Annual Report

Clinical Research Program

SUBMITTED BY
STAVROULA OSGANIAN, MD, ScD, Director



ANNUAL REPORT OF THE CLINICAL RESEARCH PROGRAM FY 2005

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Program Overview

The Clinical Research Program (CRP) is a scientific, inter-disciplinary research program that provides methodologic assistance to investigators on the design, conduct, and analysis of clinical research studies and an infrastructure for the data coordination of extramurally sponsored studies.

The mission of the Clinical Research Program is to enhance the quality of clinical research at Children's Hospital through scientific leadership in clinical research methodology (including biostatistics, epidemiology, and informatics); collaboration or consultation on the design, conduct, and analysis of clinical research studies; and educational activities targeting the clinical research community including residents, fellows, faculty, and study coordinators.

Various types of support are provided to investigators at all stages of protocol development, study implementation, and analysis. The CRP also works closely with the General Clinical Research Center (GCRC), funded by the National Institutes of Health, to optimize the infrastructure for the conduct of effective clinical research at Children's Hospital.

Since its inception in 1998, the Program has sustained significant growth in staff and resources and increased visibility among the clinical research community. The CRP staff has grown to 29 full- or part-time staff from various disciplines, including epidemiologists, biostatisticians, application developers, research associates, data coordinators, and data entry staff. The Program occupies approximately 3000 square feet of space located in 333 Longwood Avenue.

Key accomplishments over the past year include:

- Participation and leadership on major clinical research initiatives of the Clinical Research Executive Committee (CREC);
- Successful collaborations with several CHB investigators and other institutional Programs;
- Successful implementation of three multi-site clinical research protocols for the Glaser Pediatric Research Network;
- Increased funding of CRP staff on various CHB investigator initiated projects;
- Expansion of educational offerings for Clinical Research and organization of a new Core, the Clinical Research Education Core;
- Successful staff hiring and expansion.

Acknowledgement

We wish to thank Dr. Mandell, CEO, Ms. Fenwick, COO, and the hospital leadership for the continued and generous financial support provided to the Program. This support has made it possible for the Program to provide valuable assistance to the investigator community and achieve many of its accomplishments.

Overview of FY05 Activities and Accomplishments

This section highlights the major activities and accomplishments of the CRP staff, which serve to support and enhance the clinical research enterprise, support the investigator community, and improve Program operations.

1. CLINICAL RESEARCH EXECUTIVE COMMITTEE

During the past year, Dr. Osganian played a significant role with the CREC in developing a 5-year strategic plan for Clinical Research. The CREC is chaired by Dr. Jane Newburger and its members include Dr. Richard Grand, Dr. Ellis Neufeld, Dr. Tina Young Poussaint, Dr. Bart Cilento, Dr. Tom Jaksic, Dr. Voula Osganian, Dr. Scott Pomeroy, Dr. Deborah Waber, and Dr. Jean Emans. Ex-officio members include Sandra Fenwick, Dr. Carleen Brunelli, and Patrick Taylor. The strategic plan proposes growth in clinical research faculty, increases in the number of pilot projects to support junior investigators, growth in infrastructure to support the design, conduct and analyses of clinical research studies, growth in space, and improvements in administrative operations to support the clinical research community. A Preliminary Report was completed and presented by Drs. Newburger and Osganian to the hospital leadership and Research Board of Trustees in May 2005. The final report is scheduled to be presented to the Research Board of Trustees in spring 2006. Key initiatives of the CREC in FY2006 will include efforts to implement the strategic plan, increased fundraising activities for clinical research, a strategic plan and vision for clinical research education, and efforts to respond to the NIH Roadmap Initiative on Clinical and Translational Research Science Awards.

2. PROGRAM ORGANIZATION

Having recognized a need to organize and expand clinical research education activities for the institution, the Clinical Research Program formally established the Clinical Research Education Core and successfully recruited Dr. Jenifer Lightdale as its Director and Kristi Lawrence as educational administrative coordinator. Under the direction of Dr. Lightdale, the Clinical Research Education Core will be responsible for the planning, organization, and implementation of all CRP sponsored seminars and short courses. A major initiative for FY06 will be to work with the CREC to develop a vision for clinical research education and to continue to expand the educational offerings of the CRP so as to continue to promote excellence among our investigators.

3. PROGRAM UTILIZATION AND GROWTH

The Program continues to support over 300 requests for assistance from nearly 200 investigators in the institution. Of note, the Program has observed a substantial increase in funding from such collaborative projects with CHB investigators, from 45 projects funding CRP services in FY04 to 75 projects funding CRP services in FY05. This increase in the number of projects funding CRP staff has resulted in nearly a \$400,000 increase in funding from grants, programs, or Departments for the Program.

4. BIOSTATISTICS CORE

Under the direction of Dr. David Wypij, the major activities and accomplishments of the Biostatistics Core staff in 2005 include:

a. Continuation of Collaboration and Manuscript Preparation

CRP biostatisticians continue to collaborate and publish with Children's Hospital clinical investigators. FY2005 highlights include an observational study of hyponatremia among runners in the Boston Marathon (with Dr. David Wypij), a clinical trial of prone vs. supine positioning in children with acute lung injury (with Drs. David Wypij and Mei-Chiung Shih), a clinical trial studying hand sanitizers and hand hygiene education in reducing illness transmission (with Dr. Mei-Chiung Shih), effects of a low-glycemic load diet on cardiovascular disease risk in obese young adults (with Dr. Henry Feldman), psychometric evaluation of quality of life inventories (with Dr. Mei-Chiung Shih), studies of vancomycin use (with Dr. Henry Feldman), the prognostic value of measures of acid/base balance in malaria (with Drs. Clarissa Valim and David Wypij), and the impact of a quality improvement program in children with asthma (with Mr. Peter Forbes and Dr. David Wypij). A full list of recent publications is included in Appendix B.

b. New Grant Applications

CRP biostatisticians work closely with various Children's Hospital clinical investigators on the development of protocols and grant applications, for federal and foundation and other non-federal awards. New NIH grants that support CRP biostatisticians include those of Dr. Bryn Austin on sexual orientation and health disparities in adolescence (with Dr. David Wypij), Dr. Alison Field on weight control and weight change among adolescents (with Dr. Carl de Moor), Dr. Jane Newburger on a SCCOR grant in pediatric heart development and disease in children with tetralogy of Fallot (with Dr. David Wypij), Dr. Jane Newburger on outcomes in adolescence after repair of d-TGA (with Dr. David Wypij), Dr. Stephen Porter on ParentLink technology (with Dr. Leslie Kalish and Mr. Peter Forbes), Dr. Lydia Shrier on mood and HIV risk in depressed adolescents (with Dr. Carl de Moor), and Dr. David Ludwig on reducing sugar-sweetened beverage consumption in overweight adolescents (with Dr. Henry Feldman). A full list of federal and non-federal grants that CRP staff have collaborated on is included in Collaborative Projects on page 39.

c. Teaching to the Clinical Community

CRP biostatisticians are integrally involved with the teaching of the Introduction to Clinical Research course, taught twice yearly by the CRP. In addition, CRP biostatisticians have made numerous presentations to hospital seminar series and at national meetings. Dr. Henry Feldman has presented at an American Heart Association seminar series on the epidemiology and prevention of cardiovascular diseases, Drs. Mei-Chiung Shih and David Wypij have taught courses in biostatistics at Harvard School of Public Health, and Dr. David Wypij has presented at biostatistics short courses in Brazil and Italy. The Biostatistics Core also runs a biostatistics seminar series at Children's Hospital. A full list of teaching accomplishments that CRP biostatisticians have performed are described in Education and Training (page 23) and Staff Accomplishments (page 49). The Biostatistics Core is planning to increase education opportunities at Children's Hospital in the coming year.

d. Funding from Departments/Divisions

To best support Departments and Divisions at Children's Hospital who require more than a brief consultation with a biostatistician, the CRP Biostatistics Core has sought out collaborative relationships with these groups. In FY05, new Departmental funding of CRP Biostatistics Core staff came from Psychiatry and Adolescent Medicine, with planning for a new joint hire with Gastroenterology. Additional Departments and Divisions are expected to share funding of CRP biostatisticians from Department/Division funds and research grants.

e. New Hires

The CRP Biostatistics Core continued to grow in size and energy in FY 2005 with the addition of two new staff members, Dr. Dionne Graham and Ms. Parul Aneja. Growth in CRP biostatistics staff has primarily come from collaborative efforts with various Departments and Divisions in the hospital, including Departmental funds, the new Program for Patient Safety and Quality, and grant funding with Children's Hospital clinical investigators.

5. DATA MANAGEMENT CORE

Under the direction of Dr. Carl de Moor the major activities and accomplishments of the Data Management Core staff in 2005 include:

a. Study Coordinator Orientation and Seminar Series

DMC staff, led by Senior Clinical Research Specialist Maureen Clark, established a bi-monthly Orientation for all new study coordinators and research assistants and a monthly seminar series for study coordinators focused on project and data management. The Orientation covers many of the relevant topics that coordinators require information about in order to be adequately prepared to conduct clinical research studies at Children's Hospital, Boston. The Coordinators Rounds provides attendees with valuable information from experts and opportunities for open discussion on relevant topics. Seminar topics have included "Documenting Protocol Errors," "Patient Recruitment," and "Obtaining Informed Consent."

b. Safety Event Administrative Management Application

The applications development team collaborated with the Program for Patient Safety and Quality (PPSQ) to design case management software for the PPSQ risk management staff. The Safety Event Administrative Management Application (SEAMA), highlighted in detail in this annual report, provides risk managers with an invaluable tool to investigate, document and report on safety events occurring throughout the hospital. Set to launch in FY06, SEAMA will become the central tool for all PPSQ event tracking.

c. New Informatics Applications for the General Clinical Research Center

The DMC continued its informatics support of the General Clinical Research Center (GCRC). Led by Joseph Rezuke, the applications development team completed the replacement of the GCRC's legacy administrative program (CAMP). The new application (CREMA) enhances the Center's administrative capabilities by integrating Core Lab data management within central administration. Furthermore, it provides staff with the ability to import data directly from the Hospital's IRB database and export data pre-formatted for NIH annual reporting.

In collaboration with the ISD, Mr. Rezuke used Microsoft Sharepoint Services to develop a new program designed to facilitate the GCRC protocol review process. This new innovative service provides GCRC scientific reviewers with a central online workspace to review and comment on research protocol submissions.

d. Support and Development of SPSS Databases

The CRP commitment to SPSS database development continued throughout the year. Specifically, the DMC provided support and database development to over 35 new and ongoing research projects. In addition, Sharon Wong, the lead SPSS database developer, attended a weeklong, in-depth training course on SPSS technologies and development techniques.

e. Support and Development of Clinical Data Management Systems (CDMS)

The DMC developed and deployed several new large-scale data management systems in 2005. Specifically, the applications development team implemented these systems for use in Cardiology, Endocrinology, Neurology and Hematology. The DMC now supports over 12 clinical data management systems in the field and anticipates adding several more in the upcoming year.

In addition, the applications development team further enhanced its CDMS framework during the year. The development project, led by Team Leader Jason Rightmyer, added several new features including: offline database export utilities, enhanced reporting services, improved data transformation, and CRF layout capabilities. Lastly, the team added 2 new physical servers to provide isolated data storage and access to CDMS implementations directly using the Internet.

f. New Hires

The DMC hired one new staff member, Aruna Jayashankar. Ms. Jayashankar is a Clinical Research Specialist who provides support to investigators by developing case report forms, manuals of operation, and study-specific data management and quality assurance procedures.

6. GLASER PEDIATRIC RESEARCH NETWORK

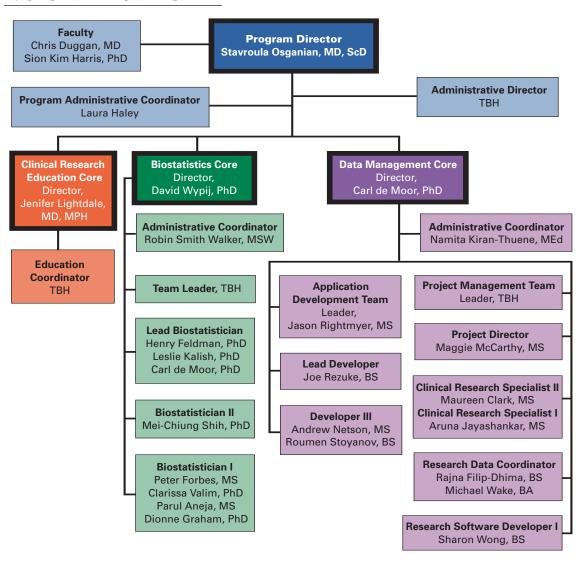
The Program continues to serve as the Design, Analysis, and Coordinating Center for the Glaser Pediatric Research Network and support activities in the areas of data management, data entry, biostatistics, Data and Safety Monitoring Board reports, manuscript preparation, and Glaser fellow education. The Core contract between CRP and GPRN, covering review of developing studies and conduct of training seminars for the fellows, was renewed in 2005 for a second three-year term. Three additional contracts were in operation for coordination and statistical analysis of GPRN-funded research:

- A multi-site Phase I/II trial of rituximab in children with chronic immune thrombocytopenic purpura, for which GPRN provided 5 of 10 sites, completed its primary evaluation period and published the findings in *Blood*.
- A trial of metformin in obese adolescents attained full enrollment of 76 patients and will complete the one year intervention period in 2006.
- A registry for clinical data on necrotizing enterocolitis in newborns moved out of the design phase and reached a total enrollment of 250 patients.

