease entity, setting of care, and other factors. For example, consumers play an important role in the choice of treatment for allergic rhinitis while the market for lung cancer treatment is driven mainly by key opinion leaders.

The next task is to identify specific information needs for each stakeholder. For example, evidence of superior clinical performance is a prime consideration for key opinion leaders located in academic medical centers while community physicians might look for inclusion in treatment guidelines. Managed care organizations want evidence that a product offers a balance of good patient outcomes with efficient use of resources, while price might be the main consideration for a group purchasing organization.

Stakeholder information needs can be restated in terms of value messages. Comparing the product development program with evidence needed to support specific messages may indicate a need to refocus messages or modify the development program. Here are some examples.

- A value statement for a new rheumatoid arthritis product states that the product is “the most cost-effective treatment option on the market”. But cost-effective relative to what comparator? If the company has not conducted comparative clinical trials or attempted to model the expected incremental benefits of the product relative to competitor agents, then the value statement cannot be supported. A lower drug acquisition cost alone would not be sufficient to support the proposed value statement.
- The value statement for a new asthma controller therapy indicates that it “reduces costs associated with asthma exacerbations”. However, evidence to support this state-

ment will be derived from a short-term (12 week) trial that does not fully capture exacerbation data, and does not collect resource use associated with exacerbations.

- Another value statement for the new asthma controller therapy indicates that it provides “more convenience and is easier to use” than competitor therapies. However, the clinical trials did not include a validated and reliable patient questionnaire that asked about the convenience and ease of use of the product.

Meeting every stakeholder’s information needs is usually not feasible due to resource constraints. Therefore, a final task is to set priorities for information generation and dissemination. Following this step-by-step process will ensure the design of an HEOR program based on strategic consideration of market need for evidence of value and structured to generate that evidence with maximum efficiency.

For more information, contact clark.paramore@unitedbiosource.com, greg.delissovoy@unitedbiosource.com or audra.boscoe@unitedbiosource.com. 

Results of Workshop on Minimal Clinically Important Differences in COPD

Now Available in *Journal of Chronic Obstructive Pulmonary Disease*

Papers presented at the workshop on Minimal Clinically Important Differences in COPD Outcomes, held in Bal Harbour, Florida, January 11-13, 2004 have been published in the March 2005 issue of the *Journal of Chronic Obstructive Pulmonary Disease*. Organized by Barry Make, M.D., Richard Casaburi, M.D., and Nancy Kline Leidy, Ph.D., the workshop brought together methodologists with experience in the development of interpretive guidelines for new outcome measures, and recognized experts with an understanding of the current state of knowledge of the clinical interpretation of key outcome measures in COPD, to discuss the state of the science in this disease and make recommendations for further research. The meeting was an excellent opportunity for clinical scientists to benefit from the debate and empirical accomplishments of the patient reported outcome (PRO) world by applying some of these same questions and issues to traditional clinical endpoints. Conversely, it was an opportunity for PRO methodologists to benefit from the data and experiences of experts in clinical research.

The goals of this meeting were to: discuss the significance of and methodology for determining minimal clinically important differences (MCID) in health outcomes of importance in chronic obstructive pulmonary disease (COPD); review the current knowledge about MCID in outcomes of importance, including dyspnea, quality of

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Spotlight
on
SCIENCE

Recent Publications

- **Beusterien KM**, Leigh N, Jackson C, Miller R, Mayo K, **Revicki D**. "Integrating preferences into health status assessment for amyotrophic lateral sclerosis: the ALS Utility Index." *ALS and other Motor Disorders*. In Press.
- **Davies A**, Ridley S, **Hutton J**, Chinn C, Barber B, Angus DC. "Cost effectiveness of drotrecogin alfa (activated) for the treatment of severe sepsis in the United Kingdom." *Anaesthesia* 2005; 60:155-162.
- **Fleurence RL**. "The cost-effectiveness of pressure relieving devices for the prevention and treatment of pressure ulcers." *International Journal of Technology Assessment in Health Care*. In Press.
- Meltzer EO, Hadley J, Blaiss M, Benninger M, **Kimel M**, **Kleinman L**, Dupclay L, Garcia J, Leahy M, Georges G. "Development of questionnaires to measure patient preferences for intranasal corticosteroids in patients with allergic rhinitis." *Otolaryngol Head Neck Surg* 2005 Feb; 132(2):197-207.
- **Leidy NK**, Wyrwich KW. "Bridging the gap: using triangulation methodology to estimate minimal clinically important differences (MCIDs)." *COPD: Journal of Chronic Obstructive Pulmonary Disease* 2005; 2:157-165.
- Make B, Casaburi R, **Leidy NK**. Editorial: "Interpreting results from clinical trials: understanding minimal clinically important differences in COPD outcomes." *COPD: Journal of Chronic Obstructive Pulmonary Disease* 2005; 2:1-5.

