Health Technology and Public Policy:

Issues and Innovations Shaping the Future

The RTI Fellows Symposium
Abstracts and Presenter Biographies

December 2-3, 2004

Radisson Governors Inn
150 Park Drive
Research Triangle Park, North Carolina

The RTI Fellow Program

Designed to recognize and integrate the best technical talent at RTI International into our business strategy, the Fellow Program provides professional opportunities for exceptionally talented staff who are committed to science in support of RTI's mission. RTI Fellows are active in research projects and serve as consultants in key areas of scientific accomplishment. RTI relies on the Fellows to provide scientific leadership to their colleagues, to their research programs, and to the Institute at large. The Fellow program fosters scientific originality and innovation. In this way, RTI Fellows not only influence the future of RTI, but also enhance the impact of our research on society.

Current members of the RTI Fellow Program are as follows:

Distinguished Fellows

Dr. Paul P. Biemer
Dr. F. Ivy Carroll
Dr. Kathleen N. Lohr

Senior Fellows

Dr. Derick W. Brinkerhoff
Dr. James Chromy
Dr. Jerry Cromwell
Dr. David S. Ensor
Dr. F. Reed Johnson
Dr. Edo D. Pellizzari
Dr. Joshua M. Wiener
Blake S. Wilson

The RTI Fellow Program

The RTI Fellow Program (www.rti.org/fellowprogram) is the home for exceptionally talented RTI staff to be active in science and research projects, to serve as RTI-wide consultants in key areas of scientific accomplishment, and to provide strategic technical and scientific leadership to RTI. Annual symposia are one component of this service to RTI. The ***Health Technology and Public Policy: Issues and Innovations Shaping the Future*** symposium in 2004 draws on the leadership and experience of Fellows in health and social services research, policy research, the statistical sciences, science and engineering, and international development. Our goals are to explore the links between technology and health being made across nearly all units within RTI and to draw out the profound social, economic, and ethical implications of the highly complex technologies revolutionizing health care here and abroad.

Session Moderator Biographies

Paul Biemer, PhD
RTI International
Research Triangle Park, NC

Paul Biemer is an RTI Distinguished Fellow and holds a joint appointment with the University of North Carolina at Chapel Hill. Dr. Biemer has been associated with RTI since 1991, when he took the position of principal scientist and director of the Survey Methods Program.

Dr. Biemer received his PhD in statistics from Texas A&M University in 1978. His PhD dissertation examined nonsampling errors in surveys, which has continued to be his major research interest. He is the author of a book, with Lars Lyberg, *Introduction to Survey Quality* (New York: John Wiley, 2003) and is the lead editor of *Measurement Error in Surveys* (New York: John Wiley, 1991).

Upon completing his graduate work, Dr. Biemer joined the U.S. Census Bureau as a mathematical statistician where he led major quality improvement projects for the 1980 Decennial Census and the current surveys program. He advanced to the position of assistant division chief of the Statistical Research Division. Dr. Biemer left the Census Bureau in 1986 to take an associate professor position at New Mexico State University. At NMSU, Dr. Biemer assumed the positions of head of the Department of Experimental Statistics and director of the University Statistics Center. He continued his research on nonsampling errors with funding from the Census Bureau and the National Agricultural Statistics Service.

Derick Brinkerhoff, PhD
RTI International
Washington, DC

Derick W. Brinkerhoff is Senior Fellow in International Public Management and is an associate faculty member at George Washington University's School of Public Policy and Public Administration. He is a specialist in policy implementation, strategic management, democracy and governance, decentralization, citizen participation, and organizational change. He has worked with public agencies, NGOs, and the private sector, across a broad range of development sectors in 30 countries, with an emphasis on Africa. He served as Principal Social Scientist at Abt Associates for 10 years, where he spearheaded the research program of USAID's Implementing Policy Change Project, managed a USAID-World Bank support program for African agricultural and NRM research systems, and worked on health sector reform under USAID's Partners for Health Reform Project. Prior to joining Abt in 1993, he spent 10 years with the University of Maryland's International Development Management Center, including 6 years as the Center's associate director for research and 4 years as resident advisor to Haiti's planning ministry; 2 years in USAID's Science and Technology Bureau; and several years freelance consulting both in the U.S. and overseas. He was also a Peace Corps volunteer in Chad for 3 years. Dr. Brinkerhoff has published extensively, including six books and numerous articles and book chapters. He holds a doctorate in public policy and administration from Harvard University and a Master's in public administration from the University of California, Riverside.

James Chromy, PhD
RTI International
Research Triangle Park, NC

James Chromy, Senior Fellow, Statistics, has over 40 years of experience in sampling theory and application, survey design, and statistical analysis. Before joining RTI in 1966, he served as a statistician for the USDA's Statistical Reporting Service. At RTI, he has led many large-scale surveys and has held a number of administrative roles including department manager, center director, and research vice president. He helped design the sample and data collection methodology for the National Assessment of Educational Progress (NAEP) first conducted by RTI in 1969 and served as project direct for sampling and administration of NAEP from 1977 to 1983. He has experience in all aspects of area probability sampling and household interview surveys. Among his most noted work, Dr. Chromy developed the theory and computational algorithm for selecting minimum replacement probability proportional to size samples, and he developed a computer algorithm for efficient sample allocation that minimizes total survey cost subject to satisfying multiple variance constraints. He holds the PhD in mathematical statistics and the MS in experimental statistics from North Carolina State University, and a BS in technical agricultural economics, from the University of Nebraska.

Jerry Cromwell, PhD
RTI International
Waltham, MA

Jerry Cromwell, a Senior Fellow, received his PhD in economics from Harvard University in 1974 before developing a career in health economics research. He has led many technical and evaluation projects for federal agencies that focused on cost containment and disparities in access to health care. He founded Health Economics Research in 1978 (recently acquired by RTI), building a core of interdisciplinary researchers studying hospital and physician payment issues and the cost effectiveness of clinical interventions and new regulatory and payment policies. He has testified on health issues in Congress and sat on scientific review boards evaluating new technologies. Dr. Cromwell has published widely on health economics issues and taught health economics courses at Tufts and Brandeis Universities.

David S. Ensor, PhD
RTI International
Research Triangle Park, NC

David S. Ensor is the director for the Center for Aerosol Technology and is an RTI Senior Fellow. Dr. Ensor received his PhD in engineering at the University of Washington. For over 30 years Dr. Ensor has conducted contamination control, aerosol, and indoor air quality research. He is a founding editor of *Aerosol Science and Technology*. He has served as President of the American Association for Aerosol Research and the International Aerosol Research Assembly. He is the convenor of ISO Working Group 14744-7 (glove boxes, minienvironments, isolators and clean hoods). His current research activities include immune buildings, homeland security technology verification for air cleaning, electrospraying/electrospinning, and bioaerosol sampling. Dr. Ensor is a Fellow of the Institute of Environmental Science and Technology and American Society of Heating, Refrigerating and Air-Conditioning Engineers.

Brett Hauber, PhD, MA
RTI International
Doylestown, PA

Brett Hauber is the Director of the Benefits Valuation Group at RTI Health Solutions. He has over 10 years of academic, research, and government experience in health and environmental economics. His primary area of specialization is discrete choice analysis of revealed- and stated-preference data of consumer demand. He also has extensive experience in conducting health economic studies based on disease progression models. In most projects, he applies advanced statistical techniques to the analysis of discrete choice, epidemiologic, and clinical trial data. His most recent work has included conjoint studies of patient and physician preferences for diabetes treatments and chemotherapies, the development of a number of disease progression models, and studies of the theoretical and empirical relationships among various health utility measures. In addition, he has focused on communicating the value of theoretically sound health economics to decision-makers. Dr. Hauber's research has been published in *Pharmacoeconomics*, *Clinical Therapeutics*, *ISPOR News*, *Land Economics*, and the *Journal of the American Agricultural Association*. He received his PhD in economics from the University of Delaware.

Paul Kizakevich, MS, PE
RTI International
Research Triangle Park, NC

Paul Kizakevich, Principal Investigator for Medical Simulation and Training, conducts research and development in medical training, virtual reality simulation, and physiological modeling with emphasis on interactive simulated patients. His efforts include 3D-interactive and physiological simulation of bioterrorism, chemical terrorism, and trauma patients in pre-hospital, emergency, and primary care domains. Mr. Kizakevich holds a degree in electrical engineering from Carnegie-Mellon University and a master's degree in biomedical engineering from the University of Miami. During his 26 years at RTI, he has completed and published on a variety of projects and studies.

David Kroll, PhD
RTI International
Research Triangle Park, NC

David J. Kroll, PhD, is a Research Pharmacologist in the RTI Natural Products Laboratory, Center for Organic and Medicinal Chemistry. Dr. Kroll earned a BS in toxicology (1985) from the Philadelphia College of Pharmacy and Science and interned in the Department of Drug Metabolism at then-SmithKline & French Laboratories. He then earned a PhD in pharmacology and therapeutics (1989) from the University of Florida College of Medicine, studying the biochemical regulation of the anticancer drug target, DNA topoisomerase II. After a postdoctoral fellowship in Medical Oncology and Endocrinology at the University of Colorado Cancer Center, he joined the faculty of the University of Colorado School of Pharmacy in 1992 and was promoted in 1999 to Associate Professor of Pharmacology and Toxicology with tenure. Following sabbatical work in 2000 at the Duke University Medical Center, he joined the Duke Center for Integrative Medicine in 2001. Collaborations there with natural products researchers at RTI led to his joining RTI full-time in January 2002.

Dr. Kroll's primary area of research expertise is the molecular pharmacology of natural and semi-synthetic anticancer drugs, mechanisms of anticancer drug resistance, and the interaction of herbal dietary supplements with cancer chemotherapy. He is also recognized as a health sciences educator on herbal medicines and was named a President's Teaching Scholar of the University of Colorado in 2000. Dr. Kroll as authored or co-authored over 40 peer-reviewed research publications, reviews, and book chapters. He is co-author of *Clinical Guide to Medicinal Herbs and Other Therapeutic Natural Products* and co-editor of a series of 16 consumer books on dietary supplements.

Judy Lessler, PhD
RTI International
Research Triangle Park, NC

Judith T. Lessler is Vice President, Partnerships for Genomics and Molecular Epidemiology, RTI. She is leading a group of scientists from across RTI who are focusing on development of capabilities in genomics and bioinformatics. Dr. Lessler's research has focused on methods for the design and execution of health surveys and epidemiological studies. Dr. Lessler was a key player in the use of cognitive laboratory methods for evaluating the quality of self-reports in clinical and epidemiological studies and in the creation of audio-computer-assisted-self-interviewing.

Dr. Lessler has a PhD in biostatistics from the University of North Carolina at Chapel Hill. She is a fellow of the American Association for the Advancement of Science and the American Statistical Association.

Kathleen N. Lohr, PhD, MPhil, MA
RTI International
Research Triangle Park, NC

Kathleen N. Lohr, RTI Distinguished Fellow, is also the Co-Director of the RTI-University of North Carolina Evidence-based Practice Center, developing systematic reviews and evidence reports on a wide array of clinical and health policy topics. Between 2000 and 2003, she was Chief Scientist at RTI in Health, Social, and Economic Research. From 1996-2000, Dr. Lohr directed an RTI program of research in health services and health policy, involving more than 40 researchers in quality of care, evidence-based practice, Medicare and Medicaid evaluations, health communications, and similar fields. In addition, she is Research Professor, Health Policy and Administration, at the University of North Carolina School of Public Health, Senior Research Fellow, Cecil G. Sheps Center for Health Services Research, Senior Investigator for UNC's Program on Health Outcomes (across the five health sciences schools) and a Co-Investigator on UNC's Center for Education and Research in Therapeutics and PROMIS cooperative agreements.

Before coming to RTI, Dr. Lohr spent 9 years at the Institute of Medicine (IOM), National Academy of Sciences, where she was Director, Division of Health Care Services. At the IOM, she had overall responsibility for administrative, personnel, and substantive tasks related to the division's portfolio of studies in health care delivery, organization, financing, quality of care and clinical evaluation, practice guidelines, health workforce, public health, and related topics. She directed studies of various IOM expert committees and served as author and/or editor on numerous publications reporting on these studies, including *Medicare: A Strategy for Quality Assurance* (1990) and *Guidelines for Clinical Practice: From Development to Use* (1992). During her 12 years at The RAND

Corporation before joining the IOM, she served as lead analyst, co-principal investigator or project leader, lead author, analyst, coordinator of staff activities, or senior editor on a variety of health care projects, particularly the RAND Health Insurance Experiment between 1974 and 1987.

Dr. Lohr is a Fellow of AcademyHealth (formerly, the Association for Health Services Research) and chairs its Distinguished Investigator Award committee. She serves on various advisory boards for federal agencies and projects and on expert committees for the IOM and the National Academy of Sciences. Dr. Lohr is widely published in the fields of quality of care, practice guidelines, evidence-based practice, and health status assessment. She has a PhD in public policy analysis from the RAND Graduate Institute, a MPhil in policy analysis from RAND Graduate School, and a MA in education from Stanford.

Lauren McCormack, PhD
RTI International
Research Triangle Park, NC

Lauren McCormack has over 12 years of professional experience in health services research, policy analysis, and health communication with an emphasis on the older adult and lower educated populations. She is currently the Director of RTI International's Health Communication program in the Center for Health Promotion Research, overseeing a staff of 13 individuals. Dr. McCormack has led multiple federal, state, and commercially funded research projects, including studies to communicate and evaluate health-related information, measure consumer knowledge of various public health issues, assess trends in employer-sponsored health insurance, and monitor indicators of access to and quality of health care. She has extensive experience developing, testing, and implementing survey and other data collection instruments; performing statistical analysis of large- and small-scale databases; and conducting qualitative analysis, including focus groups, case studies, and in-depth, cognitive and usability testing interviews. Her experience also includes designing and testing various types of health education materials, including those that are print, video, and computer-based. Dr. McCormack is currently Principal Investigator of a 3-year Centers for Disease Control and Prevention (CDC)-funded project to promote informed decision making about prostate cancer testing.

Prior to coming to RTI in 1997, Dr. McCormack was a Senior Researcher at Health Economics Research Inc./Center for Health Economics Research. She received her PhD from the University of North Carolina at Chapel Hill in health policy and administration.

Edo Pellizzari, PhD
RTI International
Research Triangle Park, NC

Edo Pellizzari, RTI Senior Fellow for Analytical and Environmental Health Sciences, became Director of Proteomics in 2003 after serving as a research vice-president for 20 years. After receiving his PhD in analytical biochemistry from Purdue University he served as a U.S. Public Health Service Postdoctoral Fellow in the Houston Medical Center and then joined RTI in 1971 as a chemist.

Dr. Pellizzari is nationally and internationally recognized for his technical contributions to environmental health sciences. He has served on several National Academy of Sciences committees, on EPA's Science Advisory Board, Committee on Drinking Water, has participated in dozens of workshops and panels for major government agencies (e.g., EPA, NIEHS, HHS, NSF, and DOE) in the areas of air and water pollution, characterization of pollutants in environmental and biological media, and synfuel production. He has served on and chaired numerous NIEHS's grant review committees since 1986. Dr. Pellizzari has provided his expertise to government agencies to review major research programs in analytical chemistry at the National Laboratories (Argonne, Battelle Pacific Northwest, Oak Ridge, Lovelace, Lawrence Livermore). He has been invited to make plenary lectures on pollution topics at agencies in Canada and Sweden that are the equivalent of the U.S. EPA. He has published over 220 papers in peer-reviewed journals.

George Van Houtven, PhD
RTI International
Research Triangle Park, NC

George Van Houtven is Director of RTI's Economics of Environment, Health, and Development Program and has over 10 years of project management experience. Dr. Van Houtven specializes in the measurement of environmental, health, and natural resource values and the application of these measures to evaluate environmental and risk management policies. He has extensive experience in the implementation of preference elicitation methods, including the design of survey instruments and the econometric analysis of stated preference data. He has also coordinated several interdisciplinary studies that link environmental and economic models and that apply benefit transfer approaches to support cost-benefit analyses of environmental regulations. In addition, he has conducted research to examine the effectiveness of unit-based pricing policies for solid waste management, and he has employed econometric techniques to assess the implicit role of cost-benefit factors in environmental regulatory decision-making. Dr. Van Houtven is a member of the American Economic Association and the Association of Environmental and Natural Resource Economists. He has published in the *Journal of Environmental Economics and Management*, the *RAND Journal of Economics*, *Land Economics*, *Environmental and Natural Resource Economics*, *Applied Economics, Risk Analysis, Economics Letters, Vaccine,* and *Public Finance Review.* Previously, Dr. Van Houtven was an assistant professor of economics at East Carolina University where he taught courses in microeconomics and environmental economics. He received his PhD in economics from the University of Maryland and a BA in economics from Johns Hopkins University.

Joshua M. Wiener, PhD
RTI International
Washington, DC

Joshua M. Wiener is a Senior Fellow and program director for aging, disability and long-term care at RTI International. He is the author or editor of eight books and over 100 articles on health care for older people, long-term care, Medicaid, health reform, health care rationing, and maternal and child health. Prior to coming to RTI International, Dr. Wiener did policy analysis and research for the Urban Institute, the Brookings Institution, the Health Care Financing Administration, the Massachusetts Department of Public Health, the Congressional Budget Office, the New York State Moreland Act Commission on Nursing Homes and Residential Facilities, and the New York City Department of Health. He received his BA from the University of Chicago and his PhD from Harvard University.