Program Organizational Structure

The Program includes 26 full-time and 3 part-time staff organized into three major cores: the Biostatistics Core, the Data Management Core, and the Clinical Research Education Core. The staff of the Biostatistics Core assists clinical investigators with protocol and grant development, study design, including sample size calculations, statistical analysis plans, and interim monitoring, and final data analyses and manuscript preparation. The staff of the Data Management Core assists clinical investigators with database development, data form design, randomization methods, and project initiation and management. The Clinical Research Education Core directs the development and implementation of various seminars and lectures that target clinical investigators and study coordinators. Topics cover clinical research study design and data analysis, human subject protection, and the logistics of conducting clinical research.

A. ORGANIZATIONAL CHART



B. STAFF ROLES AND BIOGRAPHIES

Staff publications can be found in Appendix B.

PROGRAM DIRECTOR



Stavroula Osganian, MD, ScD, MPH, Program Director

Dr. Osganian is a physician-epidemiologist with considerable experience in the design and conduct of epidemiologic and clinical research studies. Dr. Osganian's research interests and activities focus on studies of youth health promotion and chronic disease prevention with an emphasis on preventive cardiology. She has had a leadership role in one of the largest, nationally recognized NIH-funded school-based studies of cardiovascular health promotion in the United States, the Child and Adolescent Trial for Cardiovascular Health (CATCH). The work of the CATCH collaborative

group has led to significant contributions to the design, conduct, and institutionalization of school-based health promotion programs and the study of cardiovascular risk factors in youth.

Dr. Osganian presently serves as Director of the Clinical Research Program at Children's Hospital Boston and Associate Director of the NIH-funded General Clinical Research Center at Children's Hospital. She holds an appointment as Assistant Professor of Pediatrics at the Harvard Medical School and is an attending in the Optimal Weight for Life Clinic at Children's Hospital Boston.

CLINICAL RESEARCH FACULTY

Christopher Duggan, MD, MPH, Clinical Research Faculty

Dr. Christopher Duggan is a pediatric gastroenterologist and nutrition physician whose research interests include the nutritional management of acute and persistent diarrhea, clinical trials of micronutrient supplementation, and general aspects of nutritional support in catabolism. In studies in developing and industrialized countries, he is applying state of the art nutritional assessment techniques to patients with diarrhea, HIV/AIDS, inflammatory bowel disease, short bowel syndrome and cancer.

Dr. Duggan has been a member of several large multi-center clinical trial groups, including the Glaser Pediatric Research Network, a multi-center research network for cutting edge pediatric studies based at Children's Hospital, Boston as well as Stanford, UCSF, UCLA, and Baylor. He is an Assistant Professor of Pediatrics at Harvard Medical School, an Assistant Professor of Nutrition at the Harvard School of Public Health, and Director of the Clinical Nutrition Service at Children's Hospital Boston.

Sion Kim Harris, PhD, Epidemiologist and Survey Design Specialist

Dr. Harris has over ten years of experience in survey/questionnaire design, implementation, and data analysis and provides consultation to investigators throughout Children's Hospital in the design and implementation of surveys. Dr. Harris also has extensive experience in public health epidemiology, psychometric analysis methods, adolescent health research and program evaluation, and qualitative research methods. She has collaborated in the development and psychometric testing of various measures, including a comprehensive adolescent health status questionnaire called the Child Health and Illness Profile (CHIP-AE), a brief screen for adolescent alcohol and drug abuse used in primary care settings (the CRAFFT), a member survey for teen pregnancy prevention coalitions to assess

functioning and capacity for action, and a sedation assessment tool for use with critically ill infants and children, among others.

Dr. Harris received her doctorate from the Johns Hopkins Bloomberg School of Public Health in 1996, after which she worked for the Mass. Department of Public Health as the Project Manager of Adolescent and School Health for the Office of Statistics and Evaluation in the Bureau of Family and Community Health. She provided oversight and leadership in research and program evaluation projects related to teen births, teen pregnancy prevention, school health and school-based health centers, and youth risk behaviors. She continues to provide consultation to them on a number of survey and program evaluation projects.

BIOSTATISTICS CORE



David Wypij, PhD, Director of Biostatistics

Dr. Wypij joined the CRP in July 1999. He has considerable experience in the leadership of biostatistical and data coordinating center efforts for single-and multi-center studies, with special expertise in pediatric cardiology, child growth and development, ICU management and surgical follow-up, and malaria in children. He is also an Associate Professor of Pediatrics at Harvard Medical School and Associate Professor of Biostatistics at Harvard School of Public Health.

Dr. Wypij's methodologic research interests lie in the areas of longitudinal data analysis, spline and smoothing methods, the analysis of discrete data, and models for vaccine efficacy. He has collaborated on cardiac surgery clinical trials and follow-up studies at Children's Hospital since 1989, including the Boston Circulatory Arrest Study, the Boston pH Study, and the Boston Hematocrit Study. He also collaborates with many other Children's Hospital clinical investigators on their projects and supervises the data management and biostatistical activities of the Glaser Pediatric Research Network. Since 1997, he has been the Director of Biostatistics for the NIH-funded Severe Malaria in African Children clinical research network, which is conducting observational studies and clinical trials in five African countries. Dr. Wypij is an award-winning lecturer who has taught biostatistics at Harvard School of Public Health since 1989, as well as short courses in Brazil, Gabon, Greece, Italy, and Portugal.

Henry A. Feldman, PhD, Lead Biostatistician

Dr. Feldman joined the CRP in September 2001, bringing long-held interests and extensive experience in medicine, public health, and biological science. He is actively collaborating as Co-Investigator on a variety of research proposals, particularly in the areas of endocrinology and nutrition, and contributing to research training through consultation with fellows and teaching residents. His research publications include clinical and community trials, epidemiological surveys, experiments in human and animal physiology, studies in cellular and biochemical kinetics, and methods for experimental design, data analysis, and mathematical modeling.

Mr. Feldman taught biostatistics full-time at Harvard School of Public Health from 1979-89 and, as Principal Research Scientist at New England Research Institutes from 1990-2001, served as lead analyst and Co-PI for the multi-site Child and Adolescent Trial for Cardiovascular Health (CATCH). He is a Fellow of the American Heart Association Council on Epidemiology and Prevention and a faculty member of the Council's annual postdoctoral training course, the Ten-Day Seminar on Epidemiology and Prevention of Cardiovascular Disease.

Leslie A. Kalish, ScD, Lead Biostatistician and GCRC Director of Biostatistics

Dr. Kalish joined the CRP in April 2003. The focus of Dr. Kalish's professional career has been the design, coordination, and analysis of clinical trials and epidemiologic cohort studies. His statistical research has applied optimal statistical design methodology to treatment allocation procedures for clinical trials and to the selection of control groups in observational epidemiologic studies. Translating this work into practice, he has collaborated on clinical research in many areas, including HIV and other infectious diseases, transfusion medicine, alternative medicine, and oncology. Currently, he serves as the Director of Biostatistics for the General Clinical Research Center.

Before coming to Children's Hospital, Dr. Kalish held leadership positions in the coordinating centers of several multi-center studies at the New England Research Institutes and the Dana Farber Cancer Institute and taught in the Department of Biostatistics at Harvard School of Public Health.

Mei-Chiung Shih, PhD, Senior Biostatistician

Dr. Shih joined the CRP in September 2001. Dr. Shih's statistical research interests focus on statistical methods for genetic epidemiology studies of complex diseases, gene by environment interactions, design and analysis of group sequential clinical trials, and statistical methods for analyzing longitudinal data. She has participated in numerous projects including single- and multi-center clinical trials, genetic association studies of prostate cancer and ovarian cancer, and studies of quality of life in pediatric patients receiving hematopoietic stem cell transplantation and in brain tumor patients. Dr. Shih is also an Assistant Professor of Biostatistics at Harvard School of Public Health.

Prior to joining the CRP, Dr. Shih worked as a Research Statistician at Schering-Plough Research Institute from 1995-1998, and as a Postdoctoral Fellow at Stanford University School of Medicine from 1999 to 2001.

Clarissa Valim, MD, ScD, MSc, SM, Biostatistician

Dr. Valim has a multidisciplinary background, with graduate studies in medicine, epidemiology, and biostatistics. She joined the CRP in June 2003, supporting and collaborating with other investigators in clinical research on protocol development and data analysis. In addition, Dr. Valim works on her methodological research in the estimation of vaccine efficacy and on the team of the NIH-funded Severe Malaria in African Children clinical research network.

Before joining Children's Hospital, Dr. Valim worked in research and taught in Brazil until coming to Harvard for her doctoral studies. Dr. Valim's research interests and activities have focused on epidemiological, methodological, and clinical research in infectious diseases and health services research.

Dionne Graham, PhD, Biostatistician

Dr. Graham joined the CRP in April 2005. She holds a doctorate in biostatistics from Harvard University and a Master's degree in biomedical engineering from Johns Hopkins University. She provides statistical support to hospital researchers, from grant writing and protocol review to the design and analysis of clinical trials. She is also a statistician for the Program for Patient Safety and Quality, for which she assesses the efficacy of various safety and quality initiatives as well as develops measures for monitoring hospital performance.

Dr. Graham's methodological work includes the development of statistical methods for the dimension-reduction and analysis of HIV genotype data as well as for the design of pooled-specimen studies for population-based estimation of the prevalence of drug-resistant HIV. Prior to pursuing her doctorate, she worked as a bioengineer at Advanced Tissue Sciences, Inc. where her research focused on the development of a tissue-engineered vascular graft for use in cardiovascular bypass surgery.

Peter Forbes, MA, Biostatistician

Mr. Forbes joined the CRP as a biostatistician in October 2000. His responsibilities include data cleaning and data set creation, SAS programming, data reporting, data analysis, statistical graphics, and participation in the writing of grants and papers. Before joining the CRP, Mr. Forbes worked at Children's Hospital in the Department of Psychiatry's Learning Disabilities Research Center. His areas of interest include statistical software and programming, data analysis, sample design, and survey research methods.

Daniel Kinnamon, MS, Biostatistician

Mr. Kinnamon joined the CRP in April 2004. He earned a Master's degree in Statistics and a Bachelor's degree in Economics and Latin American Studies from Stanford University. Over summers, he worked in research positions at Strong Capital Management, the World Bank's Mexico City Office, and Criterion Economics, LLC. He also completed the first semester of the PhD program in economics at the Massachusetts Institute of Technology before deciding to pursue his strong and growing interest in Biostatistics by joining the CRP. His responsibilities include data cleaning and data set creation, statistical programming and data analysis, statistical graphics, and participation in the writing of grants and research papers.

Parul Aneja, MS, Biostatistician

Ms. Aneja joined the CRP in August 2005. Before this she was at Brown University, completing her Masters in Biostatistics, which she finished in July 2005. She received her Bachelor's degree in Statistics from Delhi University, India. Her Master's thesis focused on handling dropout in longitudinal data. As a research assistant at Brown, Ms. Aneja developed proficiency in SAS and data handling methods while learning about statistical analysis for medical data.

Her primary CRP responsibilities include data handling, statistical graphics and statistical analysis. She will be primarily working with Adolescent Health for the analytic needs of post doctoral fellows and researchers.

Xi Deng, BS, Biostatistics Research Assistant

Ms. Deng is a doctoral student in Biostatistics at Harvard University. She joined the CRP in July 2004. Before joining the CRP, Ms. Deng was a student at Tsinghua University in China.

Samuel McDaniel, MPhil, Biostatistics Research Assistant

Mr. McDaniel is a doctoral student in Biostatistics at Harvard University. He joined the CRP in August 2003. Before joining the CRP, Mr. McDaniel worked at the University of the West Indies, Jamaica, as a Lecturer in Applied Mathematics.

DATA MANAGEMENT CORE



Carl de Moor, PhD, Director, Lead Biostatistician

Dr. de Moor joined the CRP in September 2004. Dr. de Moor's statistical research interests focus on methods for analyzing longitudinal data, group randomized trials, and optimal methods of assigning participants to treatment conditions. Dr. de Moor has participated in numerous projects in behavioral science including studies in smoking prevention, smoking cessation, cancer screening, fruit and vegetable consumption, quality of life, alcohol consumption, and stress and immune functioning. Prior to joining the CRP, Dr. de Moor

was an Associate Professor of Biostatistics at the University of Texas, Houston School of Public Health (UTHSPH). At UTHSPH he also served as Associate Director of Design and Analysis at the Center for Health Promotion and Prevention Research. Prior to this position, Dr. de Moor was Associate Professor at the University of Texas MD Anderson Cancer Center (UTMDACC) in the Department of Behavioral Sciences and the Department of Biostatistics, and Section Chief, Behavioral Statistics, in the Department of Behavioral Science.

APPLICATIONS DEVELOPMENT TEAM

Jason Rightmyer, MS, Applications Development Team Leader

Mr. Rightmyer joined the CRP in March 2003, and brings extensive experience in clinical research informatics. As the team leader of applications development, he is responsible for directing all software development activities, including setting standards for data management system design and promoting informatics in clinical research. Mr. Rightmyer holds a graduate degree in Health Informatics from the University of Minnesota.

Before joining Children's Hospital, Mr. Rightmyer served as Project Director and Systems Programmer at New England Research Institutes. There he worked primarily on the co-design and development of a proprietary Web-based data management system for clinical and epidemiological research. He has co-authored several NIH Small Business Innovation Research grant proposals and directed a number of additional projects including the development of a computer application for scientific randomization, an evidence-based smoking cessation program, and an expert system for clinical specialists.

Joseph Rezuke, BS, Lead Applications Developer and GCRC Informatics Manager

Mr. Rezuke joined the CRP in August 2002. As a Lead Applications Developer, he has designed several systems for clinical studies, including a laboratory inventory and specimen tracking system for the Pulmonary Medicine Tissue Bank project. Mr. Rezuke also serves as the Informatics Manager for the General Clinical Research Center (GCRC). His current project entails designing and developing a new comprehensive administration system for the GCRC.