MEDTAP welcomes comments and inquires about our scientific work. In each issue we feature a list of current publications and industry presentations. For more information, please call 301-654-9729 or email MEDTAP@unitedbiosource.com.

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 Cardiology Annual Scientific Session 2005

MARCH 6-9, 2005 ■ ORLANDO, FL, USA

"Cost-effectiveness of Cardiac Resynchronization Therapy With or Without a Defibrillator in COMPANION Heart Failure Patients" Feldman AM¹, de Lissovoy G^{2,3}, Bristow MR⁴, Saxon LA⁵, De Marco T⁶, Kass DA³, Boehmer J^{7,8}, Singh S^{9,10}, Whellan DJ¹, Carson P^{9,10}, Boscoe A², Baker T³, Gunderman MR¹¹. ¹Dept. of Medicine, Jefferson Medical College, Philadelphia, PA, USA; ²MEDTAP International, Inc., Bethesda, MD, USA; ³Dept. of Health Policy Management, Johns Hopkins School of Public Health, Baltimore, MD, USA; ⁴Div. of Cardiology, Univ. of Colorado, Denver, CO, USA; ⁵Div. of Cardiology, Univ. of Southern California, Los Angeles, CA, USA; ⁶Div. of Cardiology, Univ. of California, San Francisco, CA, USA; ⁷Div. of Cardiology, Johns Hopkins Univ. School of Medicine, Baltimore, MD, USA; ⁸Div. of Cardiology, Hershey Medical Center, Hershey, PA, USA; ⁹Dept. of Medicine and Pharmacology at Georgetown Univ. School of Medicine, Washington, DC, USA; ¹⁰Veterans Affairs Medical Center, Washington, DC, USA; ¹¹Guidant Corp., St. Paul, MN, USA.

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.

2005 Medical Futures Forum

MARCH 23-24, 2005 ■ NEW YORK, NY, USA

KEYNOTE ADDRESS:

"Evidence Based? Caveat Emptor!" Bryan R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.

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 D¹, De Cock E², Sorensen S³, Baker T³, Resch A⁴, Hardewig J⁴, Duttagupta S⁵. ¹Berlin, Germany; ²The MEDTAP Institute at UBC, London, UK; ³The MEDTAP Institute at UBC, Bethesda, MD, USA; ⁴Pfizer GmbH, Karlsruhe, Germany; ⁵Pfizer, Inc., New York, NY, USA.

Healthworld 2005 Conference

APRIL 11, 2005 ■ ATHENS, GREECE

"The Value of Investing in Health: The U.S. Experience" Bryan R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.

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

APRIL 20-23, 2005 ■ DENVER, CO, USA

SATELLITE SYMPOSIUM

Wednesday, April 20, 1:00pm - 5:00pm
(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 R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.

CONTEMPORARY ISSUES SESSION

Friday, April 22, 11:45 am - 12:45 pm

"The Evidence-Based Medicine Initiative" Bryan R. Luce, Ph.D., MBA, The MEDTAP Institute at UBC, Bethesda, MD, USA.



Setting Priorities for Research: The Role of Economics

By Rachael Fleurence, MBA, M.Sc.

Setting priorities for research using economic as well as scientific criteria makes sense if scarce resources are to be allocated efficiently. Current priority-setting methods have so far been developed for public research funding bodies, but applications to research in the pharmaceutical industry provide an exciting new area to investigate.