Plenary Sessions

RTI International

RTI International seeks to improve the human condition through objective, innovative, multidisciplinary research, development, and technical services and to set the standard for scientific and professional excellence. In furtherance of that mission, the RTI Fellow Program is the home for exceptionally talented RTI staff to be active in science and research projects, to serve as RTI-wide consultants in key areas of scientific accomplishment, and to provide strategic technical and scientific leadership to RTI. Since 2001, this country has redoubled its efforts to address issues of terrorism, and, in planning this first Fellows Symposium, the Fellows identified "Homeland and Health Security: Understanding Today's Necessities, Tomorrow's Needs" as a critical national issue central to RTI's mission and work. The symposium will foster transdisciplinary work within RTI and with outside partners, including not only the founding universities — University of North Carolina, Duke University, and North Carolina State University — but also universities and institutes with which we already collaborate in relevant areas such as bioterrorism preparedness. Especially important areas for future research and policymaking that were examined at the symposium included medicine and public health, statistical issues in bioterrorism and surveillance, technical approaches to monitoring and detection, economic impacts of terrorism, safety of agriculture and the food supply, and innovative approaches to training for emergency preparedness.

Victoria Franchetti Haynes, PhD
RTI International
Research Triangle Park, NC

Dr. Victoria Haynes is President and Chief Executive Officer of RTI International. Her career of more than 27 years has focused on technology leadership, management, and new business development. She has developed expertise in strategic business alignment and management of technology resources, the identification, evaluation and commercialization of emerging technologies for significant new business opportunities, and the development of science and technology in multidisciplinary organizations directed toward complex problems.

Before joining RTI in 1999, she was Vice President of the Advanced Technology Group and Chief Technical Officer at BF Goodrich Company. She also held managerial roles at Monsanto Corporation. Her doctoral and master's degrees are from Boston University in Boston, Massachusetts, and her undergraduate degree in chemistry is from the University of California, Berkeley.

Dr. Haynes is a member of several corporate boards, including the board of directors for Lubrizol Corporation, Nucor Corporation, PPG Industries, and Ziptronix. She also serves on advisory boards and committees for a number of universities and the federal government.

Plenary Session 1:

Identifying and Promoting Truly Cost-Effective Technology Innovation

Measuring the Aggregate Impact of Medical Innovation on Health

Frank Lichtenberg

I will survey econometric evidence about the overall impact of medical innovation during the last few decades on health. Most of this evidence is about the impact of new drugs on the longevity of Americans, since drugs are the best-measured (and most widely used) innovations, longevity is the best-measured health outcome, and the United States has the best data. But the methods of evaluation used are general, and I will also present some evidence about other types of innovation (e.g., laboratory tests), other health outcomes, and other countries.

Frank Lichtenberg, PhD
Courtney C. Brown Professor of Business, Columbia University School of Business
New York, NY

Frank R. Lichtenberg is Courtney C. Brown Professor of Business at the Columbia University Graduate School of Business, and a Research Associate of the National Bureau of Economic Research. He received a BA with Honors in history from the University of Chicago and an MA and PhD in economics from the University of Pennsylvania.

Mr. Lichtenberg previously taught at Harvard University and the University of Pennsylvania. He has served as an expert for the Federal Trade Commission, the U.S. Department of Justice, and state Attorneys General, and has testified before Congress. He has worked for several U.S. government agencies, including the Department of Justice, the Congressional Budget Office, and the Census Bureau, and been a visiting scholar at the Wissenschaftszentrum Berlin, the University of Munich, and elsewhere.

Some of Professor Lichtenberg's research has examined how the introduction of new technology arising from research and development affects the productivity of companies, industries and nations. Recently he has performed studies of the impact of pharmaceutical innovation on longevity, the effect of computers on productivity in business and government organizations, and the consequences of takeovers and leveraged buyouts for efficiency and employment. His articles have been published in numerous scholarly journals and in the popular press. His book *Corporate Takeovers and Productivity* has been published by MIT Press. He was awarded the 1998 Schumpeter Prize for his paper, *Pharmaceutical Innovation as a Process of Creative Destruction,* and a 2003 Milken Institute Award for Distinguished Economic Research for the paper, *Pharmaceutical Knowledge-Capital Accumulation and Longevity.*

He has been awarded research fellowships, grants, and contracts by the National Science Foundation, the National Institute of Standards and Technology, Merck and Co., the Fulbright Commission, the Brookings Institution, the Alfred P. Sloan Foundation, the German Marshall Fund, the American Enterprise Institute, and other organizations. He has served as a consultant to private organizations and government agencies including the Securities Industry Association, Pfizer, Inc., the Community Preservation Corporation, the RAND Corporation, the New York City Water Board, Touche Ross and Co., The Walt Disney Company, McGraw-Hill, and the National Pharmaceutical Council. He is a Director of the economics consulting firm LECG, LLC.

Evidence Meets Politics in the Management of Technological Change

Annetine C. Gelijns and Alan J. Moskowitz

In few fields of public policy are the use and cost of services so powerfully driven by technological change as in medicine. To manage technology, policymakers have expanded their investment in evaluative research. This presentation will address three under-examined challenges in using evidence: those inherent in the dynamics of technological change itself, those inherent in the analytical enterprise, and those inherently political factors that shape the translation of evidence into policy decisions. The design of institutional arrangements and processes that seek to blend evidence with politics merit closer attention and existing cross-national arrangements deserve careful study.

Annetine Gelijns, PhD
Director, International Center for Health Outcomes and Innovation Research (InCHOIR)
Department of Surgery and Columbia University Medical Center
New York, NY

Annetine Gelijns is Co-Director (with Alan Moskowitz) of the International Center for Health Outcomes and Innovation Research (InCHOIR), and an Associate Professor of Surgical Sciences in the Department of Surgery, College of Physicians and Surgeons, and the Division of Health Policy and Management of the Mailman School of Public Health, Columbia University, New York City. She is also a Division Chief in the Department of Surgery. Her current research focuses on measurement of the long-term clinical outcomes and economic impact of clinical interventions, patient safety research, and the factors driving the development and diffusion of medical technology. She has special expertise in cardiovascular disease, particularly in the design, coordination, and analysis of multi-center left ventricular assist devices (LVAD) trials. She has been the director of the Data Coordinating Center for the National Institutes of Health (NIH)-sponsored REMATCH trial, and is the PI or co-PI of several newer generations of LVAD trials. She also will direct the Data Coordinating Center for the SCCOR grant on the biology of long-term LVAD implantation, for which NIH funding is pending. Before coming to Columbia in 1993, she directed the Program on Technological Innovation in Medicine at the Institute of Medicine, National Academy of Sciences. Dr. Gelijns has been a consultant to various national and international organizations, including the World Health Organization (WHO) and the Organization for Economic Cooperation and Development (OECD), Paris, France. She holds a PhD from the medical faculty and the department of science policy, University of Amsterdam, and a master's degree in law from the University of Leyden, the Netherlands.

Alan J. Moskowitz, MD
International Center for Health Outcomes and Innovation Research (InCHOIR)
Department of Surgery and Columbia University Medical Center
New York, NY

Alan J. Moskowitz, MD, is Co-Director (with Dr. Annetine Gelijns) of the International Center for Health Outcomes and Innovation Research (InCHOIR), and an Associate Professor of Clinical Medicine, Surgery and Public Health in the Departments of Medicine, Surgery, College of Physicians and Surgeons, and the Division of Health Policy and Management of the Mailman School of Public Health, Columbia University, New York City. Dr. Moskowitz trained in internal medicine and completed a National Library of Medicine Fellowship in Clinical Epidemiology, Clinical Decision Making and Medical Computer Science at Tufts University, New England Medical Center. His current research focuses on advanced heart failure, particularly long-term mechanical circulatory support. He has been the director of the Clinical Coordinating Center for the National Institutes of Health (NIH)-sponsored REMATCH trial, and is the Principal Investigator or Co-Principal Investigator of clinical trials of newer generation, continuous flow, left ventricular assist devices (LVADs). Dr. Moskowitz has special expertise in the analysis of economic and quality of life endpoints, and along with Dr. Gelijns, oversees the analysis of these endpoints for REMATCH. Dr. Moskowitz will be the co-principal investigator for the SCCOR grant on the biology of long-term LVAD implantation, for which NIH funding is pending. Dr. Moskowitz is a practicing Internist and is a member of Columbia University's Institutional Review Board. He has been a consultant for the Organization for Economic Cooperation and Development (OECD), Paris, an invited speaker for the National Academy of Engineering, and a grant reviewer for the National Institutes of Health.

Plenary Session 2:

Technologies across the Spectrum of Chronic to Acute Life-threatening Diseases

The New Age of Aging

Daniel Perry

The United States and much of the developed world are in the throes of a longevity revolution. This demographic tsunami challenges and confounds governmental efforts to avoid crushing financial and social burdens associated with increasing incidence of chronic age-related health problems. Millions of older patients with chronic, long-term conditions portend increasing costs of health care and long-term nursing care. Though many bemoan rising costs of health care and the huge national investment in new medical technologies, the argument is made here that still larger wagers on innovation are the in the long-term national interest. As the United States girds for the impending Age Boom, medical advances from frontline research will be crucial to meeting high public expectations for better lives and ultimately for taming the fires of medical cost inflation. Recent technological advances that allow better and more cost-effective care of diseases of old age will be detailed and a new study from Rand of expected breakthroughs for healthier aging in the near future will be presented.

Daniel Perry
Executive Director
Alliance for Aging Research
Washington, DC

Daniel Perry is the Executive Director of the not-for-profit Alliance for Aging Research in Washington, DC. Mr. Perry's organization is the nation's leading citizen advocacy organization for promoting a broad agenda of medical and behavioral research to improve the health and independence of older Americans.

Mr. Perry's background spans a wide range of health policy, governmental, political and journalistic experience. Mr. Perry held staff positions for more than a dozen years on Capitol Hill, including special assistant to the Majority Whip of the U.S. Senate. He was appointed by Health and Human Services Secretary Louis Sullivan during the first Bush Administration to the Federal Task Force on Aging Research and named by President Clinton to the Advisory Board of the White House Conference on Aging. As part of the influential Jackson Hole Group on healthcare issues, Mr. Perry helped establish the groundwork for the Foundation for Accountability, or FACCT, and served as Chairman of the FACCT Board of Directors.

Mr. Perry is the current President of the Coalition for the Advancement of Medical Research (CAMR), leading over 80 advocacy organizations in the fight to advance stem cell research.

Extracorporeal Life Support: Assessment of an Advanced Technology in the Pediatric Intensive Care Unit

Keith C. Kocis

Extracorporeal Life Support (ECLS) is a technology that was first used to save critically ill children over 30 years ago. ECLS will serve as a case study for discussing the introduction and utilization of advanced technology in pediatric patients. We will review the development of ECLS; current indications for use; outcomes in specific pediatric subgroups; and the business model of an ECLS program.

Keith C. Kocis, MD, MS
University of North Carolina
Department of Pediatrics
Chapel Hill, NC

Keith C. Kocis, MD, MS, is an Associate Professor of Pediatrics at The University of North Carolina, Chapel Hill, and Chief, Division of Pediatric Critical Care Medicine. He is board certified in pediatrics, pediatric cardiology, and pediatric critical care medicine. He received a Master's degree in Clinical Research Design and Statistical Analyses from the School of Public Health at the University of Michigan.

Lunch Session

Health and Technology Assessment: An International Perspective

Peter Littlejohns

The National Institute for Clinical Excellence (NICE) offers health professionals in England and Wales advice on providing their patients with the highest attainable standards of care. NICE guidance includes:

- the use of individual health technologies (Technology Appraisal Guidance); and
- the management of specific conditions (Clinical Guidelines).

In producing both forms of guidance, the Institute is required to take account of both clinical and cost effectiveness. NICE has generated considerable interest and not a little controversy and this presentation will share the experiences of the first 5 years.

Professor Peter Littlejohns, MBBS, BSc, MD, FRCP, FFPHM, MRCGP, DRCOG
National Institute of Clinical Excellence (NICE)
London, United Kingdom

Peter joined the National Institute for Clinical Excellence (NICE) as Clinical Director in 1999. He was formerly Professor of Public Health at St. Georges Hospital Medical School and Director of the Health Care Evaluation Unit. His previous research unit was commissioned by the National Health Service Executive to appraise potential national guidelines. His research interests include developing new approaches to assessing the cost-effectiveness of clinical care and translating research findings into practice.

He was coordinator of a 10 country research programme funded through the European Union investigating the basis of variation in international guideline recommendations. This research resulted in the establishment of the AGREE instrument (**A**ppraising **G**uidelines for **Re**search and **E**valuation). He is a founding trustee of the AGREE Research Trust.

In April 2005, the public health functions of the Health Development Agency will transfer to NICE and Peter has recently been appointed to the post of Clinical and Public Health Director in this new organization

Biology and Behavior

Moderator: Judy Lessler

How Genes Influence Family Relationships and Mental Health: Implications for Prevention and Intervention

Jenae Neiderhiser

Until recently, the fields of developmental psychology, behavioral genetics, and prevention have traveled along parallel courses with little interdisciplinary interaction. The steady accumulation of evidence for the importance of genetic factors for developmental outcomes, relationships, and stability and change has fostered an increase in the communication and collaboration between "traditional" developmentalists and those involved in behavioral genetic research. This has helped to advance both fields dramatically and to increase our understanding of adaptive and maladaptive development and the complementary roles of genetic and environmental factors. The next logical step is to translate and utilize these findings in prevention and intervention research. For example, understanding how children evoke or actively shape certain reactions and relationships with others (i.e., parents) is of critical importance for a relationship-based prevention strategy. These findings may also help to explain why some interventions show a great deal of variation in terms of their effectiveness across individuals.

This paper will focus on the role of genetic and environmental factors in explaining associations between parenting and the development of psychopathology in children and adolescents. Studies that have examined these associations using genetically sensitive designs have found that genetic factors play an important role and there has been a flurry of new research specifying genotype x environment interactions using both quantitative and molecular genetic approaches. Genetic influences on measures of parenting and on the associations between parenting and child adjustment can only be understood in terms of genotype-environment correlation and interaction. The implications of these findings for prevention science and their potential application and specification will be discussed. Although the integration of genetic research and prevention science is only just beginning, it is likely to advance at a rapid pace. For this reason, understanding how biology and prevention can be integrated is critical.

Jenae Neiderhiser, PhD
George Washington University
Washington, DC

Jenae M. Neiderhiser received her PhD in human development and family studies from The Pennsylvania State University in 1994. She is currently an Associate Professor in the Department of Psychiatry and Behavioral Sciences at The George Washington University. She joined the Center for Family Research (a division of the Dept. of Psychiatry) in 1994 as a postdoctoral fellow. Her work has focused on understanding the interplay between genes and the environment with a focus on family environment, and parenting in particular. Dr. Neiderhiser's research includes both quantitative genetic and molecular genetic designs in order to maximize her ability to understand the processes involved in development across the lifespan. Most recently, she has been focused on integrating genetic research and findings with prevention and intervention efforts.

Dr. Neiderhiser is currently leading a population-based study of twin mothers and fathers of adolescent children in Sweden, focused on understanding how parents' genes influence their parenting, their marital relationships and their adjustment as well as examining twin parents and their children together to tease apart the type of genotype-environment correlation operating. She has just completed a young adulthood follow-up to a large national study of adolescent twins and siblings and their parents, adding DNA collection to the design. Finally, she is co-investigator on a prospective adoption study focused on understanding genotype-environment interaction and correlation.

Cognitive and Emotional Regulatory Functions Predict Correctional Treatment Response in Inmates

Diana H. Fishbein, Monica Scott, Christopher Hyde, Ralph Serin, David Newlin, and Rob Hubal

A small number of correctional treatment programs are reportedly "effective" for a statistically significant number of inmates; however, these numbers do not provide support for their widespread clinical utility in aggressive offenders. There is invariably a substantial and important subgroup that does not respond favorably, exhibiting high levels of aggressive behavior within and outside of the correctional environment. It is critical that underlying mechanisms for these differential effects are identified to improve treatment efficacy. Integrity of neurocognitive function and its modulation of emotional responses may represent key dimensions of regulatory processes involved in antisocial behavior and may play a principal role in differential responses to treatment programs. Neurocognitive capabilities specifically related to higher-order executive cognitive functions (ECF) are of particular interest given their role in impulsivity, sensitivity to consequences, decision making, and social skills. There is strong evidence for ECF and emotional impairment in a significant proportion of aggressive offenders, which may be related to their recidivism and resistance to authority and standard treatments. The primary premise of this 3-year prospective study is that neuropsychological and emotional deficits contribute to differential responses to treatment interventions. This study is designed to assess (1) the role of ECF and emotional deficits in aggressive inmates; (2) the usefulness of neuropsychological and emotional measures in characterizing this subgroup; and (3) the ability of these measures to predict treatment response and institutional misconduct. Understanding the mechanisms that underlie differential responses to treatment will maximize the return on investment that correctional administrators direct toward intervention strategies by making it possible to triage inmate subgroups based on programming needs.