Andrew Netson, MS, Senior Applications Developer

Mr. Netson joined the CRP in March 2002. He has a Master's in Engineering and many years of experience as a programmer and applications developer. He has extensive skills and knowledge using a number of database, Web, and application technologies, including Microsoft .NET, Java, and Oracle. He has previously worked for a number of technical companies and healthcare institutions, including the Research and Development Department at Partners Healthcare System.

Roumen Stoyanov, BS, Senior Applications Developer

Mr. Stoyanov has a Bachelor's degree in Computer Science and is a Microsoft Certified Solutions Developer. He is an expert in the analysis, design, and building of software solutions based on Microsoft technologies. Before joining the CRP in July 2003, he worked as a consultant at New England Research Institutes. During his tenure there, he developed a speech recognition software system for clinical evaluation of working memory of geriatric patients and treatment allocation software for randomized clinical trials. Current projects of Mr. Stoyanov include a risk management application for the Program for Patient Safety and Quality and clinical trials data management systems for the Glaser Pediatric Research Network.

Alan Tam, BS, Applications Developer

Mr. Tam has a Bachelor of Science in Systems Engineering and over nine years of programming and applications development experience. He has extensive expertise in C/C++, Microsoft, and other Web technologies. He joined the CRP in January 2003. He works closely with CRP staff members and investigators building applications for clinical research data storage and management.

PROJECT MANAGEMENT TEAM

Maggie McCarthy, MS, MH, Project Director

Ms. McCarthy has an MPH from Harvard School of Public Health and a Master of Clinical Immunology degree from Hahnemann University in Philadelphia. She has been working in the CRP since April 2002 on a number of multi-center studies funded by federal and foundation sponsors. In the past year, she has been instrumental as the Project Manager on three multi-center studies funded by the Glaser Pediatric Research Network, assisting in protocol development, developing CRFs and a manual of operations, and assisting programmers in the development of specifications for data management systems.

Ms. McCarthy has many years of experience in the clinical arena working as a Laboratory Manager and Senior Research Technician. More recently, she had worked for five years as a Clinical Research Associate/Research Scientist at the New England Research Institutes, where she was the Project Director for a number of NIH-funded multi-site studies.

Maureen Clark, MS, Senior Clinical Research Specialist

Ms. Clark joined the CRP in June 2003. Her responsibilities include collaborating with investigators to develop and document clinical research protocols, advising investigators regarding data management systems and data collection tools for their research projects, in addition to developing study-specific data management and quality assurance procedures.

Ms. Clark has a Master's Degree in Clinical Physiology. She has 11 years of experience in clinical trials management. Before joining Children's Hospital, Ms. Clark worked as Manager of Clinical Trials at Massachusetts General Hospital in Pediatric Psychopharmacology and as a Project Manager in the Cardiovascular Division at Brigham and Women's Hospital.

Amy Kroeplin, BA, MPH, Clinical Research Specialist

Amy Kroeplin has 4 years experience in the management of clinical research studies. She has a Bachelor's degree in Biology and Anthropology and a Master's degree in Epidemiology and Biostatistics from Boston University. Ms. Kroeplin is certified in Coordinating Clinical Trials and a member of the Society of Clinical Research Associates (SOCRA) and American Public Health Association (APHA).

Ms. Kroeplin collaborates with principal investigators to develop data collection forms and study manuals of operation, and to train research staff in the conduct of the research protocol. Ms. Kroeplin works closely with the Applications Development group and is responsible for developing detailed specifications of the data management system functionality such as range and logic checks, inter- and intra-form dependency and protocol tracking. Ms. Kroeplin is also committed to developing quality control procedures, data coordination for research studies and managing the flow of data received from study staff. She is responsible for training data entry staff both internal to the Clinical Research Program and personnel hired by the principal investigator to ensure accurate data entry.

Aruna Jayashankar, MS, Clinical Research Specialist

Ms. Jayashankar joined the CRP in August 2005 as a Clinical Research Specialist. She holds a Master's Degree in Biomedical Engineering from the University of Southwestern Medical Center/ University of Texas Arlington and is an active member of the Association of Clinical Research Professionals (ACRP).

Her primary responsibilities include developing data management tools like case report forms, study manuals of operations, and other study-specific quality assurance procedures for the clinical investigators. She prepares training materials and lectures for CRP sponsored courses. Ms. Jayashankar assumes the responsibilities of a Project Data Manager for data management projects including data entry, building databases in SPSS Data Builder, and training the research staff in conducting clinical trials.

Sharon Wong, BS, Research Study Coordinator

Ms. Wong has been working at the CRP since September 2001. Over the summer of 2005, Ms. Wong was promoted to Research Software Developer from her original position of Research Study Coordinator. The promotion was due to one of Ms. Wong's main responsibilities of programming databases. Collaborating with principal investigators and their research teams, she uses SPSS Data Entry Builder to build databases. Ms. Wong also creates specifications for the databases, assists in the creation of the databases with the use of tutorials and supervision, tests the databases, and trains data entry staff.

Ms. Wong is responsible for different tasks for consultation and collaboration-based projects including several single and multi-site studies. The responsibilities include randomization, testing databases, coordinating study data, data entry, data cleaning, performing quality assurance checks, investigating any missing and/or conflicting data, and training and monitoring CRP data entry staff. She also assists the clinical research specialists, and is responsible for generating reports for CRP education courses and studies.

Rajna Filip-Dhima, BS, Research Data Coordinator

Ms. Filip-Dhima joined the CRP in March 2004. She has a Bachelor of Science degree in Psychology and a minor in Philosophy from Northeastern University. While completing her undergraduate studies, Rajna participated in the cooperative education program and worked as a research assistant at MGH, Boston City Hall, and the Laboratory of Social Psychology and Personality at Northeastern University, which further developed her interest and enthusiasm in clinical research. One of her major projects

was a cross-cultural research study she conducted in Albania, where she collected data from 200 participants. She has used this data to study cultural differences in emotional and personality styles between the Albanian and American cultures.

Her current responsibilities include testing study-specific databases, coordinating data sent for both single and multi-center CRP coordinated studies, data-entry and error resolution, data cleaning, performing quality assurance checks on entered data, and following up on any missing and/or conflicting data with clinical center staff.

Kerwin Tang, MA, Research Data Coordinator

Mr. Tang joined the CRP in August 2004 after graduating from Boston University with a Master's degree in Medical Sciences. His research experience includes working as a research assistant in the Infectious Diseases Department at Boston Medical Center and in the Hematology and Oncology Department at Boston University School of Medicine.

Mr. Tang's role as a data coordinator at the CRP is to coordinate data flow for the Glaser Pediatric Research Network sponsored pediatric research studies. His current responsibilities include providing administrative support to the development and implementation of the studies, performing data entry of case reports, communicating with clinical center sites on data queries, and maintaining study data files to ensure organization and confidentiality as required by institutional and federal regulations.

Michael Wake, BA, Glaser Data Coordinator

Mr. Wake joined the CRP in October 2003. He has a degree in Brain and Cognitive Sciences from the University of Rochester. His current responsibilities include testing CRP-developed Web-based databases for Glaser research studies, coordinating data for Glaser studies, data entry and error resolution, data cleaning, performing quality assurance checks on entered data, and following up on any missing and conflicting data. He also assists the clinical research specialists in the editing of case report forms.

ADMINISTRATION AND FINANCE

Terrie Rogers, MS, MBA, Program Administrator

Ms. Rogers has a M.S. in Immunology and an M.B.A., both from the University of Michigan. She has over 20 years of diversified global management experience in the healthcare, CRO, pharmaceutical, biotechnology, and genomics industries. Ms. Rogers has broad expertise and a proven record of accomplishment in healthcare service sales, marketing, project management, and strategic planning. She joined the CRP in November 2003. Ms. Rogers' role in the CRP is to oversee the daily operations of the department on matters of billing, budgets, purchasing, and administrative procedures and personnel. In conjunction with the CRP Director, she is also involved in strategic planning for the CRP.

Laura Haley, Program Administrative Coordinator

Ms. Haley has worked in the administrative field for nearly 20 years. She joined the CRP in July 2003 as Lead Administrative Associate and was promoted in July 2005 to her current position. Her duties include direct administrative support to the Director as well as general Program administration and coordination of the logistics and administration of some CRP-sponsored courses. Ms. Haley is the frontline individual for investigators requesting resources from the CRP, following each new project request to ensure that it has been triaged to the appropriate Program staff.

Patricia Hopkins, BA, Administrative Associate

Ms. Hopkins has a degree in Psychology and Philosophy from Boston University and previous experience in research from working on a study as a Data Coder at the Channing Laboratory, Brigham and Women's Hospital. She joined the CRP in July 2002. Her current responsibilities include providing direct administrative support to the Director of Biostatistics, payroll responsibilities, coordinating aspects of CRP-sponsored courses, general administrative support to CRP staff, and other Program activities. She has been involved in the data entry for a large multi-center clinical trial.

Robin Walker, MSW, Administrative Coordinator, Biostatistics Core

Ms. Walker joined the CRP in August, 2005; she provides overall administrative support and financial management for the Biostatistics Core. She has spent her professional life working in the non-profit sector, most recently as the Administrative Coordinator for the Center on Media and Child Health at Children's Hospital, and as the staff and resident education program coordinator for the Department of Anesthesia at Brigham and Women's Hospital, Boston. Ms. Walker holds a Master of Social Work (M.S.W.) with a concentration in management and planning from Boston University, and a B.A. from the State University of New York (Binghamton University).

Namita Kiran-Thuene, MEd, Administrative Coordinator, Data Management Core

Ms. Kiran-Thuene has a Bachelor's degree in Business Management from Bentley University and a Master's in Education. Prior to joining the CRP in May of 2005, she was a substitute teacher in Lowell Elementary School. Her responsibilities include developing budgets in collaboration with PIs, coordinating post-award budget management, overseeing timely completion of all core staff annual performance, providing administrative support for the core director, and maintaining accurate financial information. Previously, Ms. Thuene worked for Brandeis University and Dana-Farber Cancer Institute. Her work experience includes several years of NIH funded grants management.

CLINICAL RESEARCH EDUCATION CORE



Jenifer Lightdale, MD, MPH, Director

Dr. Lightdale is an Instructor in Pediatrics at Harvard Medical School. She completed fellowship training in outcomes research first at the Institute for Health Policy Studies at the University of California, and later in the Harvard Fellowship in Pediatric Health Services Research. Dr. Lightdale received her Master's degree from the Harvard School of Public Health. She has been on clinical staff at Children's Hospital Boston in Gastroenterology since finishing her Gastroenterology fellowship here in 2001. Dr. Lightdale currently holds

a Mentored Career Development Award from the Agency for Healthcare Research and Quality (KO8 HS013675) to investigate means of improving patient safety for children receiving procedural sedation and analgesia.

Utilization of Services

The Clinical Research Program (CRP) provides a range of services to assist investigators in the design, conduct, and analysis of their clinical research studies. Limited free support has been provided for consultative services to unfunded studies while more support is provided for collaborative relationships with funding.

Services of the Clinical Research Program include:

- Protocol/Grant Proposal Development
- Case Report Form/Survey Design
- Study Design
- Data Management Systems Design
- Sample Size and Power Calculations
- Data Analysis and Interpretation
- Biostatistical Analysis Methods
- Education and Training
- Randomization
- Mentoring

SUMMARY

During FY05, the CRP worked on 326 clinical research projects (Table 1). The majority of these projects (n=251) did not provide funding for CRP staff. Seventy-five (23%) of these projects funded the CRP staff for a total of \$1,346,419.

Table 1. FY05 CRP projects by funding status

	Funding	Total	
	No CRP funds received in FY05	Any CRP funds received in FY05	
No. of Projects	251	75	326
Total CRP FY05 costs	0	\$1,346,419	\$1,346,419

^{*}Includes funding from CHB investigators and extramural funding from CRP faculty

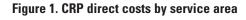
FUNDED PROJECTS

Table 2 and Figure 1 present the distribution of CRP services funded by the 75 projects during FY05 and the amount of support provided to each area. Data Management Services include the combined service areas of Project Management, Database Programming, and Data Entry.

Table 2. Direct costs by service area for 75 projects funding CRP in FY05

Service areas	No. of Projects requiring funded services	FY05 CRP Funding (% of total dollars)
PI	11	\$112,770 (8%)
Biostatistics	67	\$605,222 (45%)
Project Management	31	\$255,208 (19%)
Database Programming	23	\$271,325 (20%)
Data entry	17	\$101,894 (8%)
Total	75*	\$1,346,419 (100%)

^{*}A single project often funds several service areas.



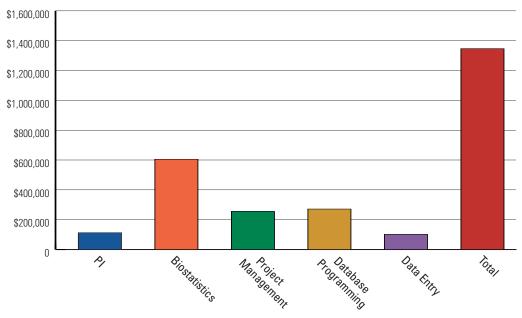


Table 3 presents the distribution of funding sources for the 75 projects providing financial support to the CRP. NIH and Foundations were the primary sources of funding for these projects (45% and 25% of funded projects, respectively). Among the 34 NIH-funded projects, 18 were funded by R01 mechanisms, 2 were R03, 2 were R21, and 6 were other funding mechanisms (K23, R37, M01, P50, etc.).

More than half (n=41) of the 75 funded projects were from collaborations with researchers from the Department of Medicine. The remainder was from various departments in the Hospital including Cardiology, Radiology, Patient Care Operations and Surgery, Laboratory Medicine, Otolaryngology, Neurology, Psychiatry, Anesthesia, and Urology. The Clinical Research Program faculty were PI's on 5 of the 75 projects.