The Role of Economics

Although it is widely recognized that health economics has an important role in informing the implementation of treatments, much less attention has been paid to the role of economics to set priorities for research.¹ Yet it makes sense that the allocation of scarce resources for research would require priority-setting methods to make efficient decisions in the same way that treatments do. A number of priority-setting methods have been proposed in the literature, although it should be noted that the vast majority of studies are conducted from the perspective of public research funding bodies that are allocating taxpayers' money to research areas and research projects. For example, such methods have been investigated in the United Kingdom for the Health Technology Assessment Programme (HTA) and the Medical Research Council (MRC).^{2,3} Adding an economic perspective to priority-setting in research can make explicit the resource allocation choices, as well as ground them in rational decision-making criteria.⁴ In this article, I first describe three main methods that have been used to set priorities for research and then look at the implications for pharmaceutical research.

Existing Methods to Set Priorities for Research

▪ Burden of Disease

Burden of disease is the most widespread way of setting priorities for research. For example, Gross et al. used it to suggest priorities for research for the National Institutes of Health in the US.⁵ A value is placed on the "size" of the

disease with the assumption that the higher the burden or cost of the disease to society, the greater the need for research. Priorities in research are then set based on the relative contribution of diseases to the total burden. The use of burden of disease estimates as a priority-setting tool for research funds has high intuitive appeal because a ranking of diseases by burden appears to be easily and directly translated into priorities for research. However, health economists have argued that, in fact, the assumption of direct translation from rankings of burden to priorities for research is highly questionable.⁶ This is not to say that the number of people affected by a disease or condition will not influence the measurement of the value of research (so that some measure of burden is necessary); indeed it will—but automatic links between burden and priorities cannot be assumed. Because of some of these "theoretical" limitations of the burden of disease approach, other approaches have been developed.

▪ "Payback"

"Payback" approaches are widespread in the literature on priority-setting in research. This method was applied to decide whether the MRC should conduct a large trial of Hormone Replacement Therapy (HRT) in the United Kingdom.⁷ In "payback" approaches, the costs and benefits of conducting and implementing research are evaluated. Typically, different scenarios are explored and the health benefits and costs that would occur if the research took place are compared to the health benefits and costs that would occur if it were not. The streams of costs and benefits are dependent on both the results of research (whether or not the treatment will prove to be effective) and the changes in clinical practice that would occur as a result of the research results.²

▪ Value of Information

This approach is based on the principle that information provided by research can be quantitatively measured and valued, and that it can inform the decision to conduct research. There are still relatively few examples in the literature, but the HTA published a pilot study last year investigating the cost-effectiveness of conducting research in a number of areas (e.g., the use of antibiotics in urinary tract infection in children, the use of manual therapy for asthma and COPD patients) using value of information techniques.³ Information is valuable because it reduces the expected cost of uncertainty surrounding the decision. The more that valid information is available, the more likely the optimal treatment will be chosen. Moreover, if perfect information were available then the possibility of choosing the less cost-effective treatment would be completely eliminated. The Expected Value of Perfect Information (EVPI) provides an upper limit on what we should be willing to pay for research, as we should not be willing to pay more for research than we should be to obtain perfect information. The EVPI can be thought of as a first hurdle to pass

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in order for research to be considered for funding. If the cost of research is higher than the population EVPI, research should not be conducted. The decision concerning the generation of further information can be broken down into a number of hurdles for proposals to pass if they are to be funded. The next hurdle is comprised of partial EVPI which can provide information on individual parameters and inform the decision to conduct research on these areas.⁸

Lessons for Industry

It would make sense for the pharmaceutical industry to employ such techniques to assess the potential cost-effectiveness of research areas and research projects. However, there are some issues with the methods discussed in this article that would need to be resolved, as currently these methods are used primarily for publicly funded research institutions. One issue is how to adapt decision rules (i.e., how a project is deemed cost-effective) to industry. While payback and value of information use a cut-off cost per QALY value to make decisions about cost-effectiveness, this value may not be applicable to the pharmaceutical industry whose objectives are different from a national health system. Another difference is the phase of development of the product to which these methods apply. These methods are currently applied to make decisions on technologies that have already been approved. However, for the pharmaceutical industry, these methods are likely to be more interesting early on in the development of the product. Once products reach, for example, Phase III, the strict regulatory constraints are likely to overwhelmingly dictate the design of research. But applying methods such as payback and value of information methods earlier on in the product development process could provide valuable information on optimal target populations and potential research endpoints other than efficacy, such as resource use and patient reported outcomes. Studies such as cost-of-illness, quality of life instruments, and go/no go models could be developed early in the product development cycle based on rational priority-setting criteria. The potential application of these methods to industry constitutes an exciting new area for research.