Diana Fishbein, PhD
RTI International
Baltimore, MD

Diana H. Fishbein has a joint PhD in criminology and psychobiology from Florida State University. She currently is a senior scientist and directs the Transdisciplinary Behavioral Science Program for RTI. Three primary themes drive this program's research agenda: (1) differentiation between drug consequences and precursor conditions; (2) underlying mechanisms in differential responses to interventions and (3) effects of psychosocial factors on neurobiological processes that influence risk for psychopathology. Consistent with these themes, studies conducted by Dr. Fishbein utilize interdisciplinary methods to evaluate neurocognitive, functional neuroanatomical, emotional regulatory, physiological, psychological and behavioral processes. Previously, she was prevention coordinator and evaluator at the HIDTA (High Intensity Drug Trafficking Area) Research Program centered at the University of Maryland and funded by the Office of National Drug Control Policy (ONDCP). Dr. Fishbein began her career as professor of criminology at the University of Baltimore and a scientific investigator, first at the University of Maryland, School of Medicine, and subsequently at the National Institute on Drug Abuse (NIDA), where she directed neurobiological studies on disruptive behavioral disorders and substance abuse. She then became a senior researcher with the U.S. Department of Justice (DOJ) to develop and evaluate crime prevention programs. Dr. Fishbein consults regularly with federal, state, and local agencies for purposes of expert witnessing in criminal court, training, technical assistance, scientific peer reviews, and development of research protocols. Publications include numerous chapters, monographs, scientific articles, and policy papers on antisocial behaviors and drug abuse. She is primary author of two textbooks, *The Dynamics of Drug Abuse* and *Biobehavioral Perspectives in Criminology*, and editor of *The Science, Treatment and Prevention of Antisocial Behavior, Volumes I and II.*

Underlying Neural Mechanisms in Differential Drug Abuse Treatment Responses

Diana Fishbein, Elliot Stein, Diana Eldreth, Thomas Ross, John Matochik, and Betty Jo Salmeron

The treatment of substance abuse and its comorbid behavioral disorders has produced inconsistent results, and relapse rates over time remain high. Although some program types and modalities are more effective than others in general, there is a substantial subgroup of substance abusers that is more recalcitrant, demonstrating a lack of improvement in psychosocial functioning. There is evidence that this treatment-resistant subgroup may be unable to process and act on information from curriculum materials that most programs use in some form. The study we will describe will elucidate moderating characteristics and explain variability in outcomes with a goal to improve treatment efficacy. Given evidence that integrity of executive cognitive function (ECF) and its modulation of emotional arousal may represent dimensions of regulatory processes related to risk for substance abuse, we hypothesize that these functions may play a principal role in differential treatment responses. We will also assess specific genetic variants and protein biomarkers, with the hypothesis that they account for a portion of the group differences (good vs poor treatment responders) in brain imaging and performance data collected.

This pilot study will prepare investigators for a 4-year study examining whether pre-existing neurocognitive, emotional, psychophysiological, and genetic differences in substance abusers relate to variability in behavioral improvements following exposure to a standard drug abuse treatment. Functional magnetic resonance imaging (fMRI), using a 3T magnet at the National Institute on Drug Abuse (NIDA) Intramural Research Program, will be used for this purpose. The proposed study will introduce two neurocognitive and an emotional task while participants are scanned to identify neural mechanisms involved in treatment responsivity. Blood will be sampled to assess gene and protein markers of treatment response. Also, a virtual reality program has been designed to simulate real-life, risky decision-making to gauge actual behavioral change. Change in neural activation patterns, cognitive function, and behavior in response to treatment will be further assessed to identify mediators of differential treatment responses. Hypothetically, favorable changes in behavioral outcomes will occur commensurate with improvement in these neurocognitive, emotional, and physiological functions. Thus, this innovative design will identify of both neural moderators and mediators of treatment outcomes.

Diana Eldreth, BA
RTI International
Baltimore, MD

Diana Eldreth obtained a BA in psychology from the University of Delaware (2000). While there, she worked with Dr. Mary Dozier on a study assessing the effects of foster care on infant development and the role of attachment relationships as mediators. During that time, Ms. Eldreth became invested in the use of salivary cortisol as a measure of hypothalmic-pituitary-adrenal axis functioning. After graduation, she consulted with the Oregon Social Learning Center (Dr. Philip Fisher) to establish a wet lab and to train staff to run cortisol assays. Ms. Eldreth interned for Dr. Stephen Suomi of the National Institute for Child Health and Human Development (NICHD) and worked with Dr. Peter Pierre assessing the effects of nursery rearing on circadian rhythms in infant macaques. Afterwards, Ms. Eldreth worked with Dr. Allyson Bennett at Wake Forest University, where she established a neonatal nursery and assessed macaque behavior. At Wake Forest, Ms. Eldreth also learned DNA extraction and became familiar with serotonin transporter gene polymorphisms. Since July 2002, Ms. Eldreth has worked with Dr. Fishbein as project manager of two studies: (1) a position emission tomography (PET) study assessing the effects of polysubstance use on neurocognition and (2) a study examining differences in neurocognition and psychophysiology between children with and without conduct disorder. She now manages Dr. Fishbein's fMRI pilot study to identify the neural substrates of drug abuse treatment response. Ms. Eldreth's main research interests are on early environmental and genetic influences on childhood and adult psychopathologies.

New Methodology for Health Measurement

Moderator: Paul Biemer

MASSC-ing Microdata: A Method for Disclosure Avoidance

David Wilson

The credibility of a data producer is at stake if the respondents in a database do not have confidence in the confidentiality of their sensitive information collected by the producer. In a scenario known as 'disclosure by response knowledge', the respondent identifies his own record from the database and is concerned about its disclosure by someone who might know enough about the respondent to identify his record.

The MASSC[SM] method developed at RTI addresses the above problem using a probabilistic framework that allows for random, but controlled, perturbation and suppression. The MASSC[SM] method views a database as a population and relies on the analogy between releasing an untreated database and conducting a census of the population.

Survey sampling methods that are used to minimize cost subject to bias and precision constraints are used in MASSC[SM] to provide simultaneous control, and measurement of, disclosure risk and information loss. The methods used in MASSC[SM] consist of four steps: **M**icro **A**gglomeration for partitioning the database into risk strata, probabilistic **S**ubstitution for perturbation, probabilistic **S**ubsampling for suppression, and sampling weight **C**alibration for preserving estimates for key variables. Analysis of data sets processed by the MASSC[SM] system can be carried out using standard analysis software.

David Wilson, PhD
RTI International
Research Triangle Park, NC

David Wilson is a Research Statistician who has been with RTI since 1998 and received his PhD in statistics from North Carolina State University in 2002. He has experience in statistical computing, survey design, survey analysis, disclosure analysis, and analysis of data from multi-center studies. He has been on the development team for RTI's SUDAAN software for the analysis of correlated data since 2000. His work over the last 2 years has primarily centered around the development of RTI's Statistical Disclosure Limitation software package known as MASSC.

Disclosure Limitation via Multiply-Imputed, Synthetic Microdata

Jerry Reiter

To limit the risks of disclosures when releasing data to the public, it has been suggested that statistical agencies release multiply-imputed, synthetic microdata. For example, the released microdata can be fully synthetic, comprising random samples of units from the sampling frame with simulated values of variables. Or, the released microdata can be partially synthetic, comprising the units originally surveyed with some collected values, e.g., sensitive values at high risk of disclosure or values of key identifiers, replaced with multiple imputations. Multiple imputation is necessary to allow the user to obtain valid variance estimates. In this talk, I provide an overview of synthetic data procedures and inferential methods.

Jerry Reiter, PhD
Duke University
Durham, NC

Jerry Reiter is Assistant Professor of the Practice of Statistics and Decision Sciences at Duke University, where he has been since 2002. He received his PhD in statistics from Harvard University in 1999. His main research interests include statistical disclosure limitation, missing data methods, and survey methodology.

GenePoint – Informatics for Human Genomic Data

A. Jaime Cuticchia

Since its inception, there have been both implications and inferences that bioinformatics would serve as the "magic bullet" for the modernization of biomedical research. When the personal computer was popularized in the 1980s, the future was also envisioned as a place where people worked three days a week and the computer solved nearly every challenge. Thus a similar hope was placed on bioinformatics. While a universal three-day workweek is still outside our grasp, the maturation of bioinformatics is now beginning to approach its initial ambition. Still not a magic bullet, bioinformatics technologies now plays an important if not crucial role to most aspects of biomedical research and drug discovery. The enormity of data and the acceleration of its acquisition have placed a data bottleneck in the research process to build scientific knowledge. Here we present the employment of cutting-edge information technology to create advances in bioinformatics tools. We focus on what is largely recognized as the major area: curation and quality of data. Using technologies that represent investments of hundreds of millions of dollars by the IT industry, we have crafted a system for the curation of genomic datasets. Addressing the fact that one out of every five public biological records has at least one error, we have produced a novel community-supported method for the curation of biological data as a significant step to bettering data quality. By crafting solutions tailored to meet the needs of improving the therapeutic research process, we attempt to decrease both the cost of research as well as the time to market of new pharmaceuticals.

A. Jaime Cuticchia, PhD
RTI International
Research Triangle Park, NC

Dr. A. Jamie Cuticchia, the Director of RTI's Genomics and Bioinformatics program, has over 20 years' academic and industry experience leading groups in computational biology, genomics, high-performance computing, software engineering, and genome database construction. Dr. Cuticchia was ranked in 2001 as a *Genome Technology All-Star*, one of the Top 3 Bioinformaticians worldwide responsible for the success of the Human Genome Project

Technology-assisted Learning for Health Care

Moderator: Paul Kizakevich

Advanced Initiatives in Medical Simulation (AIMS) – Creating a National Agenda for Medical Simulation

Colonel Mark W. Bowyer, MD, FACS, DMCC

There are many and increasing challenges associated with the production of safe and competent medical care providers. Recent limitations on work hours for trainees, coupled with decreased availability of patients within the hospital, greater numbers of invasive procedures which must be taught, and less tolerance for error has created a potential patient safety crisis. The traditional apprenticeship "see one, do one, teach one model" is no longer appropriate and the use of simulation for training has great potential. Unfortunately this new technology is expensive and there has been limited investment to date. This presentation will highlight ongoing efforts to create a national agenda for medical simulation. A review of the need, the progress to date, and the plans for the future will be presented.

Mark W. Bowyer, MD, FACS, COL, MC, USAF
National Capital Area Medical Simulation Center
Burke, VA

Dr. Bowyer is the Surgical Director of the National Capital Area Medical Simulation Center. He is also an Associate Professor of Surgery, and the Chief, Division of Trauma and Combat Surgery at the Uniformed Services University. He is board certified in both General Surgery and Surgical Critical Care and actively practices trauma surgery at the Washington Hospital Center. Dr. Bowyer is the current Vice Chair (Air Force), American College of Surgeons Military Region Committee on Trauma. He has been on the forefront of adopting the use of surgical simulators as a replacement for animals in the teaching of the Advanced Trauma Life Support course. Dr. Bowyer has been involved in the teaching of medical students and residents since 1990. Over the last 2 years, he has been integrally involved in developing a simulation-based curriculum for medical students starting their surgical rotation. Dr. Bowyer has an ongoing interest and involvement in developing and validating robust trauma, laparoscopic, triage, and critical care based simulators.

Training Pediatric Examination Interaction Skills

Robert Hubal

The Virtual Pediatric Standardized Patient (VPSP) application is intended to provide practice for medical students on using verbal skills to engage pediatric patients. In three prototype scenarios of the application, students must obtain cooperation from a young girl to check her ears with an otoscope, correctly check a boy's breathing with a stethoscope, and conduct an adolescent social history with a female adolescent. The pediatric patients' behavior relies on cognitive, emotional, linguistic, gestural, and other models, as well as responses to interaction strategies that were identified by pediatric experts. VPSP is being evaluated to measure responses to the pediatric patients and monitor usage of the application.

Robert Hubal, PhD
RTI International
Research Triangle Park, NC

Robert Hubal, PhD, is a Senior Research Engineer at RTI International. In his research he explores approaches to improving learning and training effectiveness with an emphasis on cost-effective, technology-enhanced innovations in the design, development, delivery, evaluation, and management of training and assessment. He has investigated the interaction effects among cognitive task demands, expertise, and presentation of information. Most recently, he has developed behavioral software that enables virtual humans to act and behave realistically in controlled learning contexts.

Triage Simulation for Disaster Readiness Training

Paul Kizakevich

On-the job training cannot provide adequate experience for multiple-casualty disasters, because these events occur so rarely. Live exercises provide some training, but these require extensive coordination among providers and live-actors to portray casualties. Such exercises usually focus on organizational and logistical issues, with little attention to medical response. RTI recently extended our emergency medical personnel simulations to support multiple-casualty triage training. RTI's Triage Simulator presents a scenario comprising a virtual scene, trauma or medical conditions, and one or more patients. The caregiver can navigate and survey the scene, interact and converse with the virtual patient, use medical devices, administer medications, monitor data, and perform interventions. The simulation presents animated, 3-D patients with signs and symptoms related to level of exposure for recognition of the appropriate level of treatment. Each triage casualty is independent with its own injury models, physiological simulation, and signs and symptoms. Animations such as vomiting, tearing, coughing, seizure, and convulsions are dependent upon changing physiological conditions, concentration of chemical agents, and various medical intervention. The simulated patients have facial expression, gestures, body movement, and can portray anger, fright, confusion, or other emotions or behaviors based on cognitive, emotional, physiological, and pathological models. Multiple-casualty scenarios were implemented for and mixed civilian/military mass casualty events including trauma, chemical, and psychological casualties. A "Triage Card" is provided for assignment of medical priority and triage category (immediate, delayed, minimal, expectant, and deceased) consistent with the paradigm of Move, Assess, Sort, and Send. Multiple providers can coordinate and conduct triage, patient assessment, and medical care by viewing and interacting in the scenario on individual computers. An integrated learning management system provides instruction of triage protocols and assessment of provider performance.

Paul Kizakevich, MS, PE
RTI International
Research Triangle Park, NC

Mr. Kizakevich, Principal Investigator for Medical Simulation and Training, conducts R&D in medical training, virtual reality simulation, and physiological modeling with emphasis on interactive simulated patients. His R&D efforts include 3D-interactive and physiological simulation of bioterrorism, chemical terrorism, and trauma patients in pre-hospital, emergency, and primary care. Mr. Kizakevich holds a degree in Electrical Engineering from Carnegie-Mellon University and a master's degree in Biomedical Engineering from the University of Miami. During his 26 years at RTI, he has successfully completed a wide variety of projects and has published on a variety of medical and engineering topics.

Improving Health through Chemical Biology

Moderators: Edo Pellizzari and David Kroll

Neurobiological Basis and Treatment of Addictions: Impact of Recent Human Molecular Genetic Studies

Mary Jeanne Kreek

The prevalence of addiction to opiates, when one includes both heroin addiction but also addiction to prescription opiates either used illicitly or related to treatment of pain, has not been fully determined. However, approximately 1 in 3 to 1 in 5 of those who ever self-administer heroin develop not only tolerance and physical dependence (common to all chronic opiate use) but also "addiction." In our research, which began in early 1964, we presented a novel hypothesis which, in retrospect, represented a frame shift in scientific and clinical thinking, namely, that heroin addiction is a disease of the brain, with resultant behaviors, and not simply a criminal behavior or due to an anti-social personality or other personality disorder. In clinical research, we initially developed opioid agonist pharmacotherapy (methadone maintenance treatment) for heroin addiction, which remains the major successful approach for chronic treatment of this disease. Subsequently, other effective agonist and partial opioid agonist treatments have been developed. "Bidirectional-translational research" has enabled us to develop novel animal models for molecular and cell biological, neurochemical, neuroanatomical and behavioral studies to elucidate the specific components that contribute to different facets of the development of opiate, cocaine, and/or alcohol addictions and the persistent changes that lead to relapse. Complementary studies of the role of molecular genetics have also been conducted. For instance, work from our laboratory has defined multiple variants of the coding region of the mu opioid receptor and shown that the most common of these is functionally different in cellular and molecular constructs. Work of others has shown, as we predicted, "physiogenetic" as well as pharmacogenetic findings related to stress responsivity in humans with one copy of this variant. Very recently, we have shown a very strong association of this allelic variant with both opiate addiction and also alcoholism, with attributable risk due to this variant of 18% and 11%, respectively.

Mary Jeanne Kreek, MD
Professor and Head
Laboratory of the Biology of Addictive Diseases
The Rockefeller University
New York, NY

Mary Jeanne Kreek, MD, is a graduate of Wellesley College where she received Honors in chemistry and biology, and also of the Columbia University College of Physicians & Surgeons, where she received the MD degree. Dr. Kreek is now Patrick E. and Beatrice M. Haggerty Professor and Head of Laboratory, the Laboratory of the Biology of Addictive Diseases, at The Rockefeller University, and Senior Physician of The Rockefeller University Hospital in New York City. Dr. Kreek is author or co-author of over 350 scientific reports, concept papers, and review articles. She has also received several awards for her scientific research, including the prestigious R. Brinkley Smithers Distinguished Scientist Award and Lecture of ASAM, the Betty Ford Award from AMERSA, and the Nathan B. Eddy Memorial Award for Lifetime Excellence in Drug Abuse Research presented by the College on Problems of Drug Dependence, one of the highest recognitions in the field of drug abuse research. In May 2000, she was conferred with the Doctor Honoris Causa by the University of Uppsala, Sweden, and in September 2000, was made a Fellow of the New York Academy of Sciences. Dr. Kreek is an Elected Member of the American Association of Physicians and of the Harvey Society, and is a Permanent Member of the Council on Foreign Relations. In 2004, Dr. Kreek was awarded the Columbia University College of Physicians & Surgeons Alumni Association's Gold Medal for Distinguished Achievements in Academic Medicine. Dr. Kreek currently serves as President of the International Narcotics Research Conference (INRC).

The Marriage of Chemistry with Genomic Approaches for Drug Discovery

Patrick J. Casey

Biomedical science has entered an era in which collaboration across disciplines is essential to tackle complex biological problems. One of the major challenges of the post-genome era is the linking of specific gene products to pathways and regulatory networks. Determining the cellular function of a protein generally requires a means to alter that function. The most common way of doing so is via altering the gene encoding the protein. This genetic approach has been widely used in biology, but it has its shortcomings. A complementary and more direct approach employs small molecules that alter the function of proteins; this approach has recently been termed chemical genetics/genomics but in reality is what the pharmaceutical industry has been doing for over a century. This leads to the second major challenge facing biomedical scientists, and that is how they can help to enable the translation of basic research findings into products that impact on human health. The pharmaceutical industry is becoming increasingly risk-averse and shying away from both the discovery process and from developing drugs that target small-population diseases. Academic investigators and the National Institutes of Health (NIH) are responding to these challenges by launching chemical genomics initiatives designed to exploit the opportunities presented by the sequencing of the human genome. Advances in chemistry, particularly the ability to rapidly produce diverse libraries of compounds, and biological assay development, coupled with recent advances in robotics and information processing, have revolutionized the process by which small molecule modulators of protein function can be discovered. These chemical genomics initiatives will complement those in the pharmaceutical and biotech sectors by the identification/validation of new therapeutic targets and of small molecules that impact the function of these targets.