Table 3. Funding sources for 75 projects funding CPR in FY05

	No. of Projects	FY05 CRP Funding (% of total dollars)	
NIH	34	\$745,182 (55%)	
Other Federal	11	\$118,054 (9%)	
Foundation	19	\$437,657 (33%)	
Industry	3	\$16,739 (1%)	
Departmental	6	\$17,860 (1%)	
Other	2	\$10,927 (1%)	
Total	75	\$1,346,419 (100%)	

NEW REQUESTS FOR ASSISTANCE IN FY05

During FY05, the CRP received 262 new requests for assistance from 161 Children's Hospital faculty or staff. The distribution of requests according to hospital department is shown in Figure 2. The majority of requests were from investigators with appointments in Medicine (n=145) and within the Divisions of Emergency Medicine (n=13), Endocrinology (n=22), Adolescent Medicine (n=16), Hematology/Oncology (n=14), GI/Nutrition (n=21), General Pediatrics (n=7), Infectious Diseases (n=6), and Pulmonary (n=7).

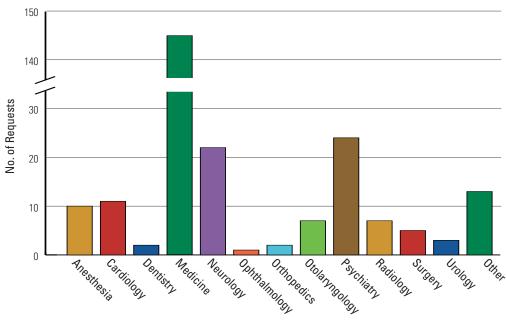


Figure 2. FY05 requests for assistance (n=262 requests)

As shown in Figure 3, investigators requesting assistance were somewhat more likely to be at the rank of Fellow (n=30), Instructor (n=31), or Assistant Professor (n=39) as compared to Associate Professor (n=23) or Professor (n=14).

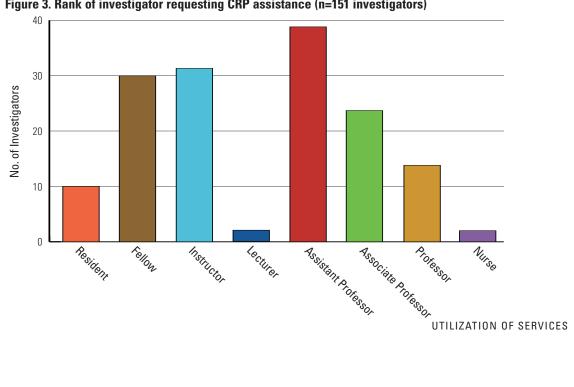


Figure 3. Rank of investigator requesting CRP assistance (n=151 investigators)

As shown in Figure 4, the majority of services were for consultation on design and analysis including estimation of sample size and power (n=104), development of a statistical analysis plan (n=138), study design (n=125), or analyses of data (n=88). Approximately 55 requests were related to data management and study implementation, including case report form development, survey design and/or database assistance.

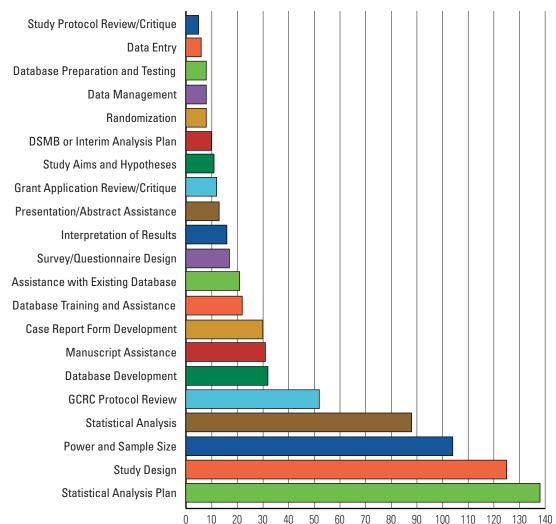


Figure 4. Services requested (n=262 requests)

About one third (n=84) of the 262 new requests for CRP resources had funding to support the project and almost one-third (n=83) were applying for funding. Among the 84 funded projects, NIH (n=27), foundations (n=15), and department funds (n=14) were the primary funding sources. Among those investigators submitting grant proposals for funding, the majority (n=64) were first submissions, whereas the remainder were mainly resubmissions (n=15) or non-competing renewals (n=4).

Among the requests applying for funding, 44 were applying to NIH, 18 to foundations, 4 to other federal, 2 to department funds, and 2 to industry. For the 44 applying to NIH, the mechanisms for funding were 19 for R01s, 3 for R03s, 6 for R21s, 6 for various K awards, 5 for other mechanisms, and 5 unspecified.

Education and Training Courses

The Clinical Research Program (CRP) provides education and training to the clinical research community at Children's Hospital through several courses and seminars offered each year. These include **Orientation** for New Study Coordinators and Coordinator Rounds, which are described below. Agendas for the courses are located in Appendix C.

A. NEW STUDY COORDINATOR ORIENTATION

1. Description

The CRP offers a bi-monthly, one day Orientation for all new study coordinators and research assistants. The Orientation covers many of the relevant topics that coordinators require information about in order to be adequately prepared to conduct clinical research studies at Children's Hospital, Boston.

The Orientation limits registration to 10-12 people per session to facilitate group discussions and allow ample time to answer questions. Topics covered include the following:

- Logistics of conducting a clinical research study;
- Approaches to reduce errors or bias in a study;
- Human subject protection responsibilities for conducting clinical research;
- The unique issues and process of obtaining informed consent in pediatric research;
- How to develop quality case report forms for effective data collection;
- How to develop manuals of operation for effective data collection;
- Approaches for effective data management;
- Approaches for monitoring the quality of data collection;
- Requirements of study audits and close-out activities;
- Organizing and storing study documents;
- How to manage the budget and bill for services or make payments.

2. Overall Evaluation

The following table summarizes participants' overall evaluation for the Orientation sessions that were offered in 2005.

	Orientation Objectives Met*
Overall quality of the Orientation	3.8
Orientation content met expectations	3.8
Orientation provided information that can be useful in clinical research rol	e 3.8
Would recommend Orientation to others	3.8

*Score Range: 1 (Poor) to 4 (Excellent)

B. COORDINATOR ROUNDS

1. Description

The CRP offers a seminar series entitled *Coordinator Rounds* that is held on a monthly basis for clinical research staff. Speakers are invited to lecture on topics relevant to clinical research study staff and address different issues or topics related to coordinator responsibilities in greater depth. Topics and speakers in the 2005 Coordinator Rounds are listed below in addition to the speaker:

Topic	Speaker
Clinical Research at Children's	Carleen Brunelli
Preparing a Regulatory Binder/Study Filing System	Eunice Newbert
Obtaining Informed Consent/Assent	Kristi Thomas
HIPAA-Overview of HIPAA guidelines and how it impacts clinical research	Susan Kornetsky
Strategies for Patient Recruitment	Carol Sweeney
Source Documentation	Vicky Turbini
IRB Submissions/Applications	Christina DiTomasso
Documenting Protocol Errors and Deviations	Eunice Newbert

C. CAREER DEVELOPMENT BLOCK

The Career Development Block (CDB) is an innovative component of training for all senior residents in the Boston Combined Residency Program in Pediatrics, introduced in 2002. Faculty and residents designed the rotation jointly to enhance the residents' knowledge and skills in several areas essential to building a career in academic or clinical pediatrics:

- Conducting pediatric research;
- Absorbing and utilizing new developments in science for clinical practice;
- Identifying and applying policy issues to advocacy for children;
- Improving quality of health care at all levels.

Over the course of the year, CDB is conducted 4 times in 3-month blocks, each block comprising approximately 9 residents. Twice-weekly meetings include seminars taught by investigators, methodologists, clinicians, and ethicists. Additionally, each resident takes on a project in research, education, or clinical practice mentored by faculty drawn from the Harvard and Boston University academic communities. A typical project might be a simple clinical research protocol; an in-depth review of current practice guidelines in a certain area; or development of a laboratory method.

A new format was introduced in 2005 for CRP participation, replacing what were formerly didactic sessions on clinical research methodology. Four times per year, the residents constituting the current Career Development Block conduct a Work-in-Progress session in which they present their projects to a team of senior CRP staff, typically consisting of one clinician and one biostatistician. Discussion and critique can cover a wide range of topics, including the following:

- Study design, including choice of time course, population, subjects, and controls;
- Recruitment and intervention, including special issues for children, groups, and foreign locales;
- Statistical considerations in study design, including sample size, power, effect size, randomization;
- Methods for measurement, data management, analysis, and interpretation of results;
- Critical evaluation of clinical research reports for application to clinical practice;
- Data and safety monitoring;
- Human subjects requirements and ethical considerations for conducting research with children.

Clinical Research Program Spotlights

A. COLLABORATIONS WITH CHB INVESTIGATORS

1. Clinical Trials for Acute Lung Injury, Martha Curley, PI

In recent years, the Clinical Research Program has collaborated with Dr. Martha Curley, Director of Critical Care and Cardiovascular Nursing Research at Children's Hospital Boston, on a variety of research projects, including two major multi-center randomized controlled clinical trials on pediatric patients with acute lung injury. The team from the CRP includes Drs. David Wypij and Mei-Chiung Shih as Senior Statisticians and Co-Investigators, Maggie McCarthy as Clinical Research Associate, Andrew Netson as Applications Developer, and Rajna Filip-Dhima as Data Coordinator.

The first trial, sponsored by the National Institutes of Health/National Institute of Nursing Research (NIH/NINR) and NIH/National Center of Research Resources, was to evaluate the effects of prone positioning on clinical outcomes in pediatric patients with acute lung injury. The rationale was that in uncontrolled clinical studies, prone positioning appeared to be safe and to improve oxygenation in pediatric patients with acute lung injury. The study was designed to enroll 180 pediatric patients from August 2001 through April 2004 at seven pediatric intensive care units (PICU) that participate in the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI), within 48 hours of meeting acute lung injury criteria. Patients randomized to the supine position group remained supine. Patients randomized to the prone position group were positioned prone within 4 hours of randomization and remained prone for 20 hours each day during the acute phase of their illness for a maximum of 7 days then remained supine. Both groups were managed using lung protective ventilator and sedation protocols, extubation readiness testing, and hemodynamic, nutrition, and skin care guidelines. The trial was stopped by the Data and Safety Monitoring Board at the planned interim analysis, after 102 patients had been enrolled, on the basis of the pre-specified futility stopping rule. The study found that prone positioning does not significantly improve ventilator-free days or other clinical outcomes in pediatric patients with acute lung injury. The primary analysis was published in this year's Journal of the American Medical Association, with an editorial discussion in the same issue (JAMA. 2005; 294:229-237). The successful completion of the study was truly a team effort. The Clinical Research Program worked closely with the Principal Investigator, Dr. Curley, and her team from the early stage of study design and grant application though study implementation and publication. In particular, as the Data Coordinating Center, the Clinical Research Program was in charge of study forms development, database development and maintenance, data management and quality control, interim and final data analyses, preparation of interim reports for the Data and Safety Monitoring Board meetings, and publications.

The CRP is also working collaboratively with Dr. Curley on a second clinical trial, a two-year pilot study to test an intervention to change sedation management in pediatric patients supported on mechanical ventilation for acute respiratory failure in the PICU, for which the Clinical Research Program also serves as the Data Coordinating Center. The rationale of the study is that humane care of mechanically ventilated infants and children involves concomitant use of comfort medications such as analgesics and sedatives. Although there is clear evidence of the benefits of medication providing comfort to acutely ill infants and children, evidence has also shown that the inadequate use of comfort medications is associated with iatrogenic injury, depressed spontaneous ventilation and thus prolonged duration of weaning from ventilation, and potential iatrogenic complications. This study, sponsored by NIH/National Institute of Child Health and Human Development (NICHD) and Pfeiffer Foundation, is a randomized controlled clinical trial with delayed intervention on sedation management in the control hospital. Specifically, two participating hospitals are randomized to receive early versus delayed intervention on sedation management. The intervention consists of (a) multidisciplinary team education and consensus building, (b) multidisciplinary team identification of the patient's trajectory of illness and daily prescription of a sedation goal, (c) a nurse-implemented sedation algorithm to guide titration of comfort medications, and (d) team feedback on clinical performance. The hypothesis is that, compared to patients receiving usual care, patients managed per sedation protocol will experience better clinical outcomes. The primary outcome is the duration of mechanical ventilation. Results of this pilot study will be used to design a larger-scale multi-center randomized controlled clinical trial of the new sedation management protocols.

Dr. Curley is also collaboratively involved in the development and psychometric testing of a number of assessment tools for use in the pediatric critical care setting. With the aid of CRP's Survey Design Specialist, Sion Kim Harris, PhD, Dr. Curley has developed the State Behavior Scale (SBS), a measure of the level of sedation/agitation of patients in pediatric intensive care, and the Family-Centered Care Scale (FCCS) which measures the degree to which parents of patients in pediatric intensive care report experiencing nursing care which embodies the principles of family-centered care. A manuscript describing the SBS and its inter-rater reliability and construct validity is currently in press and will be published by the journal, *Pediatric Critical Care Medicine*.

2. BASH-II, David Ludwig, PI

The CRP has worked collaboratively with Dr. David Ludwig and his Obesity Program on research projects targeting prevention and treatment of obesity in children. Sugar-sweetened beverages are increasingly recognized as an important source of excessive caloric intake in adolescents and thus a contributing cause to the epidemic of childhood obesity. The BASH study (Beverages and Student Health), an NIH-funded randomized controlled pilot trial, was initiated in 2002 by Drs. David Ludwig and Cara Ebbeling of the Children's Hospital Endocrine Division, with Drs. Osganian and Feldman of CRP playing a significant role in the design and implementation and serving as Co-Investigators. Dr. Virginia Chomitz, a Senior Scientist at the Institute for Community Health in Cambridge and HMS Lecturer on Medicine, also served as Co-Investigator and an important liaison with the community and schools.