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3. Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S. A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme. *Health Technol Assess.* Jul 2004;8(31):1-103.
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5. Gross CP, Anderson GF, Powe NR. The relation between funding by the National Institutes of Health and the burden of disease. *N Engl J Med.* Jun 17 1999;340(24):1881-1887.
6. Williams A. Calculating the global burden of disease: time for a strategic reappraisal? *Health Economics* Feb 1999;8(1):1-8.
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Health Related Quality of Life in the Pharmaceutical Management of Obesity

By Scott Doyle, B.A. and Patricia van Hanswijck de Jonge, M.Sc., Ph.D.

As genetic research advances we are beginning to see obesity as an incredibly complex disorder with a complex aetiology.¹ Public health interventions, commercially available diet pills, weight loss clubs, pharmaceuticals, and surgery have all failed to stem the rising tide of obesity. Behavioural, diet and exercise interventions will work for some individuals, but for the population overall the problem is growing. With smoking becoming increasingly marginalized in public use, obesity is set to overtake tobacco in the near future as the number one cause of preventable death in the western world.² The WHO estimated that approximately 1 billion adults worldwide are overweight (BMI>25) and a further 300 million meet criteria for clinical obesity (BMI >30). These prevalence rates have massive economic implications for health care providers and society generally. Direct cost estimates in the UK for obesity are pegged at £480 million per year, with a further £2 billion in indirect cost due to lost productivity.³ Estimates from the United States suggest the burden is between \$90-117 billion per year.⁴ Some experts have gone as far as estimating total global costs in terms of treatment and lost productivity to be on pace for in excess of 1 trillion dollars US per year.⁵

Pharmacological treatment of obesity has always been a controversial treatment option. Many opponents of drug treatment for obesity feel that pharmaceutical options need

...obesity is set to overtake tobacco in the near future as the number one cause of preventable death...

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Management of Obesity

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not be explored when diet and exercise alone can lead to meaningful reductions in body weight.⁶ And yet few would deny medication for sufferers of heart disease, hypertension, hypercholesterolemia, or type II diabetes, all of which are diseases that could also be treated by lifestyle interventions. Pharmacologic treatments therefore have an important place in obesity management.

The available drug treatments for obesity are limited in their effectiveness and by a significant side effect burden. Sympathomimetic/adrenergic drugs by their very nature raise blood pressure and heart rate while they increase thermogenesis. The SSRIs and sibutramine work by providing a sense of satiety and a slight raise in basal metabolic rate, but this class of pharmaceuticals come with sexual dysfunction related side-effects and some similar CNS stimulation occurrences seen with the adrenergics. Lipase inhibitors exhibit a range of bothersome GI side-effects. The side-effects from lipase inhibitors can be controlled by eliminating fatty foods from the patient's diet, but given the nature of the patient group, this can be challenging.

These medications do show meaningful health benefits.⁷ The clinical benefit may not always be matched by a benefit in terms of health related quality of life (HRQL) because the treatments do not reduce weight by a sufficient amount. This in turn can negatively impact the long term adherence to this medication. It is well recognized that obesity affects HRQL and that large weight losses can improve HRQL in the obese patient.⁸ However the typical weight loss seen in clinical trials may not be sufficient to lead to HRQL improvements. Perhaps a more significant issue is that very little work has been undertaken to develop a disease specific measure of HRQL in this area which can robustly capture data on the impact of treatment benefits, weight loss and side effects.⁹

Medication will not be the only approach to the treatment of obesity. This very complex disease needs to be attacked at every different level from social and psychological influences through to genetic and biochemical factors. Given the severity of obesity as a public health issue, it is surprising how poorly understood the disease remains. A greater understanding of the burden of the disease for individual patients in terms of HRQL and their preferences will improve our understanding of why some interventions work and others do not.

References

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² Allison DB, Fontaine KR, Manson JE, Stevens J, & Van Italliw TB. Annual deaths attributable to obesity in the United States. *JAMA* 1999; 282: 1530-1538.

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⁷ Institute for Clinical Systems Improvement: Technology Assessment Report. Pharmacological approaches to weight loss in adults. February 2003.