Patrick J. (Pat) Casey, PhD
James B. Duke Professor of Pharmacology and Cancer Biology
Director, Duke Center for Chemical Biology
Duke University Medical Center
Durham, NC

Dr. Casey received his PhD in biochemistry from Brandeis University in 1986. He did postdoctoral work in the Department of Pharmacology at the University of Texas Southwestern Medical Center. He joined Duke University Medical Center as Assistant Professor of Molecular Cancer Biology and of Biochemistry in 1990. Dr. Casey's research interests are in the areas of lipid modifications of proteins, particularly modifications important for the functions of the Ras family of oncogene products, and in delineating novel signaling processes controlled heterotrimeric GTP-binding regulatory proteins (G proteins). Dr. Casey has received a number of awards for his work, including the Basil O'Connor Scholar Award from the March of Dimes, an Established Investigator Award from the American Heart Association, and the 2000 Amgen Award from the American Society of Biochemistry and Molecular Biology.

Dr. Casey is the founding Director of the Duke Center for Chemical Biology - an organization of Duke scientists dedicated to research and training in the application of fundamental chemical and physical principles to the study of biology and the basis of disease and therapies. The Center is dedicated to bringing together expertise from across the University, including the Schools of Medicine, Arts and Sciences, and Engineering, and it has established itself as a model for research in chemical biology and the translation of these findings into new research tools to interrogate biological processes and new therapeutics.

Proteomic Approaches for Drug Discovery

Jim Stephenson

Over the last 15 years, developments in the field of mass spectrometry have had a profound impact on the field of biology. For example, the automation of high resolution separation techniques combined with mass spectrometry is now standard operating procedure for the majority of pharmaceutical companies. Not only does mass spectrometry play a critical role in the quantitation of drug candidates and their metabolites, but also is central to understanding the basic mechanism of action of drug candidates at the protein level. Current techniques that interrogate the protein complement of a cell can produce datasets in excess of one million mass spectra per experiment. In the rational use of automated mass spectrometry-based protein identification methods, researchers must consider the rate of false positive and negative peptide identifications in large datasets. Here we report the first use of peptide isoelectric point combined with statistical methods that limit the false positive identification rate to <1%, while increasing the number of total identifications by limiting false negatives. The second element in the process determines whether the top-ranking peptide match is significantly different than other returned matches by comparing it with the mean value of these other matches. This presentation will describe the relevance of this methodology in the drug discovery field by emphasizing the importance of correct peptide and protein identifications on mechanistic studies. The approach has been successfully applied to filter large (up to 1.5 million spectra) datasets from complex samples, and allowed us to realize increases of 54% and 39% more peptide and protein identifications respectively.

James L. Stephenson, PhD
RTI International
Research Triangle Park, NC

Dr. Stephenson received his BS degree in biochemistry at East Carolina University in 1984. He was first employed at California Analytical Laboratories East, in Richmond, VA, as an analytical chemist, where he first became interested in mass spectrometry. Subsequently, he spent time as an applications chemist and field engineer in San Jose, CA, at Finnigan MAT (a division of Thermo Electron Corporation) in the field of mass spectrometry. He returned to graduate school at the University of Florida in Gainesville, FL, and received his PhD in analytical chemistry in 1995. His research focused on photodissociation of biological molecules in the quadrupole ion trap. While at the University of Florida, Dr. Stephenson was given a prestigious American Chemical Society Fellowship. Upon Graduation Dr. Stephenson took a postdoctoral fellowship for 2 years in the Laboratory of Dr. Scott McLuckey at Oak Ridge National Laboratory (ORNL). Dr. Stephenson then accepted a Research Scientist Position in the Organic and Biological Mass Spectrometry Research Group at ORNL, where his research focused on the areas of protein chemistry, instrumentation, and gas-phase ion chemistry. In November 2001, Dr. Stephenson accepted a position of Senior Program Director for Mass Spectrometry Research at RTI International. He has been actively involved in starting a research program in the field of proteomics. Dr. Stephenson has over 45 publications in refereed journals, has authored several book chapters, and has over 75 presentations (many of those invited) here in the early part of his career. He also has served on a variety of study sections for the National Institutes of Health (NIH) and as an ad-hoc reviewer for the National Science Foundation (NSF).

Health Status and Quality of Life Measurement Techniques

Moderator: Kathleen N. Lohr

Creation of Instrument Short Forms: Methods and Applications

Carla M. Bann, Cheryl D. Hill, and Valerie S.L. Williams

Given time and budget constraints, as well as the desire to reduce respondent burden, researchers are frequently tempted to develop an alternative form of a psychosocial scale that contains fewer items. However, in many cases, these short forms may not be suitable replacements for the long form. Some common pitfalls include relying on a single statistical method for item elimination/retention decisions, failing to consider content specifications, and not sufficiently evaluating the psychometric properties of the short form. This presentation will provide an overview of the development of instrument short forms while avoiding what critics refer to as the "sins" of short form development. We will summarize useful psychometric techniques from classical and modern test theory, including exploratory and confirmatory factor analysis and parametric item response modeling, and discuss their advantages and disadvantages. The development of the Motivation and Energy Inventory Short Form (MEI-SF), a health-related quality of life measure designed for patients with depression, is used to illustrate the development process and psychometric techniques. Future directions for short form development, such as multidimensional item response theory, causal indicator modeling approaches, and computerized adaptive assessment, are discussed.

Carla Bann, PhD
RTI International
Research Triangle Park, NC

Dr. Carla Bann received her PhD in quantitative psychology from the University of North Carolina at Chapel Hill. She is a Senior Research Psychometrician at RTI International with over 10 years of experience in the design and statistical analysis of questionnaires, particularly in the areas of health-related knowledge, quality of life, and informed decision-making. Dr. Bann has developed and psychometrically evaluated several instrument short forms, including the Diabetic Foot Ulcer Scale – Short Form (DFS-SF) and the reduced form of the National Science Foundation Factual Knowledge of Science scale.

Valerie Williams, PhD
RTI International
Research Triangle Park, NC

Dr. Valerie Williams has more than 15 years of experience applying psychometric and statistical methods to topics in psychological measurement. She has directed the psychometric evaluation of instruments related to educational achievement, health care, quality of life, and a variety of psychosocial constructs, using techniques from classical and modern test theory. Dr. Williams has created audio-assisted computer-adaptive tests and surveys and published and presented on topics related to measurement and quantitative psychology.

Development and Psychometric Evaluation of a Bipolar-Specific Functional Status Measure: A Case Study in Patient-Reported Questionnaire Development

Sheri Fehnel, Lori McLeod, and Meghan Wills

Bipolar Disorder (BPD) is a mental illness that is generally characterized by recurrent episodes of depression and mania. While there is a wide range of medications proven to alleviate acute symptoms, as well as to reduce the frequency of future depressive and manic episodes, each has a number of side effects and, like the disorder itself, may impair patients' ability to function. In addition to the direct effects on quality of life, functional impairment is a common reason cited by patients for sporadic medication use, which ultimately increases the frequency of acute episodes. The purpose of this study was to develop a sensitive, psychometrically sound patient-reported instrument to measure functionality of patients with BPD with the ultimate goal of facilitating comparisons among long-term treatment options.

Informed by consultations with key opinion leaders, literature review, and individual in-depth interviews with BPD patients, a draft questionnaire was developed to address eight domains (e.g., social functioning). The draft questionnaire was then tested and revised through iterative sets of cognitive interviews with additional patients. The resulting 33-item questionnaire addresses all constructs considered central to the functional status of patients with BPD. The psychometric validation of the new instrument is currently underway. In particular, we are collecting data from 600 bipolar patients across the country in an effort to establish the internal consistency, test-retest reliability, and validity of the new instrument.

Sheri E. Fehnel, PhD
RTI International
Research Triangle Park, NC

Dr. Sheri Fehnel is the Global Head of Patient-Reported Outcomes in RTI Health Solutions. Since joining the RTI staff in 1988, she has combined the study of clinical psychology and psychometrics with practical research and clinical experience. She specializes in the development and evaluation of questionnaires designed to measure quality of life, patient satisfaction, resource utilization, and other patient-reported outcomes. This work has involved a wide range of therapeutic areas including ITP, depression, attention-deficit disorder, bipolar disorder, insomnia, incontinence, oncology, cardiovascular disease, asthma, chronic obstructive pulmonary disease, sexual dysfunction, obesity, cystic fibrosis, chronic pain, and sexually transmitted diseases including herpes and HIV/AIDS. As part of the questionnaire-development process, Dr. Fehnel has moderated countless focus groups, conducted cognitive interviews with a wide variety of patient and professional populations, and assessed potential sources of measurement error through cognitive forms appraisal. She has also evaluated the psychometric properties of numerous survey and clinical instruments using techniques such as factor analysis, structural equations modeling, and item response theory. Dr. Fehnel received both her MA in clinical psychology, as well as her PhD in quantitative psychology from the University of North Carolina at Chapel Hill. She has presented her work at many professional conferences and has published in a number of peer-reviewed journals, including *Quality of Life Research*, *Medical Care*, and *Pharmacoeconomics*.

The NIH Roadmap and Dynamic Assessment of Quality of Life

Bryce Reeve

The benefits provided by modern measurement theory and informatics for improving health outcomes measurement have been recognized by the National Institutes of Health (NIH); several Institutes and Centers (ICs) have taken major steps to encourage development, application, and demonstration of these methods through its grants and contracts mechanisms. One project generating excitement is NIH's 5-year, $25 million interdisciplinary Roadmap Initiative to develop the Patient Reported Outcomes Measurement Information System (PROMIS). The project purpose is to build a public domain Web-based resource to measure key health symptoms (e.g., pain, fatigue) and health-related quality of life (HRQOL) domains (e.g., depression, social well-being) relevant to a variety of chronic diseases. PROMIS will administer individually tailored health outcomes questionnaires via secure platforms such as computers, the Internet, handheld devices, and telephones; collect outcomes data for research and improvements to the system; and provide instant health status reports tailored to patients, providers, and researchers.

Serving as a psychometrician and program director for the outcomes research branch of the National Cancer Institute, I will talk about the advantages of integrating modern measurement theory and computer technology to build computerized-adaptive testing (CAT)-based instruments for measuring health outcomes domains. I will also discuss the process for building CATs and some of the challenges we face in the PROMIS project. Concluding remarks will hope to demonstrate the need for the NIH-sponsored PROMIS system and its potential impact on the health outcomes research field.

Bryce Reeve, PhD
National Institutes of Health
Bethesda, MD

Dr. Bryce Reeve is a Psychometrician and Program Director at the National Cancer Institute (NCI), Division of Cancer Control and Population Sciences, Applied Research Program, Outcomes Research Branch. At NCI, his work is focused on the evaluation and development of instruments measuring patient-reported outcomes such as health-related quality of life, patient satisfaction, and economic burden. His goals are to integrate the tools of psychometrics into the field of health outcomes research to improve the measures of cancer patient reported outcomes.

Dr. Reeve serves as a NIH Science Officer on the Patient-Reported Outcomes Measurement Information System (PROMIS) Network to build a public domain Web-based resource to dynamically administer, collect, and report data on key health symptoms and quality of life domains relevant to a variety of chronic diseases. He serves as program director on a number of grants and contracts to support methods development in cancer outcomes research. In 2004, he organized an international conference on improving health outcomes measures using tools available from modern measurement theory and computer technology. Attended by over 230 members from government, academia, and industry, this conference sparked a lot of interest in the field and provided a foundation to explore the new arena of application of computerized-adaptive testing (CAT)-based assessment

Dr. Reeve received his PhD (2000) in quantitative psychology from the University of North Carolina at Chapel Hill. His training was in test theory and multivariate statistics with an emphasis on item response theory modeling.

Cost Effectiveness of Health Technologies

Moderator: Jerry Cromwell

Assessing Effectiveness of New Technology in Everyday Clinical Practice: Methodological Challenges and Potential Solutions

Sujha Subramanian

Randomized controlled trials (RCTs) are the current gold standard for assessing new technologies but may not reflect the "real-world" impacts due to restricted patient selection. Observational studies provide information on effectiveness in the real world setting but are potentially less reliable due to the lack of random assignment. The objective of this study is to evaluate the usefulness of RCTs and observational studies to assess real-world impacts. A systematic evaluation of studies assessing percutaneous coronary interventions (PCI), which includes stent placement and percutaneous transluminal coronary angioplasty (PTCA), was performed to address this objective. Overall, RCTs indicate that there is a 50% reduction is revascularization rates with the use of stents versus PTCA, but results from observation studies show only a marginal improvement. RCTs enrolled patients who are similar to the underlying population with coronary artery disease on demographics (age, sex, race) but differ in terms of clinical manifestation (comorbidities, disease severity), treatment delivery (physician expertise, patient compliance) and clinical setting (type of hospital, geographic location). Observational studies on PCI are confounded by selection bias, as stent patients are overall younger and healthier. Studies have attempted to control for this bias but the design of these observational studies can and should be improved with better data sources and methods. RCTs provide safety and efficacy data for initial adoption but high-quality observational studies are necessary to provide valuable information to foster evidence-based delivery of patient care.

Sujha Subramanian, PhD
RTI International
Waltham, MA

Dr. Sujha Subramanian, a Research Health Economist at RTI international, has extensive experience performing technology assessments utilizing large-scale database analysis, systematic reviews, outcome evaluations, cost-effectiveness studies, and retrospective cohort analysis. She has directed numerous studies to evaluate new technology including those involving pharmaceuticals, devices, and diagnostics. She has studied the outcomes and cost of stent placement versus angioplasty to compare restenosis rate and mortality in everyday clinical settings compared with outcomes reported in clinical trials. Dr. Subramanian is currently directing a study evaluating racial differences in outcomes among asthmatics treated with specific medications using Medicaid claims and is the principal investigator on an NCI-funded grant to study the outcomes and cost associated with duodenal and colonic stenting. She is currently the principal investigator on a study evaluating the effectiveness and cost associated with the National Breast and Cervical Cancer program directed by the Centers for Disease Control and Prevention. Dr. Subramanian is in the process of developing composite measures to evaluate the programs. In her previous role as health economist in the medical device industry, she participated in efforts to develop comparable measures to assess net benefits of early stage technologies. Dr. Subramanian has studied outcomes associated with cardiac care, cancer, pulmonary embolism, renal failure, and reproductive health. She has authored several peer-reviewed articles that have been published in journals including *Value in Health*, *Obstetrics and Gynecology*, *American Journal of Preventive Medicine*, *Journal of Gasteroenterology*, and *Journal of Vascular and Interventional Radiology*.

Estimating the Potential Cost-Effectiveness of a "Polypill" for Patients with Type 2 Diabetes

Thomas J. Hoerger and Katherine Hicks

A recently published report of a proposed "polypill" to prevent heart attacks and stroke may have important implications for reduction of cardiovascular disease (CVD) among persons with diabetes. The polypill would contain a statin, three blood pressure lowering drugs each at half standard dose, folic acid, and aspirin. The polypill is estimated to reduce heart attack by 88% and stroke by 80%. We examined potential benefits of the polypill in a diabetic population using a Markov lifetime model of diabetes progression and costs that RTI previously developed for the Centers for Disease Control and Prevention (CDC). We simulated a cohort of all males and females newly diagnosed with type 2 diabetes mellitus and followed the cohort through death. The control group received tight glycemic control, tight hypertension control as necessary, and cholesterol reduction as necessary. The intervention group received tight glycemic control and the polypill. The intervention has a cost-effectiveness ratio of $11,356 per quality-adjusted life year (QALY). Life years increased by 2.3 years. The lifetime incidence of stroke decreased from 16.9% to 9.5%, and the lifetime incidence of coronary heart disease (CHD) decreased from 36.4% to 8.9%. The analysis demonstrates how an existing cost-effectiveness model can be used to examine the potential benefits of a new treatment and identify the factors that are most likely to affect cost-effectiveness.

Thomas J. Hoerger, PhD
RTI International
Research Triangle Park, NC

Dr. Hoerger is Director of the RTI-UNC Center of Excellence in Health Promotion Economics, which was recently awarded a 3-year, $3 million grant from the Centers for Disease Control and Prevention (CDC) to study the economics of health promotion and disease prevention. Dr. Hoerger also serves as Co-Director of RTI's Health Economics and Financing Program. His research interests include health care markets, Medicare policy, health care reform, and cost-effectiveness analysis. For the CDC, he has served as Project Director for RTI's Economic Studies and Prevention Effectiveness Task Order contract, which has included 56 studies to date. Dr. Hoerger has directed many CDC-sponsored studies including the development of a lifetime disease progression model for type 2 diabetes, estimates of future diabetes prevalence, analyses of the costs of clinical laboratory regulations, evaluation of an intervention to reduce cardiovascular risk factors in women, and cost and cost-effectiveness analyses of vision loss. For the Agency for Healthcare Research and Quality (AHRQ), Dr. Hoerger has examined the cost-effectiveness of strategies for screening adults for type 2 diabetes and participated in an effort to perform systematic reviews of cost-effectiveness studies. He has also directed a series of Medicare studies for the Centers for Medicare & Medicaid Services (CMS). Dr. Hoerger has published widely in peer-reviewed journals, including the *Journal of Health Economics*, *Journal of the American Medical Association, Health Care Financing Review*, the *Journal of Risk and Uncertainty*, *Review of Economics and Statistics*, *American Journal of Cardiology*, *PharmacoEconomics*, *Medical Care*, *Diabetes Care*, *Medical Decision Making*, and *Annals of Internal Medicine*. Dr. Hoerger joined RTI in 1995.