The novel BASH intervention involved delivering a regular supply of sugar-free substitute beverages to adolescents' homes, along with educational and promotional materials and motivational counseling via telephone to discourage consumption of sugar-sweetened drinks. This pilot-scale trial was conducted at Cambridge Rindge and Latin High School, and Star Markets contributed both the supply and the delivery of substitute beverages. The successful results, a differential loss of approximately 5 lb over the 25-week program in the more obese adolescents, will be published in *Pediatrics* in 2006.

Close on the heels of BASH comes BASH-II, a 5-year full-scale multi-site randomized trial that was approved and funded by NIH in 2005 and will be launched in the coming year. Again the Principal Investigator is Dr. Ludwig, with Dr. Ebbeling as Co-PI and Drs. Osganian, Feldman, and Chomitz as Co-Investigators. In BASH-II the key feature of the intervention will again be home delivery of sugarfree beverages at no cost to the participants. Education and behavior modification will be directed at both the adolescent subjects and their parents, at home and at school. An important new direction, driven by the results of the pilot trial, is that enrollment will be restricted to obese adolescents (>85th percentile for age and sex), in whom the program was proven to produce weight loss. The BASH-II intervention will be applied for a longer duration (1 yr vs 25 wk) and to more adolescents (240 vs. 103) in more schools (4 vs 1), covering a wide geographic range around Boston: besides Cambridge Rindge and Latin, which will again participate, agreements are in place from Billerica Memorial High school, Dedham Public Schools, and Somerville High School. Final evaluation will take place at two years, i.e., one year *after* cessation of the intervention. The implicit hypothesis is thus that the benefits of the intervention will carry over beyond the period of free delivery, owing to the concurrent education and motivational counseling.

3. The Center for Adolescent Substance Abuse Research, John Knight, MD

The Center for Adolescent Substance Abuse Research (CeASAR) at Children's Hospital Boston was established in 1999 by Dr. John Knight to discover new ways to identify and reduce substance abuse and related disorders in children and adolescents and to provide national leadership in the prevention, diagnosis and treatment of substance-related disorders as they affect children and adolescents. The Center conducts research, teaching and training in the field of adolescent substance abuse, and provides clinical services through the Adolescent Substance Abuse Program (ASAP). Through its research, CeASAR is developing evidence-based strategies to help pediatricians and other health care providers identify adolescent substance use at its onset and intervene before serious harm results. In addition to Dr. John Knight, the Center also includes Dr. Sharon Levy and Dr. Celeste Wilson, both clinician researchers. The CRP has supported the work of CeASAR since its inception, and contributed to its growth over the years, through consultation on grant proposal development, study design and implementation, assessment methods, psychometric evaluation of instruments, and statistical analysis provided by Dr. Sion Kim Harris, Epidemiologist and Survey Design Specialist with the CRP and an Associate Investigator with CeASAR, and Dr. Carl de Moor, Lead Biostatistician with the CRP.

One key research area in which CeASAR is a demonstrated leader is brief screening of adolescents for substance use problems by health care professionals in medical office settings. CeASAR investigators developed and tested a brief screening tool, known by the mnemonic, CRAFFT, based on the first letter of a key word in each of the 6 easy-to-remember yes/no questions. Initial studies of the psychometric properties of the CRAFFT supported its reliability and validity. Due to its ease of use and published psychometric properties, the CRAFFT screen is now widely used by health care providers throughout the U.S. and internationally. Most recently, a large scale implementation of CRAFFT screening was conducted of over 2,000 adolescent patients from a diverse network of 6 medical office sites serving youth throughout New England, called the New England Partnership for Substance Abuse Research (NEPSAR).

In addition, the CeASAR team conducts studies on new methods of brief office-based therapeutic interventions. In 2004, CeASAR was awarded two 5-year R01 grants by the National Institute of Drug Abuse. In one study, a CRAFFT screening and brief intervention program that is appropriate for youth at all levels of substance use and can be easily applied by busy primary care providers is being developed and evaluated. The other study is a randomized controlled clinical trial of a 3-session motivational enhancement intervention for adolescents who have potentially serious levels of drug and alcohol use.

4. Patient Registries

In an effort to enhance the collection and utilization of data collected on patients, the CRP is collaborating with investigators and departments on pilot projects to develop patient registries. In FY05, Dr. Voula Osganian, Dr. Dionne Graham, and Ms. Maureen Clark worked with Dr. Joe Wolfsdorf, Dr. Maryanne Quinn and others in the Diabetes Program to develop a pilot of a registry for patients receiving their diabetes care at Children's Hospital Boston. The goal of the registry is to track patients over time from initial diagnosis through follow-up outpatient clinic visits. Data that will be collected include demographics, prescribed treatments, clinical characteristics, and laboratory data. The database will be used to assess the quality of care provided by the Diabetes Program as well as provide a rich source of data for future health services and clinical research projects. During FY05, the group worked together to identify variables and create data forms. These forms are now being piloted in the clinics. In FY06, the forms will be finalized and database construction and implementation are scheduled to take place.

B. COLLABORATIONS WITH EXTERNAL INVESTIGATORS AND INSTITUTIONS

1. A School Nurse-delivered Smoking Cessation Intervention for Adolescents, University of Massachusetts Medical School

Dr. Osganian has worked collaboratively as Co-PI on a subcontract with the University of Massachusetts Medical School to develop and evaluate a school nurse-delivered smoking cessation intervention for adolescents (*Evaluation of a School Nurse-Delivered Tobacco Cessation Intervention for Adolescents*, Massachusetts Department of Public Health, School Health Unit: Lori Pbert, PI; Stavroula Osganian, Co-PI and Director of Evaluation; 2002-2003).

Smoking is the largest preventable cause of disease and premature death in the United States, with smoking during adolescence being the greatest predictor of adult smoking. The DPH funded, school nurse-delivered intervention tested in the pilot study was a patient-centered counseled approach, based on social cognitive theory and the Public Health Service (PHS) clinical practice guideline, which is endorsed by the American Academy of Pediatrics for use by pediatric providers for the treatment of tobacco use and dependence in adolescents. The pilot was a cluster randomized controlled school-based trial conducted in 72 public high schools in Massachusetts with 1148 students enrolled in grades 9-12. Students completed a self-administered survey at baseline and 6 weeks and 3 months after baseline to assess smoking status. The primary outcome was defined as no smoking in the past 30 days. The proportion of students who reported quitting smoking, defined as not smoking any cigarettes in the past 30 days, was significantly greater in the intervention schools compared to control schools at both six weeks (OR=7.3; 95% CI 3.4-15.6) and three months after baseline (OR=5.9; 95% CI 3.6-9.6). The pilot study found that a smoking cessation counseling intervention for adolescents was feasible for school nurses to conduct in the school setting and successful in assisting

some students who are interested in quiting smoking to quit smoking in the short-term. The results have been submitted to *Preventive Medicine* for publication. Although the findings from the pilot were very encouraging, limitations of the study included lack of biochemical validation of smoking status and lack of long-term follow-up. Drs. Pbert and Osganian worked collaboratively on a subsequent application to NIH that was recently funded by the NCI to conduct a 4-year school-based randomized controlled trial to evaluate the effectiveness of this same intervention in increasing 30 day abstinence rates over a 1-year period and with biochemical validation of smoking status.

2. Fulbright-Sponsored Teaching and Study Collaboration in Brazil

For three weeks during April-May 2005, Dr. David Wypij served as a Fulbright Senior Specialist focusing on Public/Global Health at the Federal University of Ceara, in Fortaleza, Brazil. Dr. Wypij presented three short courses (one each week) to faculty, staff, and students at the university, with applications to epidemiology and infectious diseases. The three courses focused on (1) methodology for clinical trials, with practical applications in the design, conduct, and analysis of trials; (2) longitudinal data methods, including methods for clustered observations and time series; and (3) modern graphical methods for regression analysis, including smoothing, splines, and generalized additive models, with several real data sets that used these methods (see below). This was Dr. Wypij's third trip to Brazil related to teaching and collaboration with Brazilian colleagues. Dr. Ligia Kerr-Pontes of the Federal University of Ceara hosted Dr. Wypij's visit.

In addition to the short courses, Dr. Wypij collaborated on studies of HIV risk reduction habits, binge drinking, and drug use among MSM (men who have sex with men) in a large study of 600 men from three cities in the state of Ceara. He worked with faculty members and students on data cleaning, definition of composite variables, descriptive statistics, and regression methods. One abstract from this work was recently submitted; Dr. Kerr-Pontes and two Brazilian students continue to work on this data (one a doctoral student in epidemiology, the other a physician in a Master's program), and several papers will be completed in the coming years.

After leaving Fortaleza, Dr. Wypij spent several days at the Institute of Social Medicine at the University of the State of Rio de Janeiro. There he presented an extended afternoon lecture on the use of generalized additive models in the analysis of epidemiologic data. One highlighted example was the recent work of Dr. Chris Almond and others at Children's Hospital, who worked with Dr. Wypij and Dr. Clarissa Valim of the CRP to study predictors of hyponatremia among runners in the Boston Marathon (published in the New England Journal of Medicine in 2005). In that work, generalized additive models were used to demonstrate that weight change and race duration had linear effects on the logit scale to predict hyponatremia, but body mass index had a clear non-linear (nearly quadratic) relationship, with runners with either lowest or highest body mass index having increased risk of hyponatremia. A second example involved work of Dr. Wypij with Dr. Jane Newburger and others at Children's Hospital looking at the effects of duration of deep hypothermic circulatory arrest in infant heart surgery on late development (published in the Journal of Thoracic and Cardiovascular Surgery in 2003). In that work, nonparametric regression and piecewise linear models suggested that neurodevelopmental outcomes at age 8 years were not linearly related to duration of circulatory arrest, but that there was a threshold effect. Little to no effect was observed for shorter durations, but there was a strong, linear decline in outcomes beyond an estimated threshold of 41 minutes.

C. GLASER PEDIATRIC RESEARCH NETWORK

Since September, 2002, the CRP has held a contractual agreement with the Glaser Pediatric Research Network (GPRN) to serve as Design, Analysis, and Coordinating Center for the network's program of pediatric research and training, with Dr. David Wypij as Principal Investigator. The contract was renewed in 2005 for a three-year term.

Based at Stanford University, and including a Boston site as well as four others in Texas and California, GPRN is a component of the Elizabeth Glaser Pediatric AIDS Foundation, a privately funded organization created in 1988. The Foundation has an international reach and a broad agenda including prevention, advocacy, and research in AIDS. The research network was launched in 2000 with the mission of conducting collaborative research on other serious pediatric illnesses, drawing from the diverse patient populations and the deep pool of investigators available at five major pediatric research institutions. An important adjunct mission is to draw young investigators into collaborative research careers through a sponsored fellowship. The organization of GPRN is detailed in Table 1.

Table 1. Glaser Pediatric Research Network

Scientific Director			
Charles Prober, MD	Stanford University		
Site Directors			
Darrell Wilson, MD Lisa Bomgaars, MD Christopher Duggan, MD Ted Moore, MD Emily von Scheven, MD	Lucile Salter Packard Children's Hospital, Stanford University Medical Center Texas Children's Hospital, Baylor College of Medicine Children's Hospital Boston, Harvard Medical School Mattel Children's Hospital, University of California, Los Angeles Children's Medical Center, University of California, San Francisco		
Design, Analysis & Coordination Center			
David Wypij, PhD	CRP, Children's Hospital Boston, Harvard Medical School		

In 2005 GPRN significantly advanced its research activities with intensive participation and leadership from CRP. Drs. David Wypij, Henry Feldman, and Stavroula Osganian each acted as coordinating-center PI for one GPRN multi-site study. Maggie McCarthy, Project Director at CRP, devoted the bulk of her time to managing operations for these studies. Highlights include the following:

- The CRP contract was extended thru 2008.
- The multi-site Phase I/II trial of rituximab in children with chronic immune thrombocytopenic purpura, for which GPRN provided 5 of 10 sites, completed its primary evaluation period and published the findings in *Blood*.
- CRP contributed substantially to the preparation of a submitted article on the trial of alendronate for osteoporosis.
- The drug-treatment trial of obese adolescents attained full enrollment, published several abstracts from baseline data, and made two reports to the Data and Safety Monitoring Board including an interim conditional power analysis.

A development of potential significance was the July, 2005 report of an ad hoc GPRN External Review Committee. Among its findings, the committee endorsed the role of CRP in the network's operations and found it had worked effectively with the investigators from different centers. The committee also cited the GPRN training program, in which CRP plays a central role, as the "most mature" component of the network. For the future, the committee recommended building on current strengths, expanding study design capability, seeking funding partners, and increasing the number of sites with selection based on merit. Each of those recommendations, if implemented, would indicate an expanded role for CRP.

CRP functions in several ways in the operations of the Glaser Research Network. First, it serves as a Core resource, lending expertise in the design and conduct of clinical research to help the network develop and foster its programs. CRP Core Investigators, including Drs. Wypij, Osganian, Feldman, and Kalish, participate in the evaluation of new research proposals and attend periodic meetings of the GPRN leadership at which progress of current projects is reviewed. CRP is also consulted *ad hoc* by the Glaser Scientific Director as issues arise in the conduct of ongoing studies (including those predating the CRP agreement, in which CRP has no direct role), particularly where statistical or design questions are concerned.