⁸ Kolotkin RL, Meter K, William GR. Quality of life and obesity. *Obesity Reviews* 2001; 2: 219-229.

⁹ Fontaine KR, Barofsky I. Obesity and health-related quality of life. *Obesity Reviews* 2001; 2: 173-182.

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MEDTAP Welcomes New Staff

Wen-Hung Chen, Ph.D. is a Senior Research Analyst whose responsibilities include statistical design, analysis, programming, and research on related psychometric issues with a focus on the development and validation of patient reported outcomes instruments. His areas of expertise include item response theory, classical test theory, and estimation methods. Dr. Chen earned his Bachelor's degree in Science from Chengchi University in Taipei, Taiwan, and his Master's degree and Doctorate in Quantitative Psychology, with a minor in Biostatistics, from University of North Carolina at Chapel Hill.

Dennis Govro, B.A. is a Research Assistant with responsibilities including conducting literature and web searches, reviewing literature, developing tables and spreadsheets, and data collection and organization. Dennis received a Bachelor of Arts degree in English and American Literature and Language from Harvard University.

Laurie A. Smith, M.L.I.S. is the Librarian/Manager of Scientific Information Services for MEDTAP. Ms. Smith is responsible for managing all functions related to electronic research and document delivery, managing MEDTAP's paper-based book and journal collection, and conducting literature reviews. She has experience searching within a wide variety of databases (such as PubMed, Cochrane Library, Dialog, etc.), as well as designing internal

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databases. Ms. Smith holds a Masters of Library and Information Sciences from Simmons College in Boston, MA and a Bachelors of Arts in Anthropology from Boston University. She also completed a Graduate Certificate Program in Knowledge Management from The George Washington University in Washington, DC.

Alexander Wade, B.A. is a Research Assistant with responsibilities including conducting literature searches, Web searches, developing tables and spreadsheets, data collection and organization, and assisting in the review, preparation and editing of reports and manuscripts. Mr. Wade graduated with honors from Duke University, receiving a Bachelor's degree in History.

Meghan Werner, B.A. is a Research Assistant with responsibilities including 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. Werner graduated Phi Beta Kappa with her Bachelor of Arts

degree in Comparative American Cultures and a minor in Writing Seminars from the Johns Hopkins University in 2004. She is currently completing her Master's degree in Public Policy with a concentration in International Health and Economic Development at the Johns Hopkins University Institute for Policy Studies. 🌐

MEDTAP Congratulates Staff on Promotions

Rachael Fleurence, M.B.A., M.Sc. and **Kellee Howard, M.A., M.Sc.**, both located in our Bethesda, MD office, have been promoted to Senior Project Managers.

Erwin De Cock, M.Sc. from our London office and **Sarah Dewilde, B.Sc., M.Sc.**, located in Belgium, have been promoted to Senior Research Associates. 🌐

MEDTAP Center for Pricing & Reimbursement Announces New Managing Director

Beth A. Hahn, Ph.D. has joined The MEDTAP Institute at United BioSource (UBC)'s Center for Pricing and Reimbursement as a Managing Director. Her leadership will strengthen MEDTAP's Center for Pricing and Reimbursement (CPR) in its ability to provide comprehensive strategic solutions in the areas of reimbursement and product economics. Dr. Hahn has over a decade of experience 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 ten years with GlaxoSmithKline, where she held a variety of positions in the commercial and R&D organizations. Her work with the commercial organization included developing and implementing reimbursement strategy 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.

Dr. Hahn has developed, managed, and executed health outcomes strategy in a broad range of therapeutic areas, including neurology, psychiatry, and gastroenterology. Dr. Hahn earned her Ph.D. in Sociology from the University of Illinois, and has applied her background in statistical analysis and demographics to international projects on health behaviors and quality of life studies. Her work in clinical therapeutics has led to publications in journals such as *Pediatrics*, *The Journal of International Medical Research*, *Medical Care*, *Digestive Diseases and Sciences*, and the *American Journal of Gastroenterology*.

Dr. Hahn has also provided expert guidance on reimbursement and pricing issues to GlaxoSmithKline's Pharma RTP business unit, and recently as a Practice Executive in management consulting, she has interpreted the implications of Medicare Modernization Act Part D for product marketing and contractual issues.