Managed Care Barriers to the Diffusion of Cost Effective Technologies: How High Are They?

Jerry Cromwell

It is commonly agreed that rapid technical innovation and diffusion have been responsible for much of the growth in health care spending in the United States. Concern has also been raised about the medical necessity of many new devices and drugs—at least for some patients. High expectations exist for public and private managed care plans to reign in and rationalize the diffusion and utilization of new technologies. Discussions with device and drug manufacturers, however, indicate that managed care, alone, will not discourage future research and development (R&D) investments. An aging U.S. population and a burgeoning world market are only two factors that may be drowning out any depressing effects of managed care. Doubts among R&D strategists about the longevity of vigorous managed care—especially directed at the voting elderly—simply reinforce demographic and global trends. It is also debatable whether managed care administrators can "fine tune" denials and approvals of the most cost-effective technologies. Medicare rate setting, by contrast, appears to be a much more serious threat: no coverage, no market, no R&D. This paper considers the pitfalls of relying on "managed medicine" to modulate the development and adoption of costly new technologies. It then concludes with the proper role of competition and regulation and a complement to managed care.

Jerry Cromwell, PhD
RTI International
Waltham, MA

Jerry Cromwell, PhD, is a Senior Fellow in Health Economics at RTI International. He has over 30 years' experience conducting technical and evaluation studies of public and private payment systems for hospital and physician services. He has led several Medicare and Medicaid studies of hospital competition on the basis of new technologies as well as the diffusion of medical devices into the physician's office. He developed cost estimates for the Health Care Financing Administration (HCFA) of the Medicare prospective capital payment system in the early 1990s and analyzed differences in the availability of high-tech services between urban/rural, teaching/non-teaching, and large/small hospitals. He has conducted interviews with device and drug manufacturers on the long-run trends in technical innovation in the health sector and the potentially constraining impacts of managed care and public rate setting systems. He also directed the first comprehensive evaluation of HCFA's Centers of Excellence demonstration of a global inpatient payment for Medicare bypass surgery. Currently, he is leading the Centers for Medicare & Medicaid Services (CMS') Congressionally mandated study of the impacts of high-tech heart and orthopedic surgical hospitals on patient referral patterns and access to care in six communities nationwide. Dr. Cromwell has published extensively in health economics journals and testified before Congress on physician payment and Medicaid federal-state cost-sharing issues.

Aerosol Technology and Health

Moderator: David Ensor

Integration of Aerosol Exposure Technologies with Alterations of Asthma Severity and Potential Mitigation Steps

Nathan Rabinovitch

Personal monitoring has generally been considered to be impractical and pose an excessive burden, especially in school-age children. However, newly developed, small portable monitors that can measure respirable endotoxin exposure may be more acceptable than previous models. Utilizing this technology, we examined the relationship between personal exposure to ambient particulate and childhood asthma. For a spatially homogenous pollutant such as ambient particulate, concentration-dependant measurement error may occur despite high correlations between outdoor concentrations and personal exposures. In our studies, central ambient monitors underestimated pulmonary function effect sizes by 70% compared to estimates determined by personal exposures. We also examined the relationship between personal endotoxin exposure and asthma health effects; quantifying levels of endotoxin to which asthmatic children are exposed on a daily basis, examining how well stationary monitors estimate endotoxin exposures and determining whether furry pets are associated not only with dust concentrations but also with increased personal endotoxin exposures. In this way, a direct association between endotoxin exposure and disease severity in children with asthma could be documented.

Nathan Rabinovitch, MD
Assistant Professor
Department of Pediatrics – Allergy and Clinical Immunology
National Jewish Medical and Research Center
The Children's Hospital
Denver, CO

Nathan Rabinovitch, MD, is an Assistant Professor in the Department of Pediatrics – Allergy and Clinical Immunology at National Jewish Medical and Research Center. He is also an Assistant Professor of Pediatrics at The Children's Hospital in Denver.

Dr. Rabinovitch received his undergraduate degree from Yeshiva University in New York, and in 1989, he earned his Doctor of Medicine from McGill University School of Medicine in Montreal, Canada. His pediatric residency and board certification were completed in 1992 with the Albert Einstein College of Medicine, and his fellowship training was done here at National Jewish.

Dr. Rabinovitch is also certified by the American Board of Allergy and Immunology and is a member of the American Academy of Allergy Asthma and Immunology and the American College of Allergy and Immunology. He has been honored with awards and grants, is a member of several committees, is a current reviewer for the *Journal of Allergy and Clinical Immunology,* and has numerous medical publications, presentations and investigations credited to his name.

Dr. Rabinovitch's current research focuses on the role of environmental triggers in asthma. These focus on the effects of ambient air pollution, environmental tobacco smoke and bioaerosols on asthma severity in children with moderate to severe disease.

Quantification of Asthmatic Children's Exposure to Aerosol Size-Specific Endotoxin

Karin K. Foarde and Charles E. Rodes

RTI has supported a series of adult and children's research panel studies for governmental and private clients in the past 10 years to establish links between exposures to environmental contaminants and adverse health consequences. These efforts were facilitated at the outset by development of robust, particle size-specific miniature personal exposure sampling systems under internal research and development (IR&D) grants to the Center for Aerosol Technology (CAT) and a joint CAT/Microbiology Department (MD) IR&D to develop expanded, integrated bioaerosol capabilities. Complementary analytical technologies were subsequently developed that could be conducted on the very small sample collections inherently provided by battery-operated personal exposure samplers. These included extremely sensitive gravimetric analysis methodology developed within CAT, and more recently, new proprietary technology were devised in the MD to allow endotoxin and other biocontaminants analyses of personal exposure samples. Partnering these "enabling" exposure sampling and analysis tools with medical research specialists has advanced the classic health risk paradigm from simply characterizing media to linking all elements of the process from sources to health outcomes.

This talk describes selected aspects of the development processes for the children's personal exposure system, as well as the enhancements made in the associated endotoxin analytical methodology. A not-as-successful trial technology will be described that illustrates the difficulties in applying low burden technologies to childrens' studies. Spin-off supporting methodologies have also been developed along the way that have substantially enhanced our capabilities to study both adult exposures, and the seemingly unrelated area of Homeland Security.

Karin Foarde
RTI International
Research Triangle Park, NC

Karin Foarde is a Senior Research Microbiologist with over 25 years of experience, and is the Program Director of RTI's Microbiology Department. She designs, directs, and conducts applied and basic research in microbiology and aerobiology. Her research interests focus on bioterrorism-associated biological aerosols and the environmental causes of allergy and asthma. Her bioterrorism research experience includes the detection of, the decontamination of, and protection from biowarfare agents. The asthma/allergy work focuses on researching the biological contaminants isolated from the environment to identify environmental causes of illness and to recommend methods for preventing such biological contamination and its associated adverse health effects. These organisms include airborne allergens as well as pathogens.

Charles E. Rodes, PhD
RTI International
Research Triangle Park, NC

Dr. Rodes is a Senior Research Environmental Engineer in the Center for Aerosol Technology (CAT) at RTI International. His BS ChE degree is from Clemson University in 1966, MS ChE from NC State University in 1971, and his PhD in environmental engineering from UNC in 1992. He has over 36 years of experience planning, conducting, managing, and reporting research and development studies relating environmental exposure assessment and control to human health. Technical specialty areas include: personal exposure and human activity assessments for the general population, elderly adults, and children; and indoor air quality, microenvironmental, and size-specific, speciated aerosol sampling. Recent Homeland Security studies have focused on removal of particle and gas-phase toxics in Immune Buildings, and developing low-cost bioaerosol detectors.

He is a member of the numerous technical societies and currently serves as a peer reviewer for five journals including the *Journal of Exposure Analysis and Environmental Epidemiology*, and the *Journal of Aerosol Science*. He has over 50 peer journal publications, including three book chapters on exposure assessment and indoor air characterization. His presentation "Indoor Particles – Their Sources, Fate, and Contributions to Personal Exposures" prepared for the National Research Council (NRC) is posted on the NRC website.

The Growing Opportunities for Aerosol Delivery of Medicines

Michael T. Riebe

Of the many pharmaceutical delivery modes, inhaled and intranasal are among the fastest-growing. Partly, this growth is due to the increasing incidence of asthma and chronic obstructive pulmonary disease. It is also related to the recognition that treating these diseases locally vs. systemically can provide a superior benefit/risk ratio. Approval of inhaled systemic therapies, such as insulin for Type II diabetes, will be a major milestone and should open the gate for a flood of new products. Proteins and peptide therapeutics, the heart of the biotechnology revolution, are still mostly constrained to be delivered via injection. Inhalation delivery offers a realistic alternative. It is also common for small molecule organic drug candidates to be dropped due to poor water solubility and the correlated low oral bioavailability. In contrast, the best pulmonary medicines are designed to be very lipophilic in order to reduce systemic bioavailability. The compounds lost in drug discovery could offer great opportunities if evaluated for pulmonary delivery. The lung offers a huge surface area, coated with surfactant, with rapid access to the systemic circulation, no first-pass metabolism, and low protease activity. The many barriers to the development of inhaled and intranasal pharmaceutical products, as well as the enormous opportunities available, will be addressed in this presentation.

Mike Riebe, PhD
Director, Aerosols and Drug Delivery
RTI International
Research Triangle Park, NC

Dr. Riebe is Director of Aerosols and Drug Delivery at RTI International, a not-for-profit research institute in Research Triangle Park, North Carolina. He has been in this position since the beginning of 2004 and serves as a consultant to several industry leaders in the area of pharmaceutical aerosols and delivery system design, development, registration, and manufacturing. He is also undertaking research at RTI in inhaled delivery system development related to MDIs, DPIs, and vaccines.

He has served as Vice Chair and Chair of the AAPS Inhalation Technology Focus Group and is currently an Executive Committee member. Dr. Riebe is also a current member of the USP Aerosols Expert Committee.

Previously, he was Director in New Product Supply at GlaxoSmithKline, responsible for CMC aspects of all projects in the respiratory portfolio except DPIs. This position involved the coordination of product development and manufacturing activities related to the development, registration, and introduction of new respiratory products. From 1998 until 2000, he was the Director of Inhalation Product Development at Glaxo Wellcome Inc. Past accomplishments of this group include: Serevent™ Inhalation Aerosol and Diskus, Flovent™ Inhalation Aerosol and Diskhaler, and Ventolin™ Inhalation Aerosol. From 1987 to 1990, he was a member of the Chemical Research Division at Polaroid Corporation in Cambridge, Massachusetts.

He received his BS in chemistry from Kalamazoo College in 1981 and a PhD in analytical chemistry from the University of Wisconsin at Madison in 1987.

Information Technology in the Developing World

Moderator: Derick Brinkerhoff

Back to the Future: Environmental Technologies to Improve Child Health in Developing Countries

Gene Brantly and Myles Elledge

Every year, over 10 million children under the age of five die in developing countries. Almost half of these deaths are attributed to pneumonia, diarrheal diseases, and malaria -- diseases that result, at least in part, from the environmental conditions in which poor children and their families live. Technologies for preventing and curing these diseases have long been known and proven effective, but limited funding, weak systems, and conscious policy choices have blocked efforts to expand access to them. Recent increases in funding for international public health programs and an international consensus regarding Millenium Development Goals bring new hope for progress, but also highlight the urgent need to focus on system and policy issues.

Myles F. Elledge
RTI International
Research Triangle Park, NC

Myles F. Elledge is a Program Director in the International Development Group at RTI International. Trained in international political economy, he has experience in public finance and management assessment, and sector and program evaluation. Over the last 15 years, his work has focused on national-level policy analysis and in supporting improved social infrastructure planning and service delivery at the subnational level across 17 countries in Asia and Eastern Europe. Mr. Elledge holds a master's degree in international economic and social development from the University of Pittsburgh (1988), and a BA degree in Third World studies from the University of the South (1985).

Zambia Electronic Perinatal Record System: An Archetype of Computer-based Health Information Systems in Developing Countries

Gordon M. Cressman and Godfrey Sikipa

The Zambian Electronic Perinatal Record System (ZEPRS) is an electronic medical record (EMR) system designed for public obstetric clinics and the University Teaching Hospital (UTH) in Lusaka. ZEPRS is built using open-source components and leading-edge Web software and database architecture. Medical personnel in facilities access the ZEPRS application through a Web browser over the ZEPRS wireless network. The ZEPRS wireless network connects 23 participating clinics, the UTH, Lusaka Urban Health District, the Ministry of Health, and the CIDRZ Data Center. The ZEPRS Web-based electronic referral system, electronic-first EMR, and municipal wireless network are leading-edge systems in sub-Saharan Africa.

ZEPRS provides the foundation for ARTworks™, a system for managing antiretroviral therapy (ART) for HIV/AIDS patients. ARTworks™ is currently being used in eight clinics and the UTH in Lusaka and provides reports meeting performance monitoring requirements of the President's Emergency Program For AIDS Relief (PEPFAR). Work on a version of ARTworks™ for handheld computers also is under way. ARTworks™ can store patient records in a local database or in a centralized shared network database. Work is under way to add the capability to store patient data securely on individual smart cards,

Gordon M. Cressman, MS
RTI International
Research Triangle Park, NC

Mr. Cressman is Director of the Information and Communication Technologies (ICT) program for the RTI's International Development Group. He currently leads a team applying sustainable information and communications technologies to improving living standards in developing countries. He has more than 26 years of experience in information and communications technologies, 21 of them as a professional in international development. He is experienced in every phase of ICT systems design and implementation, including assessment, strategic planning, operational planning, systems integration, procurement, installation, training, and operation. His ICT applications experience spans health, education, and governance. He has helped organizations in 13 developing countries to improve their ICT systems through sustainable strategies sensitive to local constraints.

Godfrey Sikipa, MD
RTI International
Research Triangle Park, NC

Dr. Godfrey Sikipa is a public health specialist with over 25 years' experience in both clinical practice and preventive public health. Dr. Sikipa worked in various capacities in Zimbabwe, starting as Hospital Medical Officer in several departments including internal medicine, surgery, pediatrics, and obstetrics and gynecology. He then worked as a Hospital Superintendent in charge of a 340-bed general hospital, where his duties included both patient care and administration and management. He rose through the ranks of the Ministry of Health to become Permanent Secretary of the Ministry of Health. Dr. Sikipa left Zimbabwe in 1992 to join Family Health International (FHI) as Regional Director for Africa on the USAID-funded AIDS Control and Prevention (AIDSCAP) project, based initially in Arlington, Virginia; then Nairobi, Kenya. In 1999 he joined the United Nations Joint Program on HIV/AIDS (UNAIDS) as Sub-regional Coordinator for East and Southern Africa. He joined Research Triangle Institute (RTI) International as Senior HIV/AIDS and Infectious Diseases Specialist. He is based at the RTI headquarters office in North Carolina. He currently serves on the Technical Review Panel of the Global Fund to fight AIDS, Tuberculosis and Malaria. Dr. Sikipa has advised governments, nongovernmental organizations, and private companies on various aspects of HIV/AIDS prevention, care and impact mitigation.

Quantifying Perceived Benefits of Improved Health Care

Moderator: Brett Hauber

Stated Preference: State of the Art for Measuring Patient and Physician Treatment Preferences

Ranjani Manjunath and Semra Ozdemir

Stated preference (SP) surveys are used to assess the preferences of patients and physicians to inform healthcare decision-making. Conjoint analysis (CA), an SP method, is the conceptually correct and most scientifically appropriate method for quantifying individual preferences. CA has been widely used and tested for validity and reliability in marketing, transportation, and environmental economics. Its use in health economics is recent, but has been increasing. CA is based on rigorous utility-theoretic principles and depends on ordinal utility, which is nonlinear in time and allows for diminishing marginal utility in quantity-quality tradeoff. CA accounts for both 'process' and 'outcome' factors that contribute to utility, and allow subjects to think about trade-offs between various products realistically. It also permits estimating trade-offs among attributes, including both time and money, and allows for the valuation of both the intervention and its individual attributes.

SP methods can be applied to various health-related drug treatments or programs to aid in choice-based decision-making. One application involves a diabetes primary prevention program where individuals at risk for diabetes were asked to choose between hypothetical programs to reduce their risk of developing diabetes and the option not to participate in either program. The prevention programs were described using attributes, including requirements for diet, exercise, counseling, medication, weight-loss goal, the level of risk reduction, and the cost of the program. This study suggests that participation in diabetes risk-reduction interventions is more likely for programs that include effective weight-loss goals and promise higher risk reductions. Stated preferences in this study indicate a possible need for improved risk communication and innovative interventions that reduce physical and financial impediments to risk-reduction activities

Ranjani Manjunath, MSPH
GlaxoSmithKline (GSK)
Research Triangle Park, NC

Ms. Ranjani Manjunath is a health outcomes scientist with GlaxoSmithKline (GSK). She obtained a MSPH in health policy and administration from the University of North Carolina at Chapel Hill. Within her health outcomes experience, she has conducted large survey development, data collection, and database analysis projects in the therapeutic areas of asthma, diabetes, HIV/AIDS, epilepsy, mental illness, and reproductive health. She has led patient-reported outcomes instrument development activities, conducted in-depth individual and cognitive pretest interviews with patients and physicians, coordinated expert advisory board meetings, and contributed to several manuscripts and meeting presentations. She has also developed various economic models to determine economic outcomes using methods such as, stated and revealed preference, cost-effectiveness (using decision-tree analysis), cost-utility, and cost-consequence. In addition to her health outcomes experience, she has 5 years of experience in basic science and clinical research that offer comprehensive knowledge in biochemical molecular signaling and genetics, teratogenesis and teratogen-induced birth defects, gross anatomy, and histology.