A second Core function of CRP is to act as a training resource. CRP reserves places for the GPRN fellows at its three-day course, Introduction to Clinical Research, providing an opportunity for intensive methodological orientation at the start of their first fellowship year. Following up the course with first-year fellows, Dr. Feldman organizes a monthly Work-in-Progress Seminar via telephone, at which the fellows present and jointly critique each other's protocols. In 2005 Dr. Kalish and Dr. Charles Prober, GPRN Scientific Director, instituted a similar series of Work-in-Progress conference calls for second-year fellows focused on developing K-series training award applications. In July 2005, immediately following the summer course, CRP collaborated with GPRN and Johnson & Johnson to present a short symposium in Boston featuring both technical topics and career-building perspectives. Dr. Rick Martinez, Medical Director for J&J, lectured on Career Development. Dr. Jesse Berlin, Senior Director for Statistical Science in J&J Pharmaceutical Research and Development, surveyed Statistical Power and the Ethics of Clinical Research. Finally Dr. Donald Goldmann, Professor of Pediatrics in the Infectious Diseases Division of Children's Hospital and member of the GPRN Sponsors' Committee, led a discussion of epidemiological evidence in drug-safety negotiations between the pharmaceutical industry and the Food and Drug Administration. Dr. Christopher Duggan, a member of the CRP clinical faculty and Boston site director for GPRN, organized and coordinated the event.

Finally and most substantially, CRP has served the Glaser network since 2002 as the data coordinating center for its multi-site studies, each via separate contract. As of fall 2005, agreements were in effect for two clinical trials and one registry project, listed in Table 2. Members of the CRP staff are assigned to the full variety of clinical research tasks for these studies, including statistical planning, design of case report forms, database programming, randomization, data management, preparation of data and safety monitoring reports, and presentation and authorship of final results.

Table	2.	Active	GPRN	studies
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Title	CRP role, key personnel	Start	Term (yr)	Enrollment (% of final)
Multi-center trial of metformin for treatment of obesity in adolescents	Coordinating Center: S. Osganian (PI) H. Feldman (Biostatistician M. McCarthy (Coordinator	•	4	97 baseline studies, 77 randomized (100%)
Multi-center neonatal surgical database: necrotizing enterocolitis	Coordinating Center: D. Wypij (PI)	Dec. 2002	3	249 enrolled 204 completed follow-up
Multi-center open-label Phase I/II trial of rituximab for chronic, severe idiopathic thrombocytopenic purpura in children and adolescents	Coordinating Center: H. Feldman (PI/Biostatistician) M. McCarthy (Coordinator)	May 2003	3	36 (100%)
Multi-center randomized trial of alendronate treatment for children receiving high doses of steroids	Advisory: D. Wypij	July 2002	4.5	26 (100%)
Pharmacokinetics of doxorubicin	Advisory: D. Wypij	Jan., 2003	2.5	22 (49%)
Palliative care and quality of life: children's, parents', and physicians' perceptions	Advisory: L. Kalish	Aug., 2004	2	37 (74%)

In sum, our involvement with GPRN has met expectations as a fertile and rewarding collaboration and over the next several years should help to place CRP in a prominent leadership role among U.S. pediatric hospitals sponsoring clinical research.

D. GENERAL CLINICAL RESEARCH CENTER (GCRC)

One of the most important areas in which the CRP contributes methodological support to the hospital is through its work with the General Clinical Research Center (GCRC). The GCRC provides clinical research infrastructure support for patient oriented research. At any one time, there may be over 200 active protocols with GCRC support. CRP efforts on the behalf of the GCRC are on several fronts: administrative leadership, biostatistics, informatics, and education. With additional support from other CRP staff, these efforts are directed by Dr. Stavroula Osganian, Associate Director, Dr. Leslie Kalish, Director of Biostatistics, and Mr. Joseph Rezuke, Informatics Manager.

As Director of Biostatistics for the GCRC, Dr. Kalish coordinates the biostatistical review of all protocols in which consideration is given to general study design (including control groups, randomization, and blinding mechanisms, as appropriate), statement of aims and hypotheses, eligibility criteria, predictor and outcome variables, data collection procedures, data management, statistical analysis plans, and statistical power and sample size. Prior to Institutional Review Board (IRB) review, all protocols using GCRC resources must first pass scientific review by the GCRC, including a thorough biostatistical review. Written statistical reviews are provided to the investigators and to the primary scientific reviewers for the GCRC Scientific Advisory Committee. Sixty-five written reviews were completed during Fiscal Year 2005. If the biostatistical review calls for revisions or clarifications in these areas, investigators may request CRP assistance. We encourage investigators to request these support services prior to protocol submission. In addition, once a GCRC protocol

is activated, all of the CRP support services such as assistance with case report form design, data management system, randomization procedures, statistical analyses, etc, are available through the CRP's "Request for Assistance" mechanism.

As Informatics Manager for the GCRC, Joseph Rezuke leads the CRP informatics support, which includes helping GCRC manage the scientific review process for newly proposed studies, tracking laboratory specimens, administrative management support, and database development for research projects. Recent informatics activities include designing and developing a new system, the Clinical Research Executive Management Application (CREMA), which facilitates tracking of protocol status, budgets and patient level information. A Core-Lab sample inventory and tracking system, which has been online for about a year, is now integrated within CREMA and has printed more than 4,600 bar coded specimen labels identifying the sample by protocol, subject number, type of specimen and its location. Having the lab program integrated within CREMA makes it possible to inventory specimens by patient or by study. A reporting system allows the user to access reports from CREMA using a Web browser. A Protocol Review Process System developed during the past fiscal year will soon automate many steps in the administration of the Scientific Review process, such as written communications between reviewers and investigators, automatic email notifications of document changes, and tracking the review status from submission to approval. With this system, multiple personnel can view and edit a common "shared" document, with a record of all changes kept automatically as a backup.

E. PROGRAM FOR PATIENT SAFETY AND QUALITY

In January 2005, the CRP began collaboration with CHB's newly formed Program for Patient Safety and Quality (PPSQ). Under the direction of Dr. Kathy Jenkins, the identified initiatives of this program are: (1) implementation of an improved strategy for patient safety; (2) improvement of adverse event screening, reporting, and review; (3) development of an infrastructure for hospital-based measurement; and (4) development of a meaningful hospital quality dashboard. The program has grown over the year and is currently made up of an administrative director, four nurse risk managers, two clinical research nurses, three patient safety specialists, a manager of compliance and standards, and three administrative staff. In addition to the staff are the PPSQ Measurement Committee and the PPSQ Implementation Committee, both of which are made up of clinicians, nurse researchers, pharmacists, and administrators from almost all areas of the hospital. The charge of these committees is to identify, develop, implement, and assess hospital-wide measurement strategies. As part of the collaboration with the CRP, Dr. Dionne Graham provides statistical support and expertise to program initiatives and is a member of the PPSQ Measurement Committee. Mr. Roumen Stoyanov is the program's database programmer.

One of the major accomplishments of the Program in 2005 was the development of the Comprehensive Quality Report which measures the quality of patient care in all facets of the hospital. The report will be presented to the Board of Trustees on an on-going, quarterly basis. Based on the Institutes of Medicine "Steps to Quality" which states that patient care should be effective, timely, efficient, safe, patient-centered, and equitable, examples of the 22 outcome measures comprising the report include: quarterly medication error rate, 3-year standardized mortality rate following solid organ transplant, immunization rate among 2 year olds receiving their primary care at CHB, and monthly median waiting time in the Emergency Department. Dr. Graham was involved in developing the measurement plans for the report and will be responsible for future related statistical analyses, including the development of risk adjustment models for external benchmarking of the measures.

In May 2005, the Program administered a two-part survey-one on the Coordination of Care of Complex Patients and the other regarding Trainee Supervision. Performed as follow-up to surveys administered in 2003 and 2004, 180 surveys were randomly distributed to residents, fellows, and attending physicians. The aim of the first part of the survey was to measure the effect of the new Associate Attending policy with questions regarding the communication between specialties during the care of complex patients. The second part focused on issues regarding communication between trainees and attending physicians when trainees encountered questions and critical patient events. The results of the survey, which were presented to the Senior Clinical Leadership Council, showed improvement over time in the communication between trainee and attending physicians. Dr. Sion Kim-Harris was instrumental in designing the survey and Dr. Graham was responsible for survey administration, analysis of results, and writing the final report.

In 2005 CHB, under the leadership of PPSQ, began active participation in the Pediatric Health Information Systems (PHIS) database. This large administrative database contains over five years of data on all inpatient discharges (over 3 million records) at 37 free-standing children's hospitals in the United States. The comparative nature of the data will allow for external benchmarking of several measures of the Comprehensive Quality Report as well as provide a rich source of data for various clinical, health services, and financial research projects. For example, the data from PHIS will be used to compare the risk-adjusted median LOS at CHB (a Quality Report measure) to the LOS experience by patients in the other PHIS hospitals. Further, PPSQ in collaboration with researchers in the Department of Otolaryngology have initiated a study to describe the clinical characteristics of children undergoing tonsillectomy as well as to identify predictors of ICU admission and hospital readmission following tonsillectomy. Dr. Graham will serve as PHIS liaison to hospital researchers seeking access to the database as well as perform statistical analyses related to PPSQ initiatives using PHIS.

One of the initial strategic goals of the new collaborative relationship between PPSQ and the CRP was to provide PPSQ with basic applications development assistance. Since then, this relationship has expanded and now includes more comprehensive informatics and analytical support. Currently, there are several ongoing consultative, software development and analytical projects that are addressing immediate PPSQ initiatives and improving dramatically the effectiveness of PPSQ.

The Safety Event Administrative Management Application (SEAMA) is one example of the ongoing software application development support provided by the CRP. SEAMA is a software and database application that will facilitate identifying, investigating and tracking patient safety events reported at Children's Hospital. It is planned to function as a case management and reporting tool on top of the hospital's Safety Event Reporting System (SERS) and is expected to quickly become the central tool for all PPSQ investigative operations, facilitating the work of staff to manage all clinically-reported safety events. The SEAMA system was implemented using cutting edge design and technology based on industry standard, service-oriented architectural guidelines. Specifically, the system is accessed using a Windows Smart Client application that delivers a rich graphical user interface over the hospital's secure Intranet. This client application communicates directly with the SEAMA system through a collection of Web-based services. As a result, the client can access and manage data from multiple disparate hospital databases while using a single Windows application.

The major features and functionality of the SEAMA client application include:

- Browsing safety events from multiple data sources (Figure 1);
- Importing source safety events into SEAMA cases (Figure 2);
- Grouping and managing multiple source events as a single case;
- Tracking case artifacts including documents, meetings, agency reports and site visits (Figure 3);
- Managing associations between events, cases and related clinical staff;
- Enforcing secure access through user authentication and authorization; and
- Providing asynchronous and disconnected mode of operation.

Future enhancements of the system will include implementing reporting components, integrating additional data sources, and facilitating interoperability with analytical toolsets.

The following screen-shots display the features of SEAMA.

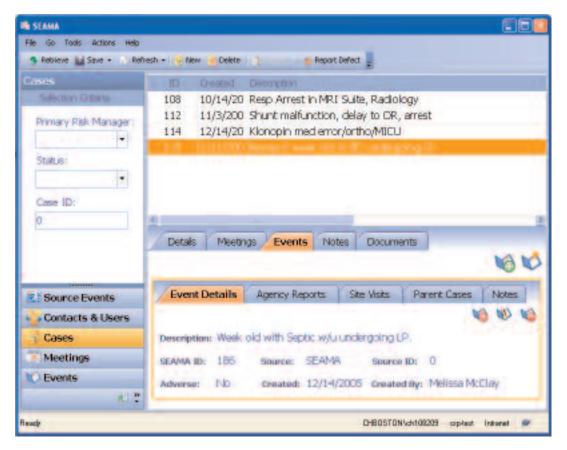


Figure 1. Browsing case events

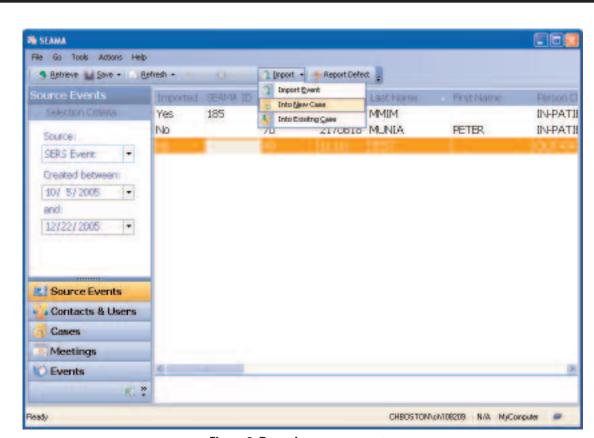


Figure 2. Browsing source events

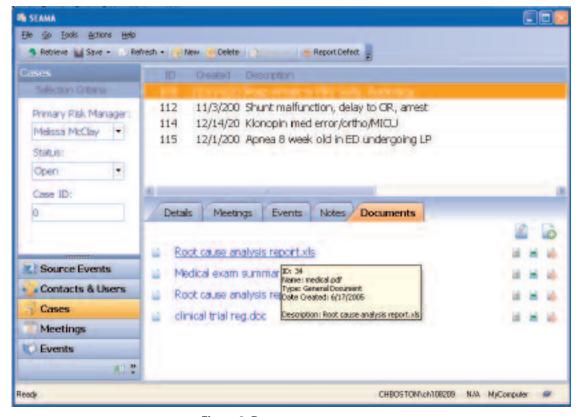


Figure 3. Document management

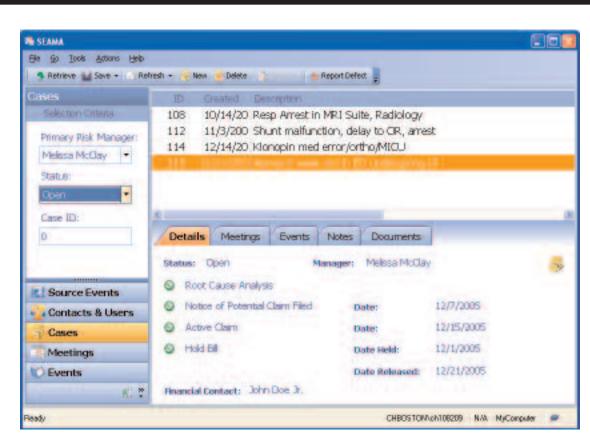


Figure 4. Browsing cases

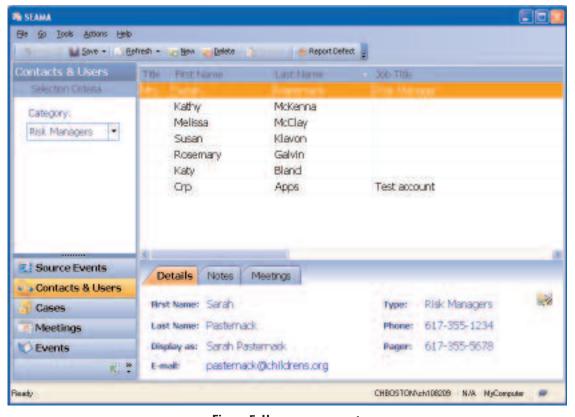


Figure 5. User management

Collaborative Projects

The Clinical Research Program works collaboratively with numerous Children's Hospital Boston investigators from a wide variety of disciplines. The program presently provides such support to the following funded studies (all dollar figures represent Annual Direct Cost).