Dr. Hahn says, "In terms of why I joined MEDTAP, I have worked with and known of both the MEDTAP and CPR groups for many years and was always impressed by the stellar research both organizations produced. Coming from a background with pharmacoeconomics and reimbursement, MEDTAP was the perfect fit of my interests and skill set in an organization with a reputation for excellence. I am thrilled to be part of MEDTAP."

For more information, contact beth.hahn@unitedbiosource.com. 🌐

MCID in COPD

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life, exercise performance, and pulmonary function, in the management of patients with COPD; apply methodologies to determine MCID using existing data for outcomes of importance in COPD; and develop recommendations for further studies to determine MCID in health outcomes of importance in COPD.

In addition to serving as co-chair of the meeting, MEDTAP's Nancy Kline Leidy, Ph.D., along with Kathleen Wyrwich Ph.D. of St. Louis University, contributed a paper proposing the use of triangulation methodology to derive guidelines for interpreting change scores on health outcome measures. Triangulation integrates results from global ratings with clinical benchmarks of change, statistical estimates of magnitude, and qualitative data from patients and/or clinicians to derive guidelines that are not field-specific or method bound. Ten MEDTAP scientists served as reviewers for the manuscripts appearing in the *Journal of Chronic Obstructive Pulmonary Disease*. The journal website is: <http://www.tandf.co.uk/journals/titles/15412555.asp>.

For more information, please contact MEDTAP@unitedbiosource.com. 

Upcoming Presentations

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

MAY 7-11, 2005 ■ SAN FRANCISCO, CA

"Overactive Bladder with Urinary Incontinence Adversely Affects Women's Sexual Quality of Life" Rogers R¹, Margolis MK², Bavendam T³, Zyczynski T³, Coyne K².

¹University of New Mexico, Albuquerque, NM, USA; ²The MEDTAP Institute at UBC, Bethesda, MD, USA; ³Pfizer, 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 R¹, Margolis MK², Bavendam T³, Zyczynski T³, Coyne K². ¹Univ. of New Mexico, Albuquerque, NM, USA; ²The MEDTAP Institute at UBC, Bethesda, MD, USA; ³Pfizer, Inc., New York, NY, USA.

American Thoracic Society (ATS) 2005

MAY 20-25, 2005 ■ SAN DIEGO, CA, USA

"Content Validation of the Breathlessness Diary (BD): A Qualitative Analysis" Leidy NK¹, Niebauer K¹, Kleinman L¹, Leibman C², Goldman M². ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²AstraZeneca, Wilmington, DE, USA.

"Content Validation of the Breathlessness Diary (BD): A Quantitative Assessment" Leidy NK¹, Niebauer K¹, Kleinman L¹, Leibman C², Goldman M². ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²AstraZeneca, Wilmington, DE, USA.

"What Do Change Scores Mean? The Development of Empirically-Based Interpretive Guidance for the Breathlessness Diary" Leidy NK¹, Leibman C², Goldman M². ¹The MEDTAP Institute at UBC, Bethesda, MD, USA; ²AstraZeneca, Wilmington, DE, USA.


14th European Congress on Obesity (ECO 2005)

JUNE 1-4, 2005 ■ ATHENS, GREECE

"A Comprehensive Review of Local and National Epidemiology of Obesity in the UK" van Hanswijck de Jonge P, Doyle S, Hutton J, The MEDTAP Institute at UBC, London, UK.

"Reported Sexual Abuse and Cognitive Content in the Morbidly Obese" van Hanswijck de Jonge P¹, Waller G², Fiennes A³, Rashid Z³, Lacey H³. ¹The MEDTAP Institute at UBC, London, UK; ²Springfield Univ. Hospital, London, UK; ³St. George's Hospital Medical School, London, UK.

"An Unexplored Mechanism for Weight Control in Rimonabant: the Role of cAMP" Doyle S^{1,2}, Harrison CD³. ¹The MEDTAP Institute at UBC, London, UK; ²Univ. of Westminster, London, UK; ³Dept. of Haematology, Queen Mary School of Medicine and Dentistry, Univ. College London, UK.

"A Comprehensive Review of the Economic Cost and Burden of Disease: Overweight and Obesity in the United Kingdom" Doyle S, van Hanswijck de Jonge P, Hutton J, The MEDTAP Institute at UBC, London, UK. 



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