Semra Ozdemir, MS, BS
RTI International
Research Triangle Park, NC

Semra Ozdemir is a health economist with RTI Health Solutions. She has worked on discrete choice experiments, particularly on conjoint analysis. She has assisted in questionnaire development in the stated preference setting, survey design, and data management. Ms. Ozdemir worked at the University of Maine, where she investigated public preferences for purchasing conservation easements to farmland, and Maine dairy farmers' decision to exit from the market. Ms. Ozdemir has experience with a number of statistical programming languages, including SAS, Stata, and Limdep.

Comparing Apples to Oranges: Quality-Adjusted Life Years (QALYs), Health-Years Equivalents, Willingness to Pay, and Willingness to Wait

Reed Johnson and Brett Hauber

While quality-adjusted life years (QALYs) provide a simple, intuitive method for incorporating quality-of-life effects in economic analyses of medical interventions, reducing complex relationships among dynamic health states to a single cardinal index requires several well-known restrictive assumptions. Using standard-gamble (SG) or time-tradeoff (TTO) measures of quality-adjusted life year (QALY) utility weights requires stronger assumptions than those generally imposed in ordinal-utility applications in other areas of applied economics. These strong and generally unrealistic assumptions effectively break the link between SG and TTO utilities and utility-theoretic preferences, and undermine the validity of quality-adjusted life year QALYs as welfare measures.

This presentation derives general "super QALYs" (sQALYs) from nonlinear, ordinal utility functions that incorporate wealth and nonhealth utility variables, as well as time in specific health states. These generalized SQALYs preserve all available information about heterogeneous individual preferences and thus are valid measures of individual welfare changes. SQALYs can incorporate patient satisfaction related to nonhealth features of health-care interventions and other utility-relevant factors for both acute and chronic health outcomes. We show how time-equivalence measures relate to money-equivalence measures derived from the same preference structures. When derived from consistent utility-theoretic preference relations, squality-adjusted life year SQALYs, willingness to pay (WTP), and willingness to wait (WTW) represent alternative and equivalent rescaling of the same preference information.

Although nonlinear, ordinal utility functions sacrifice the simplicity of constant QALY weights and linearity over time, in many cases improved validity justifies the increased analytical effort. Furthermore, obtaining valid estimates of time-equivalent and money-equivalent welfare measures requires no new empirical methods. Such estimates are readily obtainable from properly designed stated-preference surveys.

Brett Hauber, PhD, MA
RTI International
Doylestown, PA

Dr. Hauber is the Director of the Benefits Valuation Group at RTI Health Solutions. He has over 10 years of academic, research, and government experience in health and environmental economics. His primary area of specialization is discrete choice analysis of revealed- and stated-preference data of consumer demand. He also has extensive experience in conducting health economic studies based on disease progression models. In most projects, he applies advanced statistical techniques to the analysis of discrete choice, epidemiologic, and clinical trial data. His most recent work has included conjoint studies of patient and physician preferences for diabetes treatments and chemotherapies, the development of disease progression models, and studies of the theoretical and empirical relationships among various health utility measures. In addition, he has focused on communicating the value of theoretically sound health economics to decision-makers. Dr. Hauber's research has been published in *Pharmacoeconomics*, *Clinical Therapeutics*, *ISPOR News*, *Land Economics*, and the *Journal of the American Agricultural Association*.

A Comparison of Families' Willingness to Pay for Vaccines in Developing Countries

Joe Cook

The Diseases of the Most Impoverished Program (DOMI), administered by the International Vaccine Institute, works to accelerate the development and introduction of new generation of vaccines against cholera, typhoid fever, and shigellosis. This presentation will focus on one aspect of DOMI's research agenda: measuring private demand and willingness-to-pay for cholera and typhoid vaccines in several developing countries in Asia. In particular, it will present results from a conjoint study conducted in Hue, Vietnam, in 2003, and compare them to results from a companion contingent valuation study.

Joe Cook, MS, BS
University of North Carolina at Chapel Hill
Chapel Hill, NC

Joe Cook is currently a doctoral candidate in the Department of Environmental Sciences and Engineering at UNC's School of Public Health. He received his BS from Cornell University in 1996 and his MS from UNC in 2004. He has worked as a research assistant at AEMS, an environmental consulting firm, and at Resources for the Future, a nonprofit environmental and resource economics research institute. His most recent work has focused on estimating private demand for vaccines against cholera and typhoid fever in Hue, Vietnam, and Kolkata, India. His other research interests include water and sanitation policy in developing nations, the economics of antibiotic resistance, and the use of economic experiments to measure risk aversion.

Technologies to Inform Patients on Health Quality, Costs, and Access

Moderator: Lauren McCormack

Educating and Empowering Chronic Disease Patients Using Web Technology

Michael Trisolini

Research has shown that care for those with chronic conditions should be patient-centered and collaborative, and requires effective communication between caregivers and patients. Patients who are more informed, empowered, and activated are expected to have better outcomes. They are also more likely to be involved in decisions about planning and treating their illness**.** Chronically ill patients and their families have particular needs for information and education about their conditions so that they can effectively self-manage their disease.

This presentation focuses on the role of the Internet in providing information to people with chronic kidney disease. Health-related websites for patients need to be carefully designed and pre-tested, and require ongoing improvements due to common problems of poor organization, overly technical language and content, and challenging navigation. This presentation also describes an RTI project that examined the use of the Internet to provide information to patients and their families to enhance self-management capabilities. Specifically, we discuss the Dialysis Facility Compare (DFC) website, that was developed by the Centers for Medicare & Medicaid Services (CMS) for people with chronic kidney disease and their families.

The RTI team conducted qualitative interviews and focus groups with 140 chronic kidney disease patients and family members and 130 renal care professionals as part of a comprehensive evaluation and revision of the DFC website. We conducted a series of 19 focus groups, 13 triads (small focus groups), and 56 individual interviews in four regions of the country. Based on these interviews, we developed recommendations for enhancing the DFC website in a number of ways to promote patient activation and involvement, and we are currently working with CMS staff to implement those changes. For future efforts, we recommend further exploring applications of the unique features of the Internet, such as its different dimensions of interactivity, and more targeted application of behavioral change theories for website design.

Michael Trisolini, PhD, MBA
RTI International
Waltham, MA

Michael Trisolini, PhD, MBA, is a Senior Researcher in the Program on Health Care Quality and Outcomes at RTI International. He has over 20 years of experience in health services research and management. Dr. Trisolini has conducted studies on quality, access, and cost issues for people with chronic diseases, hospitals, and integrated delivery systems, substance abuse treatment services, and primary health care programs. He has led projects utilizing both qualitative and quantitative research methodologies. He has conducted focus groups and interviews with patients, family members, physicians, and a range of other health care professionals. He has led case study research on health program development in the United States and overseas. Dr. Trisolini has conducted sophisticated statistical analysis using econometrics and structural equation modeling to study health-related quality of life, factors affecting employment and exercise status for chronically ill patients, insurance status of minority groups, and hospital utilization. He has extensive experience in analysis of both patient survey data and Medicare claims. Dr. Trisolini has developed demonstration projects to improve efficiency and quality of Medicare services. He has conducted evaluations of disease management programs for end-stage renal disease, family planning programs, and international health planning efforts.

In health care management, Dr. Trisolini has conducted strategic planning for primary care organizations and hospitals, developed financial management systems for clinical programs and hospitals, designed and taught management training programs for health care professionals, and developed information systems for health planning programs, clinical programs, and hospitals.

Dr. Trisolini received his PhD from the Heller Graduate School for Social Policy and Management at Brandeis University. He received his MBA from Harvard Business School.

IT and Safe Practices: The Role of Technology in Patient Safety

Lucy Savitz

Federal agencies supported by Congressional legislation have moved to drive the upgrade and expansion of the information technology (IT) architecture in health care delivery. This has culminated in the naming of Dr. David Brailor as the National Coordinator for Health Information Technology in the U.S. Department of Health and Human Services.

Review of the reported evidence for IT-based safe practices together with a summary of policy initiatives supporting IT development for health care will be presented. This background will set the stage for a case study report. The case study reports on the electronic health record and safe practice enhancements implemented by our IDSRN partner—Providence Health System. Specifically, results from two studies focusing on the problem of medication information transfer will be presented. Improvement in safety is ascertained via a pre-post-FMEA analysis. Discussion of research findings focus on the integral and inseparable consideration of human factors in IT adoption and institutionalization.

Lucy Savitz, PhD, MBA
RTI International
Research Triangle Park, NC

Dr. Lucy Savitz holds a PhD from the Department of Health Policy and Administration at the University of North Carolina and an MBA from the University of Denver. With more than 18 years' experience in health care delivery and health services research, she has worked as a financial planner at UNC Health Care, a researcher at the Cecil G. Sheps Center for Health Services Research, as a faculty member at the UNC School of Public Health, and now as a Senior Health Services Researcher at RTI in the Health Care Quality and Outcomes Program. Prior to relocating to North Carolina, Dr. Savitz served as an economist for the Colorado Legislative Council. Most recently, at RTI, Dr. Savitz directs the Agency for Healthcare Research and Quality (AHRQ)-funded master task order, *Accelerating the Cycle of Research in Integrated Delivery Systems,* and has led several task orders including *Assessing the Information Technology Infrastructure in IDSs, Validating AHRQ's Patient Safety Indicators,* and *Estimating Risk Reduction & Cost of Enhancing Medication Information Transfer Across Patient Care Settings.* Her research expertise in evaluating the implementation of clinical process innovations, collaborative research, and translation of research into practice have been primarily funded by the AHRQ and Centers for Disease Control and Prevention (CDC). Dr. Savitz has been acknowledged as an Examiner for the 2001 and 2002 Malcolm Baldrige National Quality Program, administered by the National Institute for Standards and Technology in the U.S. Department of Commerce and the American Society for Quality. She is also a Fellow in the Intermountain Health Care Quality Institute and a Research Fellow at the Cecil G. Sheps Center for Health Services Research. She taught the core Strategic Management Course in HPAA for 7 years and currently guest lectures there as well as teaches a module in the Centers for Disease Control and Prevention (CDC) Management Academy, which is a jointly sponsored training initiative between the Schools of Public Health and Business at UNC.

The Light and Dark Sides of the Internet: Health and Risk Promoting Websites

Rebecca J. Cline

This presentation argues the value of understanding the Internet as a health communication system. Conceptualizing the Internet as a "communication system" rather than an "information system" (1) highlights the power of the Internet's social influence and communication characteristics, (2) reveals the limitations of previous research regarding the Internet's role in health, health care, and health promotion, and (3) makes evident risk-promoting functions of the Internet, a phenomenon virtually invisible in present interactive health communication research. Increasingly, consumers engage in health information seeking via the Internet. More than 70,000 websites disseminate health information; an estimated 90 to 110 million people seek health information online, with likely consequences for the health care system. The Internet offers widespread access to health information but access is inequitable; increasingly, critics question the quality of online health information; and meager information-evaluation skills add to consumers' vulnerability. Further, critics argue, with only limited research, about how the Internet influences health care interaction. Future research needs to address the Internet as part of the larger health communication system and take advantage of incorporating extant communication concepts. This presentation (1) applies premises of health communication to the Internet, (2) considers the implications of viewing the Internet as a communication system versus an information-dissemination mechanism (including the failure of the "information" perspective to account for the "dark side" of the Internet's health-related functions), (3) identifies and illustrates the array of risk-promoting functions of the Internet, and (4) encourages both interpersonal and mass communication concepts as open avenues for investigating and understanding the health-related influence of the Internet.

Rebecca J. Cline, PhD
Barbara Ann Karmanos Cancer Institute
Wayne State University School of Medicine
Detroit, MI

Rebecca J. Cline (PhD, The Pennsylvania State University) is a Senior Scientist in Communication and Behavioral Oncology at the Barbara Ann Karmanos Cancer Institute, and Associate Professor of Family Medicine in the Wayne State University School of Medicine, Detroit, MI. Dr. Cline's recent research focuses on the role of interpersonal communication in health. Her recent and ongoing research includes investigating: (1) macro-level factors that may influence the physician-patient relationship, including the Internet (cancer patients' use of the Internet; general consumer health information-seeking on the Internet; the "dark side" of the Internet) and direct-to-consumer advertising of prescription drugs; (2) parent-child interaction during painful pediatric oncology procedures; (3) interpersonal communication and HIV/AIDS, including HIV prevention, communication with people with HIV disease, and gender issues associated with communicating about HIV/AIDS. Currently Dr. Cline serves as the Liaison from the Health Communication Working Group of the American Public Health Association to the Health Communication Divisions of the International Communication Association (ICA) and the National Communication Association (NCA). She has served as Chair of the Health Communication Divisions of ICA as well as NCA and is recognized as a leader in developing health communication curricula within the communication discipline. Dr. Cline brings to this program 20 years of experience as a scholar-teacher in health communication. Dr. Cline's experience includes authorship of more than 50 research articles, book chapters, and technical reports and more than 130 presentations to professional organizations.

New Technologies for Health Measurement

Moderator: James Chromy

New CASIC Technologies for Collecting Health Data

Jay Levinsohn and Rita Thissen

In the field of research computing, technological advances regularly appear on the horizon, open new avenues for acquiring information, and either prove useful or fade from view. The most visible advances are to hardware, but improvements to software, programming techniques, and data communication channels present opportunities as well. This presentation offers a glimpse of how current RTI projects use web systems, automation, voice capture, 24/7 access, mobile computers, and emerging technologies to support research needs. A quick look forward reveals additional developments, such as wireless devices, informatics, open source libraries and smart agents, which may prove valuable for future projects. Some items, such as wearable wireless computing devices that will allow real-time monitoring and interaction with subjects, would bring data collection to levels we have not yet been able to achieve. RTI has years of experience evaluating and deploying CASIC technologies for the social sciences, expertise we now apply to health research. Whether a study seeks to understand the extent of a health-related condition, to monitor the behavior of at-risk populations, or to enable analysis and communication of health data, success hinges on the selection of appropriate technological support.

Jay Levinsohn, PhD
RTI International
Research Triangle Park, NC

Dr. Jay Levinsohn is the Manager for Technology Issues in RTI's Research Computing Division. He is a graduate of the University of North Carolina's L. L. Thurstone Psychometric Laboratory where he received a PhD with a minor in computer science in 1975. He has been at RTI since 1974 and has been involved in applying computing technology to data collection activities throughout that time. He is currently involved in developing systems for handheld computers to collect information is situations that require a mobile computing platform.

Rita Thissen
RTI International
Research Triangle Park, NC

Ms. Rita Thissen is a Senior Research Programmer/Analyst in the Research Computing Division of RTI. She has a background in both chemistry and computer science, and has worked with clinical trials, economic, public policy and survey data systems. Currently she coordinates software development and support for several survey research projects and serves as one of the computer-assisted telephone interview (CATI) system administrators for RTI's call centers.

New Technologies for International Clinical Trials

Tyler Hartwell

RTI is involved in serving as the Data Coordinating Center for several National Institutes of Health international health studies that involve providing each study with statistical leadership, data collection and management, materials development, study logistics and communication, training, and quality control. This presentation will describe some of the issues involved in collecting, managing, transmitting, processing, and reporting data collected for these studies. Issues discussed will include building and maintaining local infrastructure, developing a reliable communications system, and addressing requirements for data security and integrity. Examples will be presented of systems developed for studies in Kenya, the Democratic Republic of the Congo, and several countries in South America.

Tyler D. Hartwell, PhD
RTI International
Research Triangle Park, NC

Tyler D. Hartwell, PhD, is a Senior Statistician and RTI's Program Director for Multisite Studies. He is a member and fellow of the American Statistical Association (ASA) and past president of the North Carolina Chapter of ASA. Dr. Hartwell has over 30 years of experience in multisite studies and has served as Principal or Co-Principal Investigator on numerous large-scale studies applying a variety of statistical methods to a wide field of research areas. He has published widely in several research journals.

Biospecimen Collection in Epidemiologic Studies: Conventional Methods and Technology-driven Advances

Danny Ringer and Craig A. Hill

In the conduct of current epidemiologic studies, the collection and management of biospecimens has become an increasingly common and important research tool. The ability to collect and ship biospecimens around the world, allows today's investigator to readily combine traditional epidemiologic methods with state-of-the-art laboratory techniques. Laboratory results derived from specimens tested by traditional research assays as well as recently developed molecular based-methods not only help scientists to better understand the etiology of diseases, but also evaluate potential biomarkers that may prove helpful in early disease diagnosis and response to treatment. Moreover, advances within the field of molecular biology, specifically genomics and proteomics, are changing the ways in which collection methods were once performed. Over the past decade, studies with a specimen component (blood, urine, tissue, etc.) have not only been collected with conventional clinic-based methods by trained medical personnel but also use the increasingly popular self-administered in-home methods such as fingerstick for dried blood spots (DBS) and noninvasive oral techniques for sublingual epithelial cells, commonly referred to as "buccal cells." The latter two methods commonly include the use of a "Guthrie" card which is lightweight and compact for both transport and storage, requires little or no processing and can be pretreated to retard bacterial growth and inhibit damaging nuclease activity. No matter what the method of collection is, special attention and rigorous adherence must still be paid to initial study design, and development of study protocols to correctly collect, process, store, ship, and test specimens. Specific issues related to the stability of analytes, correct anticoagulant, appropriate packaging materials, and shipping methods must be well thought out in advance prior to study start-up. In addition, studies that include long-term banked specimens will also need suitable storage facilities, equipped with monitoring systems, and special software to monitor facility operations and full service inventory systems to store and track specimens, as well as merging analytical and demographic data with sample histories.