A. FEDERAL AWARDS

R01 HD045763 (Austin) NIH/NIMH 07/01/04-04/30/08

\$60,320

Sexual Orientation and Health Disparities in Adolescence

This project is a prospective epidemiological study of the distribution and determinants of sexual orientation group disparities in health in the *Growing Up Today Study*, a national longitudinal cohort of over 16,000 adolescents.

5 U01 CA81457 (Boyett/CHB subcontract: Poussaint)

04/01/04-03/31/09

\$188,471

Pediatric Brain Tumor Consortium (PBTC)

The primary goal of this project is the establishment of a Neuroimaging Center for the Consortium. The center will develop and coordinate imaging protocols of PBTC trials, collect images, analyze data sets, and establish a database of imaging results.

R01 DK062363 (Castillo)

09/30/02-6/30/07

NIH/NIDDK

NIH/NCI

\$391,304

Metabolism of Endothelial Dysfunction in Renal Disease

The major goals of this project are to conduct a randomized, controlled, mechanistic study of the *in vivo* regulatory mechanisms of the metabolic pathways involved in endothelial dysfunction, in end stage renal disease and chronic renal disease patients and in healthy controls.

R01 NR05336 (Curley) NIH/NINR 3/01/01-02/28/06

\$327,550

Effect of Prone Positioning in Pediatric Acute Lung Injury

The major goals of this project are to conduct a multi-center, randomized, non-crossover, controlled clinical trial comparing early, repeated, and prolonged prone positioning with supine positioning in children with acute lung injury or acute respiratory distress syndrome.

R21 HD045020 (Curley) NIH/NICHD 09/01/03-08/31/05

\$125,000

Sedation Management in Pediatric Patients Supported on Mechanical Ventilation for Acute Respiratory Failure

The purpose of this two-year project (randomized controlled clinical trial of two matched pediatric intensive care units in two different hospitals) is to pilot test an intervention to change sedation

management in pediatric patients supported on mechanical ventilation for acute respiratory failure in the pediatric intensive care unit (PICU). The hypothesis is that pediatric patients managed per sedation protocol will experience fewer days of mechanical ventilation than patients receiving usual care.

R21 DK065085 (Field) 04/01/04-03/31/06 NIH/NIDDK \$100,000

Weight Control and Weight Change Among Adolescents

The aim of this study is to assess the behavioral predictors of weight gain and the development of overweight and obesity in adolescence and early adulthood in the National Longitudinal Study of Adolescent Health.

R01 (Galler / CHB subcontract: Waber) 05/01/04-04/30/09
NIH/NIMH \$51,821
30 Year Follow-up of Mental Health Outcomes Following Childhood Malnutrition

The goal of this project is to assess the long-term cognitive and mental health consequences of infant malnutrition in adulthood. Individuals who were followed from infancy through late adolescence will now be re-evaluated as adults in order to determine whether and how effects that persisted through adolescence may be evident among adults, and if so, what their consequences are for those individuals regarding mental health and adaptation.

R01 HD043869 (Gordon) 04/01/04-01/31/08 NIH/NICHD \$180,000

Effects of Adrenal and Gonadal Hormone Replacement in Young Women with Anorexia Nervosa

A randomized, controlled trial in young women with anorexia nervosa, designed to measure the effects of an 18-month course of adrenal and gonadal steroid replacement on bone mass, markers of bone turnover, serum levels of IGF-I, and bone strength as assessed through cross-sectional geometric analysis of DXA data.

R01 HD041531 (Jaksic) 02/05/03-12/31/05 NIH/NICHD \$157,500

Protein Metabolism in Critically Ill Surgical Neonates

The project is designed to determine if the application of a hyperinsulinemic euglycemic clamp in parenterally fed neonates on Extracorporeal Life Support (ECLS) will result in an improvement in protein balance, and to elucidate the mechanisms by which the change occurs.

R01 DC05248 (Kenna) 8/16/02-07/31/06 NIH/NIDCD \$225,000

Genetics and Pediatric Nonsyndromic Hearing Loss

A prospective cohort study to describe the phenotypic pattern of temporal bone abnormalities, progression of hearing loss, and cognitive development in infants and children with Cx26 mutations in relation to other children with nonsyndromic sensorineural hearing loss.

R01 DA018848 (Knight)

NIH/NIDA

09/30/04-08/31/09 \$427,900

Screening and Brief Advice to Reduce Teen Substance Abuse

The overall goal of this project is to augment the screening/brief advice intervention with educational materials, and then to assess the efficacy of this approach within a network of primary care practices.

R01 DA014553 (Knight) NIH/NIDA

06/01/04-03/31/09 \$250,000

A Medical Office Intervention for Adolescent Drug Use

A randomized trial of a brief intervention, developmentally appropriate for adolescents and practical for use in busy clinic settings, designed to test its effect on drug use, engagement in treatment, and other substance-related outcomes. Factors that moderate or mediate the effect of intervention will be identified and measured.

R37 AI24643 (Lagakos/subcontract)

4/1/87-1/31/06

NIH/NIAID Statistical Methods in AIDS Research \$21,919 (salary only)

The major goals of this project are to conduct biostatistical research in problems arising in HIV/AIDS research.

R01 MH59532 (Laird/subcontract)

9/30/98-11/30/05 \$22,682 (salary only)

NIH/NIMH

Family Based Tests of Association for Complex Diseases

The major goal of this project is to enable the discovery of genes underlying complex traits using family-based association tests that detect linkage disequilibrium while protecting against spurious evidence of association due to population admixture.

R01 EB01998 (Levine/CHB subcontract: Estroff) NIH/BIDMC

07/01/03-05/31/08

\$184,282

MRI of Fetal Ventriculomegaly: Morphology and Outcome

Comparison of Magnetic Resonance Imaging to ultrasound for prenatal diagnosis, pregnancy management, and prediction of newborn cognitive, motor, and psychosocial development in cases of ventriculomegaly.

R01 DK59240 (Ludwig) NIH/NIDDK

4/01/02-2/28/06 \$190,739

Glycemic Index, Obesity, Insulin Resistance, and CVD Risk

Two related studies in obese adolescents: (1) a randomized controlled trial of a low-glycemic-index diet for treatment of obesity and prevention of related complications; (2) a crossover feeding study investigating the effects of weight-maintaining diets differing in glycemic index on insulin resistance and cardiovascular risk factors.

R01 DK59240-S1 (Ludwig/Botero)

NIH/NIDDK

4/01/02-2/28/06 \$103,189

Glycemic Index, Obesity, Insulin Resistance, and CVD Risk

(Research Supplement for Underrepresented Minorities)

Two related studies in obese adolescents: (1) a randomized controlled trial of a low-glycemic-index diet for treatment of obesity and prevention of related complications; (2) a crossover feeding study investigating the effects of weight-maintaining diets differing in glycemic index on insulin resistance and cardiovascular risk factors.

M01 RR02172 (Mandell)

04/01/04-03/31/09

NIH/NCRR

\$2,020,048

General Clinical Research Center

The major goal of this project is to provide the clinical research infrastructure for medical scientists who conduct patient-oriented research.

200-2003-01601 (Mandl)

09/12/03-11/30/04

DHHS/CDC

\$136,263

Pediatric Hospital Based Sentinel Surveillance Network for Vaccine Preventable Diseases

The purpose of this project is to determine the feasibility of conducting surveillance for vaccine preventable diseases.

U01 HL63411 (Newburger)

07/05/00-06/30/05

NIH/NHLBI

\$442,856

Clinical Trial of Hematocrit Strategy in Heart Surgery

The major goals of this project are to compare neurodevelopmental outcome and early postoperative course after two strategies of hemodilution during hypothermic cardiopulmonary bypass in infants undergoing reparative open-heart surgery.

P50 HL074734 (Newburger)

02/15/04-1/31/09

NIH/NHLBI

\$3,040,891 (Core A: \$246,165)

SSCOR in Pediatric Heart Development and Disease

The goal of the SSCOR is to improve the prevention, detection, treatment, and outcomes of tetralogy of Fallot (TOF). There are 3 clinical and 3 basic projects that represent the diverse, but intersecting approaches to this central objective. In addition, there are 4 Core units to support the projects. Core A will provide data management, biostatistical analysis, and administrative support for all projects part of the SSCOR.

R01 HL077681 (Newburger)

07/01/04-06/30/09

NIH/NHLBI

\$397,806

Outcomes in Adolescence After Repair of d-TGA

The goal of this project is to characterize more fully any late effects of the arterial switch operation of the d-transposition of the great arteries (d-TGA). This study will utilize the same group of 160 children whom have been followed in a previous prospective single-center study during the perioperative period, and at ages 1, 4, and 8 years (for neurologic, developmental, speech and MRI studies).

R01 HL68922 (Platt)

NIH/NHLBI

09/30/01-07/31/06 \$655,236

Genetic Modifiers of Severity in Sickle Cell Anemia

This study proposes to identify the genes that influence baseline white blood count (WBC) in sickle cell anemia (SS) by studying a large series of nuclear and extended families with an SS proband.

R01 HS014947 (Porter) DHHS/AHRQ

09/30/04-09/29/06 \$219,174

ParentLink: Better and Safer Emergency Care for Children

The goal of this proposal is to determine whether implementation of a patient-centered health information technology—ParentLink—can address system-level deficiencies and the unique "just-in-time" information needs of Emergency Department physicians and the parents of ill children. The proposed project would deliver an innovative product—an electronic interface linked to a pediatric knowledge base that integrates parent-derived data with best practices for safe and effective emergency care across five common pediatric disease conditions: occult bacteremia, otitis media, urinary tract infections, asthma, and head trauma.

FD-R-002202 (Rufo) FDA

09/30/02-09/29/05

\$149,988

Clotrimazole Enemas for Pouchitis in Children and Adults

This study is a Phase I/II double-blinded, placebo controlled, dose escalating trial that will test the efficacy of topical CLT therapy (delivered as a retention enema) in two cohorts of pediatric and adult patients with pouchitis.

1R21 MH072533-01A1 (Shrier)

04/01/05-03/31/07

NIH

\$200,094

Mood and HIV Risk in Depressed Adolescents

The goal of this project is to evaluate the association between mood and sexual activity using hand-held computers in depressed adolescents.

U19 AI45955 (Taylor/CHB subcontract: Wypij) NIH/NIAID

09/30/99-07/31/05

\$34,504

Severe Malaria in African Children: A Clinical Network

The major goals of this project are to develop a clinical trials network for severe malaria in African children, which will provide a new structure for the rapid and efficient evaluation of novel treatments for this killing disease. The network will also provide a framework for collecting the data necessary to validate clinical observations made in individual sites and to evaluate pathogenetic hypotheses, which are necessary steps in the development of new malaria interventions.

R01 MH65877 (Waber) NIH/NIMH

05/01/04-03/31/09

\$72,759

30 Year Follow-up of Mental Health Outcomes Following Childhood Malnutrition

The goal of this project is to assess the long-term cognitive and mental health consequences of infant malnutrition in adulthood. Individuals who were followed from infancy through late adolescence will now be re-evaluated as adults in order to determine whether and how effects that persisted through adolescence may be evident among adults, and if so, what their consequences are for those individuals regarding mental health and adaptation.

R03 MH65152 (Woods)

NIH/NIMH

07/01/03-06/30/05 \$50.000

HIV Prevention: Providers as Agents of Change

The goals of this new initiative will include developing and testing culturally and developmentally sensitive measurement tools specifically for adolescent girls being treated for STD's. The tools will focus on the association of provider-patient relationships and mutuality of exchange of information with return for subsequent health care visits.

B. NIH CAREER DEVELOPMENT GRANTS

K01 DK62237 (Ebbeling) NIH/NIDDK 08/15/02-06/30/05

\$118,736

Motivating Obese Adolescents to Reduce Risk for Diabetes

The Mentored Research Scientist Development Award provides support for an intensive, supervised career development experience in one of the biomedical, behavioral, or clinical sciences leading to research independence. The aim of this particular project is to evaluate a directive, patient-centered counseling style for assisting obese girls in modifying diet and physical activity behaviors and equipping their mothers to provide needed support.

K08 HS13333 (Landrigan)

09/01/02-08/31/07

DHHS/AHRQ

\$116,500

Effects of Sleep Loss and Night Work on Patient Safety

The major goal of this Mentored Clinical Scientist Development Award is to develop the investigators' expertise in the impact of sleep deprivation and night work on patient safety. The proposal aims to study the manner in which interns' work schedules and sleep deprivation affects patient safety.