Tim Wilcosky, PhD
RTI International
Research Triangle Park, NC

Dr. Tim Wilcosky, a Senior Epidemiologist in the Survey Research Division's Environmental Health and Epidemiology Program, has more than 25 years of experience as an epidemiologist in a variety of research areas, including cancer, cardiovascular disease, tuberculosis, HIV infection, environmental epidemiology, and clinical trials. While on the faculty at the University of North Carolina Department of Epidemiology, he was an editor and contributor for the first book on biological markers written for epidemiologists. Dr. Wilcosky is currently the Principal Investigator for a National Cancer Institute grant concerning agricultural pesticide exposures, the Co-PI for a National Institute of Environmental Health Sciences grant investigating the effects of perfluorooctyl compound exposures on male fertility, and the PI for a National Institute of Child Health and Human Development contract investigating the impact of environmental chemical exposures on the ability of couples to conceive a child.

Economic Evaluations of Environmental, Food Safety, and Medical Testing Technologies

Moderator: George Van Houtven

Technologies and Costs for Reducing the Risks of Transmitting Bovine Spongiform Encephalopathy (BSE) in Cattle Slaughter Plants

Mary Muth

Scientific and epidemiological studies have linked variant Creutzfeldt-Jakob Disease (vCJD), a chronic and fatal neurodegenerative disease that affects humans, to the consumption of beef products contaminated with the BSE agent. In response to the discovery of a cow infected with BSE in Canada in May 2003 and in the United States in December 2003, USDA's Food Safety and Inspection Service proposed regulations to reduce the risks of human illnesses that might arise from BSE in cattle. To support the economic analysis of the proposed regulations, we identified the technologies and processes used by cattle slaughter plants to comply with the regulations. We then developed estimates of the additional operating costs associated with these technologies and processes, and modeled the resulting market level economic effects.

Mary Muth, PhD
RTI International
Research Triangle Park, NC

Dr. Muth is Program Director of RTI's Food and Agricultural Policy Research Program and manages projects to provide support for and analyze the economic impacts of food safety, nutrition, and environmental policies and regulations. She specializes in applications of industrial organization, microeconomics, applied welfare analysis, and econometrics in evaluating policy and providing information for policy development. These applications have included meat and poultry slaughtering and processing, food processing, vegetable oils and meals, oysters, dietary supplements, bioengineered foods, and food labeling. She also specializes in developing electronic models and databases to support economic impact analyses of regulations. Before joining RTI, she conducted analyses of the structure of the beef packing industry and of the effects of the honey support program. Dr. Muth has presented her work at the annual meetings of the Allied Social Science Associations, the American Agricultural Economics Association (AAEA), the Food Distribution Research Society, and the Southern Agricultural Economics Association. She has published papers in the *Journal of Law and Economics*, the *American Journal of Agricultural Economics,* the *Journal of Agricultural and Resource Economics*, the *Agricultural and Resource Economics Review*, the *Drug Information Journal*, the *Journal of Agricultural and Food Industrial Organization*, *AgBioForum*, and *Choices*. She has also served as referee for several journals, as session organizer and moderator at the AAEA meetings, and as member-at-large for the AAEA Food Safety and Nutrition Section. Dr. Muth is an adjunct assistant professor in the Department of Agricultural and Resource Economics at North Carolina State University.

An Assessment of Avoidable National Health Care Costs through Improved Calibration Techniques for Medical Testing Equipment

Michael Gallaher

Errors in medical testing are potentially significant contributors to the high aggregate costs of heath care in the United States. By promoting improved testing methodologies, the National Institute of Standards and Technology (NIST) can help to reduce these costs. This case study, which focuses on testing methods for blood calcium levels, was performed for NIST by RTI International in cooperation with the Mayo Clinic. The researchers estimate that, for the approximately 3.5 million patients receiving screening serum calcium tests annually, systematic biases in testing equipment calibration create potential economic impacts ranging from $60 million to $199 million per year.

Michael Gallaher, PhD
RTI International
Research Triangle Park, NC

Dr. Gallaher is the director of RTI's Technology, Energy, and the Environment Program and has over 10 years of experience leading projects for NIST, the U.S. Environmental Protection Agency (EPA), and other federal agencies modeling the economic impact of new technologies. Dr. Gallaher specializes in developing baseline/counterfactual scenarios from which incremental costs and benefits can be measured and has conducted both retrospective and prospective technology assessments. Most of the projects he has led have involved modeling the adoption of new technologies and assessing the barriers to adoption. Dr. Gallaher has led over 30 economic impact assessments for agencies such as NIST, EPA, National Science Foundation (NSF), and National Telecommunications and Information Administration (NTIA), assessing the implications of technology adoption in the automotive, aerospace, computer hardware and software, chemical, iron and steel, and construction industries. Dr. Gallaher has led the review and redesign of national establishment-level surveys for NSF and EPA and has developed and implemented a wide range of survey methods, including in-person, telephone, mail, and Internet-based surveys. Dr. Gallaher has made numerous presentations at professional conferences and to federal committees and industry associations, and has provided economic analysis support for Federal Advisory Committee Act (FACA) activities.

A Health Benefits Assessment Model for Mercury Emissions Control Technologies

George Van Houtven

RTI is assisting the U.S. Environmental Protection Agency (EPA) in developing methods to assess the nationwide health benefits associated with alternative mercury emissions control approaches for coal-fired power plants. One of the main concerns associated with mercury exposures are developmental effects in prenatally exposed children. Therefore, the specific objective of this project is to estimate prenatal exposures to children due to mothers' consumption of noncommercial freshwater fish. By merging national data on fish tissue samples, fishing behaviors, watershed characteristics, and demographic characteristics, RTI has developed two general approaches for estimating numbers of exposed individuals and their corresponding mercury ingestion levels.

George Van Houtven, PhD
RTI International
Research Triangle Park, NC

Dr. Van Houtven is Director of RTI's Economics of Environment, Health, and Development Program and has over 10 years of project management experience. He specializes in the measurement of environmental, health, and natural resource values and the application of these measures to evaluate environmental and risk management policies. He has extensive experience in the implementation of preference elicitation methods, including the design of survey instruments and the econometric analysis of stated preference data. He has also coordinated several interdisciplinary studies that link environmental and economic models and that apply benefit transfer approaches to support cost-benefit analyses of environmental regulations. In addition, he has conducted research to examine the effectiveness of unit-based pricing policies for solid waste management, and he has employed econometric techniques to assess the implicit role of cost-benefit factors in environmental regulatory decision-making. Dr. Van Houtven is a member of the American Economic Association and the Association of Environmental and Natural Resource Economists. He has published in the *Journal of Environmental Economics and Management*, the *RAND Journal of Economics*, *Land Economics*, *Environmental and Natural Resource Economics*, *Applied Economics, Risk Analysis, Economics Letters, Vaccine,* and *Public Finance Review.* Previously, Dr. Van Houtven was an assistant professor of economics at East Carolina University where he taught courses in microeconomics and environmental economics.

Posters

Is Less Intensive Care Really Cost Effective? Understanding Common Biases in the Economic Evaluation of Substance Abuse Treatment

Bray, J.W.[1], Harris, K.M.[2], Zarkin, G.A.[1], and Mitra, D.[1]

Several recent cost-effectiveness studies show that less intensive modalities of substance abuse care, such as outpatient (OP) care, are less expensive and at least as effective as more intensive modalities, such as inpatient (IP) care. These findings unambiguously suggest that all patients should be sent to OP care rather than to IP care. Using simulation methods, we show that this push towards OP care may be ill advised because of a failure to consider two key aspects of substance abuse treatment. First, individuals respond differentially to the intensity of treatment depending on the severity of their substance abuse problem. IP care has a different effect than OP care for the same individual, and the same type of care will have different effects for different individuals. Second, treatment assignment is nonrandom. Treatment providers attempt to assign individuals to the type of care that yields the largest improvement in health, creating the potential for selection bias in observational studies. We find that common analysis methods often overstate the benefits of OP care relative to IP care when these two aspects apply. Because OP care is less expensive than IP care, this effect biases cost-effectiveness conclusions in favor of OP care. The resulting policy implication is to route all patients to OP care with the expectation that both health improvements and cost savings will occur. Based on our simulations, however, health outcomes are unexpectedly worse under this policy because IP clients get less health benefit out of OP care than do those patients observed in OP care. Our results demonstrate that policies limiting the availability of IP substance abuse care may have unexpected negative consequences.

[1]RTI International
[2]Office of Applied Studies, Substance Abuse and Mental Health Services Administration

Jeremy Bray, PhD
RTI International
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Dr. Jeremy Bray is the Director of RTI's Behavioral Health Economics Program. His research focuses on two primary areas of interest: the economics of substance abuse and mental health, and the cost-effectiveness of substance abuse treatment and prevention. In his work on the economics of substance abuse and mental health, Dr. Bray has examined the labor market effects of substance use, abuse, and dependence. Currently, Dr. Bray's research focuses on the impact of alcohol use and abuse on educational attainment. In his research on the cost-effectiveness of substance abuse treatment and prevention, Dr. Bray has estimated the costs and effectiveness of enhanced employee assistance program (EAP) services designed to increase employee utilization of the EAP. In addition, Dr. Bray serves as the Cross-site Evaluation Director on the Center for Substance Abuse Prevention (CSAP)-funded Young Adults in the Workplace initiative and is Co-Principal Investigator on a National Institute on Alcohol Abuse and Alcoholism (NIAAA)-funded study to determine the cost-effectiveness of combined behavioral- and pharmaco-therapies for alcohol dependence. Dr. Bray has published his research findings in peer-reviewed journals, including the *Journal of Health Economics, Labour Economics, Public Health Reports*, *Health Economics*, and *Employee Assistance Quarterly*.

RTI Obesity Cost Calculator

Eric Finkelstein, Derek Brown, Hong Chen, Ian Fiebelkorn, Katherine Hicks, Robert Hughes, Olga Khavjou, and Brent Ward

The RTI Obesity Cost Calculator is a simple software tool that allows employers, insurers, and other users to examine the costs of obesity within an employed or insured population of working age adults. The calculator performs two primary functions. (1) It estimates the costs of obesity based on demographic characteristics of a firm (employer or insurer), including costs for medical expenditures and the dollar value of increased absenteeism resulting from obesity. Costs are estimated separately for two groups of obese persons, those eligible and ineligible for bariatric surgery. (2) It also provides a module to assess the return on investment (ROI) for coverage of bariatric surgery based on specific scenarios input by the user.

The calculator generates costs based on a combination of firm-specific data provided by the user (e.g., size of the firm, average wage rate), and obesity-specific data estimated from nationally representative datasets (e.g., prevalence of obesity within an industry or state). Users may select varying levels of detail for the information that they input. ROI is calculated based on the previous set of inputs, along with additional choices selected by the user. For example, the calculator allows a user to explore the effect of changes in insurance coverage and out-of-pocket costs on ROI.

The majority of the output from the calculator is based on published research produced by RTI. Some portions of the ROI calculations are based on research in progress.

Eric Finkelstein, PhD, MHA
RTI International
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Dr. Eric Finkelstein is an economist in the Health Economics and Financing Program in RTI's Division for Health Services and Social Policy Research. He currently conducts economic and health policy research at RTI and teaches the undergraduate health economics course at Duke University. He focuses on the economic causes and consequences of health behaviors, emphasizing obesity. Dr. Finkelstein has published several peer-reviewed papers in this area and has garnered national media attention for his research. Dr. Finkelstein leads several projects concerning the causes and consequences of obesity and evaluates several obesity prevention programs for the Centers for Disease Control and Prevention (CDC) and other public and private sector agencies. He frequently speaks at conferences about the economic impact of obesity and strategies for reducing this burden.

Derek S. Brown, PhD
RTI International
Research Triangle Park, NC

Dr. Derek S. Brown is an economist in the Health Economics and Financing Program in RTI's Division for Health Services and Social Policy Research. He joined RTI in 2004, and his current work includes several obesity projects for Centers for Disease Control and Prevention (CDC) and a field study of physical inactivity and walking in older adults. His current research agenda includes these topics and econometric models of transition data and revealed and stated preference data. Dr. Brown has a strong technical background in econometric and statistical methods and computer programming. He has coauthored a number of publications in peer-reviewed journals. Prior to joining RTI, he worked in the Duke University Center for Health Policy, Law, and Management.

Handheld Computing Devices for Clinical Data Management in a Multi-Site Trial in Latin America

Steve Litavecz,[1] Norman Goco,[1] Debra Fleischmann,[1] Emily Warmoth,[1] Eduardo E. Castilla,[2] Jorge Lopez Camelo,[2] Alejandra Mariona,[2] Jeffrey C. Murray,[3] George L. Wehby,[3] Lorette Javois,[4] Linda Wright,[4] and Tyler Hartwell[1]

As the Data Coordinating Center for the National Institute of Child Health and Human Development's (NICHD) Global Network for Women's and Children's Health Research (GN), RTI International researched options for the development of a data management system for a multi-site clinical trial in Latin America and in collaboration with Estudio Colaborativo Latino Americano de Malformaciones Congénitas (ECLAMC) decided upon the use of handheld devices. The nature of the trial and diversity of the study sites required the implementation of a dynamic approach to program design and development, training, data management, and troubleshooting. This experience has provided valuable lessons to strengthen research capacity in future global efforts with this cost-effective technology.

The *Birth Defects Treatment and Prevention Program: Tertiary Prevention by Systematic Pediatric Care* is a study being conducted within the GN in partnership with NICHD, ECLAMC, the University of Iowa, and RTI. 47 hospitals affiliated with ECLAMC are participating in this trial whose objectives are to examine the impact of high-intensity pediatric care on neonatal mortality in children born with cleft lip and/or cleft palate and a systematic pediatric care strategy on the health of a child born with nonsyndromic cleft lip and palate during the first two years of life.

Palm® handheld devices were chosen because of their availability, cost, reliability, capacity, prior ECLAMC experience, and ability to function with multiple users in various settings. The selection of programming tools based on flexibility in programming to allow for rapid modifications of data entry screens and support of multiple languages (Portuguese and Spanish). Other criteria included existing programming experience, processes for deploying systems onto the handheld device, data storage, and synchronizing data between a handheld and a PC.

The challenge of working with several sites in different countries, multiple languages, differing levels of experience with computer technologies, and quality of Internet access for data transfer and maintenance all posed unique problems for implementing the handheld system. Strong teamwork, technical knowledge, and commitment among RTI and ECLAMC staff allowed for the implementation of practical and innovative strategies to bring handheld devices to users willing to learn new skills and incorporate new technologies to assist them in their work.

Financed by the Global Network for Women's and Children's Health Research (NICHD U01 HD40636) and the Bill and Melinda Gates Foundation.

[1]RTI International; [2]Estudio Colaborativo Latino Americano de Malformaciones Congénitas; [3]University of Iowa; [4]National Institute for Child Health and Human Development

Steve Litavecz, MBA, BS
RTI International
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Mr. Litavecz is a research programmer/analyst with 15 years of experience in data processing, software design, and development. Mr. Litavecz specializes in planning, coordinating, and performing software development and data processing activities. He has implemented audio computer-assisted self-interviews (ACASI) utilizing touch-screen technology. Mr. Litavecz developed a data-driven codebook capable of distributing data in SAS, SPSS, and STATA. He develops transmission systems capable of importing and exporting data from remote sites. Mr. Litavecz has also developed data-driven handheld computer systems. He is an expert in SAS and has extensive knowledge with Visual Basic and Access.

Dietary Reference Intakes in Nutrition Labeling of Foods: How Do We Gain Acceptance for New Science When It Impacts Old Policy?

Bernadette M. Marriott

Recommended Dietary Allowances (RDAs) for Americans were first published in 1941. From that time until 1997 most national policies and programs related to nutrition in the United States have used the RDA as the single numeric basis for nutrient requirements for the American population. For example, the RDA for calcium in 1980 was presented as the recommended safe intake levels for 15 different age and gender groups from infancy through adulthood plus separate values for pregnancy and lactation. The RDAs have been periodically revised since 1941 with progression of scientific understanding of nutrient requirements. As government food assistance and the understanding of the link between diet and health and resulting health promotion programs have increased in our country, so has the preeminence of the RDAs as the primary scientific basis for programs such as School Breakfast and School Lunch, Meals on Wheels, nutrition labels on foods, etc. However, the scientific community acknowledged that the multiple uses of the single value for populations and individuals was mathematically inappropriate. In 1997, the Food and Nutrition Board (FNB), National Academy of Sciences, who has been the creator of the RDAs since 1941, determined that new data not only required the revision of the RDAs but also the expansion of the RDA concept to multiple reference values to address the multiplicity of uses for nutrient references as well as specific new concepts such as an upper safe limit of intake. These new values are called the Dietary Reference Intakes (DRIs). In December 2003, the FNB released the report, *DRIs: Guiding Principles for Nutrition Labeling and Fortification.* This report was funded jointly by the Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and Health Canada. These guidelines were well received by the sponsors but highly controversial among the scientific community. The complexity and subtlety of recommended use of the multiple new values has resulted in a scientific backlash and retreat of many well-known scientists to promote the old single value concept. This poster will present the derivation of the DRIs and rationale for their use in food labeling and contrast it with the old RDA single reference value concept. It will include the current status of the debate and how better communication of the underlying principles might have avoided this policy controversy. The poster will conclude with consideration of a staged release of novel scientific concepts that have far-ranging policy implications.

Bernadette Marriott, PhD
RTI International
Research Triangle Park, NC

Dr. Bernadette Marriott joined RTI in 2003 as the Assistant Vice President, Global Strategic Planning, International Development Group (IDG). She has more than 30 years of experience in the fields of nutrition and nutrition policy, psychology, and comparative medicine, and in research settings that include government agencies, medical schools, and universities. Specifically, her research has focused on nutrition and trace minerals; behavioral correlates of food selection and intake in animals and people (including children, the elderly, and military populations); and issues in national nutrition policy, in particular dietary supplements. Dr. Marriott also has experience in a wide range of federal research compliance issues, such as protection of human and animal subjects and radiation safety. She has provided upper-level management at universities, the National Institutes of Health (NIH), and private foundations. Starting in 1995, Dr. Marriott created the congressionally mandated Office of Dietary Supplements (in the Office of the Director, NIH), initiating all programs, identifying and hiring staff, developing the office's strategic plan, providing fiscal management of the office, and working with Congress, other agencies, and professional and trade organizations in the development of dietary supplement policy. From 1989 to 1995, Dr. Marriott worked at the Institute of Medicine's Food and Nutrition Board, holding progressively more responsible positions; for 2 years she served as the Board's Deputy Director, with supervision of staff and oversight of program activities. She has published widely in her field and is active on professional boards and committees. Her PhD in psychology is from King's College, University of Aberdeen, with a BSc in Biology from Bucknell University. She also has postgraduate training in trace mineral nutrition and comparative medicine. Dr. Marriott serves as an Adjunct Professor in the Department of Nutrition (Schools of Medicine and Public Health) at the University of North Carolina at Chapel Hill.

Method Development for Speciation of Toxic Trivalent Arsenic Species MMA (III) and DMA (III)

Lisa S. Milstein, Keith E. Levine, Peter M. Grohse, and William F. Gutknecht

Arsenic (As) research has gained worldwide public interest as evidenced by the World Health Organization (WHO) and the U.S. Environmental Protection Agency (EPA) reduction of the minimum acceptable As level in drinking water from 50 μg/L to 10 μg/L. It is necessary, however, to resolve the various arsenic oxidation and complexation forms (i.e., speciation) in order to fully understand the biomedical and epidemiological pathways of the element once it is ingested. Arsenic species exhibit varying degrees of toxicity. For example, ingestion of inorganic arsenite (As III) and arsenate (As V) has caused health-related problems such as cancer, cardiovascular disease, and skin disease, such as hyperkerotosis. In contrast, species such as arsenocholine (AsC), arsenobetaine (AsB), and arsenosugar compounds, typically present in seafood, are relatively innocuous. Ironically, As III also has medicinal uses as it has been prescribed to patients in sublethal doses for treating acute promyelocytic (APL) leukemia. Trivalent arsenic metabolites monomethylarsonous acid (MMA III) and dimethylarsinous acid (DMA III), however, have become a health concern as recent studies have revealed their presence in human urine samples from individuals who were exposed to arsenic in drinking water. These compounds are more toxic to animal and human cells than inorganic arsenic species, such as arsenite (As III). These metabolites have also been present in APL patients' urine samples, further supporting the need to measure these species.

Separating and detecting DMA III and MMA III from other previously determined arsenic species is challenging because of compound instability. These compounds often oxidize in solution to their pentavalent forms prior to speciation analysis, making quantitation difficult. RTI researchers have developed analytical techniques using ion chromatography (IC) coupled to inductively coupled plasma – mass spectrometry (ICP-MS), to measure these species. The results of these studies will be discussed.

Lisa S. Milstein, PhD
RTI International
Research Triangle Park, NC

Lisa Milstein**,** PhD, research analytical chemist, is in the Trace Inorganics Department/Environmental and Industrial Sciences Division

Dr. Milstein received her PhD in analytical chemistry from the University of Cincinnati under Professor Joseph Caruso. She also received her BS in chemistry (magna cum laude) at the University of Cincinnati.

Dr. Milstein is currently directing the trace metal speciation program. She regularly conducts good laboratory practice (GLP) and non-GLP studies involving the detection of trace metals in a variety of sample matrices for government, industrial, and pharmaceutical clients. She has co-authored several publications in the area of trace element speciation and has presented at numerous international conferences.

Simulation Tool to Assess the Impact of Taxes on Cross-Border Sales

Christian Nimsch, Matthew Farrelly, Nathan Mann, Trevor Woollery, and Terry Pechacek

Problem/Objective: In recent years, there has been a dramatic increase in the average level of cigarette excise taxes and the number of states increasing their cigarette taxes. Higher cigarette excise taxes have led to renewed concerns over cigarette tax evasion/smuggling. We inform the debate on tax evasion/smuggling by providing a standalone simulation tool that can assess the impact of state excise taxes on crossborder cigarette sales for every state.

Methods**:** The Cross-Border Cigarette Sales Simulation is an Excel spreadsheet program. The underlying model for all estimations is a demand model using state aggregate tax-paid cigarette sales data. The model includes measures for short and long distance cross-border sales, taxes, state, and year effects, as well as measures of overall economic activity and well-being that vary over time within states. Using the cross-border sales measures in the aggregate model, we apply counterfactual analysis to estimate the effect of taxes on cross-border sales.

Results: The simulation tool identifies both the source and destination of smuggled cigarettes for every state. The simulation tool provides estimates for the number of packs lost/gained due to cross-border sales over time and in response to hypothetical tax increases.

Conclusions: The simulation tool provides information for policy makers to understand the impact of tax increases on cross-border sales. The information on the source and destination of smuggled cigarettes can help law enforcement to control illegal crossborder sales.

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Mr. Nimsch, Health Outcomes Scientist, has a background in applied economics and has over four years of experience in scientific and technical writing. He has published in several journals, including *Health Economics* and *Health Education and Behavior*. He has also authored numerous working papers and technical reports.

Mr. Nimsch is also experienced in project management and economic analyses, and has led numerous project tasks, programmed and analyzed data from several large-scale data sets, and is experienced in econometric modeling and forecasting techniques, such as panel and cross-sectional data modeling, factor analysis, discrete choice, logistic regression, structural equation models (SEM), and survival analysis.

Mr. Nimsch has extensive experience in the area of smoking, both through scientific research and economic analyses. He has worked on projects studying cigarette demand, smoking prevalence, nicotine addiction, and youth empowerment. Outside of health research, he has focused on the economic impact analysis of raising cigarette excise taxes as well as the analysis of the trend in market-shares, prices, sales, and promotions in the cigarette industry.

Individual and Area-level Socioeconomic Disparities in Smoking Prevalence and Quitting in Maine

Nancy Sonnenfeld, D.E. Maines, and S. Subramanian

To prevent tobacco use, Maine and other states have implemented comprehensive programs that include local community mobilization components. However, state health departments rarely have sufficient data to provide community-specific statistics. In this poster, we illustrate that consideration of area level characteristics can enhance our understanding of socioeconomic disparities in smoking and smoking cessation in Maine. Individual level data were obtained from the telephone-based Maine Adult Tobacco Use Survey from 4,713 white residents of 432 Maine towns in 1999 and 2000. Models of recent quitting included 1,006 current smokers and former smokers who reported quitting in the last year. Town demographic data were obtained from the year 2000 U.S. Census. Marginal and mixed regression methods were employed. Marginal results are presented.

At the individual and household levels, educational attainment and living with a smoker were among the variables most strongly associated with increased odds of smoking and decreased odds of quitting. After adjusting for educational attainment, household income was not associated with recent quitting. At the town level, disparities differed for recent quitting and current smoking. Town percentage of high school graduates and town unemployment rates were associated with recent quitting [town percent of high school graduates (reference = > 90%): < 80% high school graduates odds ratio (OR) = 0.35 (95% confidence interval (CI) 0.19, 0.67), 80-89% high school graduates OR = 0.58 (95%CI 0.32, 1.06); town percent of unemployment (reference = ≥5.9%) : < 3.5% OR = 0.31 (0.15, 0.62), 3.5%-5.89% OR = 0.60 (0.31, 1.16). Town percent of residents in poverty [OR = 1.46 (1.22, 1.75)] and percentage of white collar workers [OR = 1.21 (1.01, 1.44)] were associated with current smoking.

This analysis has several implications for programs aimed at reducing health disparities associated with smoking. First, the definition of socioeconomic disparity matters. We often discuss health disparities in relation to income, but at least for recent quitting, disparities related more clearly to education. Barriers associated with educational disadvantage might include limited literacy and lower perceived ability to quit. Second, households matter. Living with a smoker was a strong predictor of smoking behavior. Smoking cessation programs must target households, not individuals. Finally, the broader community matters. Even without data for individual towns, it is possible to identify characteristics of towns that matter. In this case, town educational attainment is associated with individual smoking behaviors, after controlling for individual characteristics. Interventions must address smoking-related disparities at multiple levels including the individual, household, and community.

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Dr. Nancy Sonnenfeld started working at RTI as a research epidemiologist in August 2004. She has more than 12 years of professional experience in designing and implementing epidemiological research, performing quantitative data analyses, and supporting public health initiatives in many different areas including environmental health and social epidemiology. Among the outcomes she has studied are pregnancy, cancer, tobacco use, chronic lung disease, renal function, and suicide attempts. She also has worked with public health officials to identify ways in which data can be better used to monitor the health status of populations, plan and evaluate public health programs, and develop public health policy. She has the ability to translate epidemiological data and statistics both orally and in writing for the nontechnical audience, and to function as an effective public health advocate in public and scientific settings. Dr. Sonnenfeld served as the first full-time faculty member in University of New England's graduate program in public health, as the first lead chronic disease epidemiologist for the Maine Bureau of Health, and as an epidemiologist for the Agency for Toxic Substances and Disease Registry. She received her doctorate in epidemiology at the University of North Carolina at Chapel Hill in 1997.

Metabolomics: Use in Biomarker Discovery

Susan Sumner, Timothy Fennell, Jason Burgess, Robert Jeffcoat, and James Raymer

Metabolomics, metabolite profiling, and metabonomics are terms used to describe the study of the low-molecular-weight complement of cells, tissues, and biological fluids. Metabolomics is a process that involves, in part, the use of analytical tools to capture signals for low-molecular-weight metabolites, and the use of data reduction methods to associate specific metabolite profiles with one or more classification parameters. Once patterns (or marker profiles) are recognized, the metabolites responsible for biological association can be identified. Mechanistic insights for additional discovery efforts are developed through mapping identified metabolites to biochemical pathways and determining their association with proteins and genes.

Most published metabolomic studies have been focused on the development of pattern-recognition methods to distinguish samples obtained from rodents receiving no-effect levels and effect levels of compounds with known toxicological insult. To date, most metabolomic studies have utilized nuclear magnetic resonance spectroscopy (NMR) and gas- or liquid- chromatography coupled with mass spectrometry (GC-MS, LC-MS) for metabolite detection. These studies have clearly demonstrated a powerful use of metabolomics in recognition of patterns for association with liver and kidney toxicants, and has promising application in screening pre-clinical samples. Although applications of metabolomics in human studies are more limited, there exist demonstrations of this technology in the areas of disease staging and therapeutic intervention.

While the challenges of metabolomics are complex, they can be simplified to these categories:

- Definition of the metabolome and its cellular and tissue specificity.
- Development of separation and analytical methods for capturing signals that are representative of a specified metabolome, or needed to examine a specific biological question.
- Application of data reduction tools and mathematical algorithms for association of metabolite profiles with effects; for example, disease state, therapeutic intervention, or toxicity.
- Unraveling sources of inherent variability in samples from human populations.
- Integrating and understanding of metabolomics relative to other measurements; for example clinical chemistry parameters, pathology assessment, or gene and protein expression.

This poster will described the vision for metabolomics at RTI, and the progress in the development and application of analytical approaches (GC-MS and NMR), data reduction methods, pathway mapping tools, and interpretations.

Susan Sumner
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Dr. Susan Sumner is taking a lead role at RTI International in the development of a biomarker discovery effort that includes the use of a metabolomics approach. Susan was trained (1982-1986) as a physical chemist with a specialty in spectroscopy at North Carolina State University (NCSU) following completion of undergraduate studies in the NCSU Department of Chemistry (1979-1982). She completed a 2-year staff fellowship (1987-1989) in biological applications of spectroscopy at the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH). Susan was employed by the Chemical Industry Institute of Toxicology for 13 years where she served as a principal investigator and study director. Her research was focused on understanding mechanisms of chemical-induced toxicity, cross-species extrapolation, and the relevancy of animal models in assessment of human health risk. Susan continued developing and applying spectroscopic methods for biomarker discovery and elucidation of biochemical mechanisms while employed at Paradigm Genetics, Inc. (2002-2004). She has directed both Nuclear Magnetic Resonance and Mass Spectrometry facilities for metabolite characterization and metabolomic analysis. Susan joined the Health Sciences Division of RTI International in August 2004.

Biomarkers and Cross-Species Extrapolation

Timothy Fennell, Jason Burgess, Rodney Snyder, and Susan Sumner

The development of biomarkers for disease staging, monitoring therapeutic treatment, or assessment of human health risks from exposure to compounds greatly depends on the development of mechanistic insights from dose-response studies in animal models. The extrapolation of rodent based-markers to humans is often complex due to the relatively high-dose studies conducted in rodents when compared with lower-exposure scenarios for humans. A powerful approach to defining the metabolism of a xenobiotic, and potential biomarkers, involves nuclear magnetic resonance (NMR) spectroscopy based characterization and quantitation of metabolites in biological fluids, cells, and tissues following administration of a multiple ^{13}C-labeled xenobiotic. NMR provides a non-biased method for capture of a broad range of signals for metabolites, where the spin-spin coupling patterns from adjacent ^{13}C-labels enables the distinction of the endogenous and exogenous components. Samples collected from dose-response studies conducted in rodents can be used to elucidate metabolite structures and quantitate metabolites, with subsequent development of proposed metabolic pathways. In humans, more limited and controlled low-dose studies can be conducted for the collection of urine and serum, followed by metabolite assignment and quantitation. Qualitative and quantitative comparisons can then be made to access species differences in metabolic capabilities, providing an understanding of appropriate species-specific markers as well as mechanistic insights. An example study will be presented that involves the characterization and quantitation of urinary metabolites collected from rats and mice following administration of [1,2,3-^{13}C]acrylamide, and the comparison with urinary metabolites from humans following controlled exposure to [1,2,3-^{13}C]-acrylamide. This type of methodology has more frequently been applied in assessment of environmental agents, but has a great potential for use in the development of clinical markers and assessment of therapeutic agents.

Susan Sumner, PhD
RTI International
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Dr. Susan Sumner is taking a lead role at RTI International in the development of a biomarker discovery effort that includes the use of a metabolomics approach. Susan was trained (1982-1986) as a physical chemist with a specialty in spectroscopy at North Carolina State University (NCSU) following completion of undergraduate studies in the NCSU Department of Chemistry (1979-1982). She completed a 2-year staff fellowship (1987-1989) in biological applications of spectroscopy at the National Heart, Lung, and Blood Institute at the National Institutes of Health (NIH). Susan was employed by the Chemical Industry Institute of Toxicology for 13 years where she served as a principal investigator and study director. Her research was focused on understanding mechanisms of chemical-induced toxicity, cross-species extrapolation, and the relevancy of animal models in assessment of human health risk. Susan continued developing and applying spectroscopic methods for biomarker discovery and elucidation of biochemical mechanisms while employed at Paradigm Genetics, Inc. (2002-2004). She has directed both Nuclear Magnetic Resonance and Mass Spectrometry facilities for metabolite characterization and metabolomic analysis. Susan joined the Health Sciences Division of RTI International in August 2004.

Determination of Mercury in an Assortment of Processed and Unprocessed Seafood Samples by Combusion Atomic Absorption Spectroscopy

Frank X. Weber, Keith E. Levine, Michael A. Levine, John P. Henderson, and Peter M. Grohse

A study was performed to (1) estimate the mercury content in tuna from a variety of sources and (2) assess the efficiency and accuracy of a direct mercury analyzer during such a screening process. This measurement approach involved the thermal decomposition, gold amalgamation, and detection of mercury from tissue samples by atomic absorption spectroscopy. Pre-packed and freshly caught seafood samples were lyophilized, ground to a powder, and homogenized. The powdered tissue was then directly analyzed for mercury content. The analyzer was calibrated using animal tissue certified reference materials (CRMs) and demonstrated a detection limit of less than 0.1 ng Hg and a quantitative range of between 0.5 ng and 500 ng. The analysis of a wide range of reference materials, including animal and plant tissue CRMs and standard reference materials (SRMs) as well as coal and sediment SRMs, demonstrated recoveries consistently between 85% and 115% at concentrations between 0.080 µg Hg/g and 4.6 µg Hg/g. No dissolution step was required and approximately 80 samples can be measured unattended in an 8-hour period.

The average amount of Hg found in canned tuna packed in water was 20.5 µg/serving (suggested serving size 3 ounces), canned tuna packed in oil was 16.3 µg/serving, and tuna packed in a pouch with water was 26.9 µg/serving.

The method was found to be highly sensitive, accurate, matrix-independent, and efficient. Manufacturers and regulatory agencies concerned with monitoring the lot-to-lot tuna quality may find this method an attractive alternative to the more classical acid-dissolution / cold vapor atomic absorption (CVAA) methodology.

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Mr. Weber has 14 years of experience as a chemist in the Trace Metals Department at RTI, as a chemist and laboratory manager at BOC Edwards, as a laboratory manager and chemist with American Environmental Network, and as a chemist at Rhone Poulenc. He specializes in the determination of trace metals in a wide variety of sample matrices by Inductively Coupled Plasma Mass Spectroscopy and Inductively Coupled Plasma Atomic Emission Spectroscopy.

He has extensive experience with the determination of trace metals for the U.S. Environmental Protection Agency (EPA) in the Contract Laboratory Program (CLP) using EPA methods 6020, 200.8, 6010, and 200.7.

Mr. Weber has also worked in the semiconductor industry as a quality assurance chemist and laboratory manager.