K23 HL074202 (Levy) NIH/NHLBI

07/01/03-06/30/08

\$116,500

Family Based Analysis of Modifiers of CF Lung Disease

The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. This particular project is to identify key associations between genetic variation and clinical inflammatory markers that are responsible for pulmonary disease severity in cystic fibrosis.

K08 HS013675 (Lightdale) DHHS/AHRQ

06/01/03-05/31/07 \$116,500

Improving Safety of Pediatric Sedation

The goals of this project are to define adverse outcomes associated with pediatric sedation and to develop prediction rules to help avoid adverse events during sedation for pediatric gastrointestinal endoscopy.

K23 HL075502 (Ordonez) NIH/NHLBI

07/01/04-06/30/09 \$118.225

P. aeruginosa Virulence in Cystic Fibrosis Lung Disease Progression

The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. The goal of this project is to use a functional genomics approach to identify virulence factors associated with progression of CF lung disease.

K08 HS11660 (Porter) DHHS/AHRQ 07/01/02-06/30/05 \$115,805

Informative Technology Linking Parents and Providers

Test of a computer-based system for improving health communication in the emergency department in cases of pediatric asthma. The hypothesis is that by transmitting parents' data directly to care providers, the system will improve parents' satisfaction in the domains of communication and partnership as well as asthma-specific process measures of quality of care.

K01 DP000089 (Rhodes) DHHS/CDC 09/30/04-09/29/07 \$277,708

Health Values and Treatment of Pediatric Type 2 Diabetes

The goal of this Mentored Research Scientist Development Award is to provide training in health services research, and to develop expertise in research methods and disciplines that will be used to develop health promotion and disease prevention strategies for children with, and at risk, for type 2 diabetes. The study proposed will evaluate the role of health preferences in the treatment of type 2 diabetes in children.

K23 RR016080 (Schachter)

08/01/00-07/31/05 \$116,200

NIH/NCRR

Nuclear Factor Kappa B in Pediatric Nephrotic Syndrome

The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research.

C. GLASER PEDIATRIC RESEARCH NETWORK: DESIGN, ANALYSIS AND COORDINATING CENTER

(Wypij)

09/01/02-08/31/08

\$150,856

Glaser Pediatric Research Network

Design, Analysis, and Coordinating Center (DACC)

for the Glaser Pediatric Research Network

The DACC provides leadership in protocol development and statistical design for GPRN, a consortium of pediatric academic medical centers performing multi-center research, and conducts training in clinical research methods for the GPRN Fellowship program.

(Wilson/CHB subcontract: Lenders/DACC: Osganian)

12/01/02-11/30/07

Glaser Pediatric Research Network

\$93,629

Design, Analysis, and Coordinating Center (DACC): A Multi-center, Randomized, Placebo Controlled, Double Blind Trial of Metformin in Overweight Adolescents

The purpose of the study is to determine if the drug Metformin will result in decreased obesity among obese adolescents.

(Neufeld/DACC: Feldman)

12/01/02-2/28/06

Glaser Pediatric Research Network

\$29,540

Design, Analysis, and Coordinating Center (DACC):

Open Label, Phase I/II Trial of Rituximab for Chronic, Severe

Idiopathic Thrombocytopenic Purpura in Children and Adolescents

This is a pilot phase open label study to evaluate the effectiveness of rituximab in severe or refractory pediatric ITP and to obtain further safety information on rituximab.

(Moss/CHB subcontract: Jaksic/DACC: Wypij)

12/01/02-11/30/06

Glaser Pediatric Research Network

\$76,313

Necrotizing Enterocolitis (NEC) Surgical Database

This study will develop a multi-center prospective data collection process for necrotizing enterocolitis in order to provide accurate data regarding practice of treatment and variability of care between different centers.

D. FOUNDATION/ASSOCIATION/OTHER

(Bennett)

07/07/04-06/30/06

St. Giles Foundation

\$125,000

Genetic Modifiers of Childhood Chronic Immune Thrombocytopenic Purpura (ITP)

This study has two specific aims: 1) to collect precise and detailed phenotypic data from the North American Pediatric Chronic ITP Registry to study a large cohort of patients with chronic ITP in a prospective manner; and 2) to analyze the association of candidate genes to the clinical severity of chronic ITP and its response to therapy.

(Curley)

05/01/04-08/30/06

Gustavus and Louise Pfeiffer Research Foundation

\$50,200

Sedation Management in Pediatric Patients Supported on Mechanical Ventilation

The purpose of this two-year project (randomized controlled clinical trial of two matched pediatric intensive care units in two different hospitals) is to pilot test an intervention to change sedation management in pediatric patients supported on mechanical ventilation for acute respiratory failure in the pediatric intensive care unit (PICU). The hypothesis is that pediatric patients managed per sedation protocol will experience fewer days of mechanical ventilation than patients receiving usual care.

 (Duggan)
 02/01/03-01/31/06

 Mass Vitamin Litigation Fund
 \$42,884

Body Composition in Cancer Patients Undergoing Stem Cell Transplantation

A randomized trial in children undergoing stem cell transplantation, who typically lose muscle mass as a side effect of chemotherapy, designed to test whether reduced parenteral nutrition and vitamin E supplementation will result in better tolerance of chemotherapy and their reduced levels of resting energy expenditure.

(Grand) 01/01/03-02/28/06

Crohn's & Colitis Foundation of America

\$99,456

Use of Intranasally Administered Calcitonin in the Treatment of Osteopenia and Osteoporosis in Children, Adolescents, and Young Adults with IBD: A Pilot Study

The goals of this pilot trial are to compare the effect of treatment with nasally administered calcitonin plus calcium and vitamin D supplementation to that of treatment with placebo plus calcium and vitamin D supplementation on the lumbar bone mineral density of patients with the diagnosis of IBD and low lumbar bone mineral density.

(Harris) 1/1/04-12/31/05 Aerosmith Foundation \$11.698

A Needs Assessment of Health Risk Behaviors and Protective Factors Among Students Attending Two Boston High Schools

This study is part of an ongoing collaboration between Children's Hospital adolescent health clinicians/ researchers and two nearby high schools to identify, and develop strategies to address student health needs. The first collaborative project is an anonymous needs assessment survey of all students in both schools.

(Hirsch, CHB subcontract: Osganian)
Robert Wood Johnson Foundation
Injury Free Coalition for Kids of Worcester
at the University of Massachusetts Memorial Hospital

01/01/02-12/31/06 \$7,930

This study proposed to evaluate a community-based injury prevention program that targets youth, ages 19 years old and younger. The intervention will target the more relevant injuries in the Greater Worcester area and the evaluation will consist of an injury surveillance program to monitor trends in the incidence of hospitalized injuries and fatal injuries in the communities that define the Greater Worcester area.

(Knight) 5/1/02-10/31/05

Robert Wood Johnson Foundation \$175,281

Implementation of Medical Office Screening for Adolescent Substance Abuse

The major goal of this project is to determine how screening is best implemented in different clinical settings and, most importantly, how pediatric clinicians can best respond to those who screen positive.

(Mooney)
Robert Wood Johnson Foundation
Injury Free Coalition for Kids of Boston

11/15/02-11/14/06 \$52,720

The purpose was to become the Injury Free Coalition for Kids of Boston site. The planned intervention was based upon the needs expressed by the community and data concerning injuries to children. The surveys indicated that families perceived home, fire, and pedestrian safety as their top three concerns. The interventions will include a home safety program, a community safety program, and a pedestrian safety program.

(Shrier) 09/01/04-08/31/05 Harvard Medical School 50th Anniversary Program \$24,611 Affective States and Sexual Behavior in Depressed Adolescents

The primary goal is to demonstrate the feasibility of recruiting depressed adolescents to participate in a momentary sampling study of mood and HIV/Sexually Transmitted Infections (STI) risk behavior. The secondary objective is to explore the associations of antecedent, concurrent, and subsequent positive and negative affect, and affect variability with sexual thoughts, desires, and risk behaviors among depressed adolescents.

(Taveras) 09/01/04-08/31/05

Deborah Munroe Noonan Memorial Fund \$68,182

Improving Clinical Practice to Prevent and Manage Obesity in Children

This cross-sectional study of parents of overweight children and their pediatric clinicians will collect information regarding the 1) current delivery system for overweight prevention and management in primary care, 2) services available to parents and clinicians to support overweight management, and 3) type of overweight prevention interventions that parents and clinicians think most feasible. Knowledge obtained from this study will be used to design a clinical intervention to improve prevention of pediatric overweight and management of its associated complications and disabilities.

GERAFF (Ward) 07/01/02-06/30/05 GE-AUR Radiology Research Academic Fellowship \$65,000

An Assessment of Magnetic Resonance Imaging in the Prenatal Diagnosis of Fetal Chest Masses: Impact on Diagnostic Accuracy, Clinical Decision-Making, Parental Understanding, and Prediction of Neonatal Respiratory Health Outcomes

The objective of this health services research project is to prospectively evaluate whether, after a fetal chest mass has been discovered on ultrasound, MRI provides additional and more accurate diagnostic and/or prognostic information.

E. INDUSTRY

(Laufer) 05/01/03-06/30/06
Personal Products Worldwide \$29,477

Personal Products Worldwide Assessment of the Utility of Salivary Hormonal Assays for the Determination of Menarche

The purpose of this study is to determine if consistent changes in the selected hormonal markers, introital pH, and body mass index could be used to predict menarche.

Staff Accomplishments and External Contributions

STAVROULA OSGANIAN, MD, ScD

External Teaching

Small Group Leader; sponsored by Harvard School of Public Health, Clinical Effectiveness Program; Summer 2005.

National Committee

Chair, Data and Safety Monitoring Board for the Girls Health Enrichment Multi-site Studies (GEMS); sponsored by The National Heart, Lung, and Blood Institute; 2003-present.

Member, Academic Health Centers, Clinical Research Forum, Washington, DC, 2004-present.

NIH Scientific Review Panels

NICHD, Special Emphasis Panel on "Prevention and Treatment of Childhood Obesity"; 4/18/05-4/20/05.

NHLBI, Special Emphasis Panel for Research Demonstration and Dissemination Projects (R18); 5/6/2005.

DAVID WYPIJ, PhD

External Teaching

Course Developer and Lecturer: Clinical Trials (BIO 214); Department of Biostatistics, Harvard School of Public Health; January-March 2005.

Course Developer and Lecturer: Short Course on the Analysis of Repeated Measures and Longitudinal Data; Federal University of Ceara, Fortaleza, Brazil; April 2005.

Course Developer and Lecturer: Short Course on an Introduction to Clinical Trials; Federal University of Ceara, Fortaleza, Brazil; April 2005.

Course Developer and Lecturer: Short Course on Smoothing and Semiparametric Regression Modelling; Federal University of Ceara, Fortaleza, Brazil; May 2005.

Course Developer and Lecturer: Short Course on Case Studies in Biostatistics; Summer School on Modern Methods in Biostatistics and Epidemiology, Treviso, Italy; June 2005.

Presentations

Use of Generalized Additive Models in the Analysis of Epidemiologic Data; Federal University of Rio de Janeiro, Brazil; May 2005.

National Committee

Member, Data and Safety Monitoring Board for "The Effect of Intramyocardial Injection of Immunoselected Bone Marrow Cells on Myocardial Function in LVAD Bridge to Transplant Patients"; sponsored by the National Heart, Lung, and Blood Institute, 2004-present.

Member, Data and Safety Monitoring Board for "The Impact of Diabetes on Left Ventricular Remodeling"; sponsored by the National Heart, Lung, and Blood Institute, 2004-present.

Honors

Elected to membership in the International Statistical Institute, 2005.

Fulbright Senior Specialist (visiting Brazil), 2005.

CARL DE MOOR, PhD

Scientific Review Panel

Member of the NIH study section on Community Influences on Health Behavior.

Presentations

Invited talk entitled "Measures of Tracking Dietary Intake" at Baylor College of Medicine, Houston.

HENRY FELDMAN, PhD

National Committees

Data and Safety Monitoring Board: Multi-site Trial of Activity in Adolescent Girls. National Heart, Lung, and Blood Institute, Bethesda, MD; Nov. 4, 2004; Jun. 22, 2005; Sep. 29, 2005.

Scientific Review Panel

Transdisciplinary Research on Energetics and Cancer; National Heart, Lung, and Blood Institute, Bethesda, MD, Mar. 3, 2005.

National Training Seminar

Ten-day Seminar on Epidemiology and Prevention of Cardiovascular Diseases, sponsored by American Heart Association and U.S. Centers for Disease Control. Presentations on Sample Size and Power, Biostatistics Review; participation in literature critique, research design exercise, and related faculty activity. Tahoe City, CA; Jul. 24-Aug. 5, 2005.

International Training Seminar

Four-day Science School for Post-Doctoral Fellows, sponsored by International Society for Pediatric and Adolescent Diabetes. Presentation on Statistics in Clinical Research; participation in critique of Fellows' work in progress and related faculty activity. Boston, MA; Oct. 24-27, 2005.

External Teaching

Lecturer, Statistics in Clinical Research (EPI 607, Fundamentals of Clinical Research); Power and How to Get It; Study Design Workshop (EPI 703, Special Topics in Epidemiology of Chronic Disease). University of Alabama at Birmingham School of Public Health. Birmingham, AL; Nov. 2-3, 2005.

SION HARRIS, PhD

Internal Teaching

Children's Hospital Nursing Research Conference, Lecturer: The Means to the End, Assessment in Clinical Research; 90-minute presentation; 10 attendees: Faculty and Fellows; January 2, 2005.

Children's Hospital Division of General Pediatrics Biennial Retreat, Co-Lecturer with Marjorie Beeghly, PhD: Writing for Scientific Publication; 75-minute presentation, 9 attendees: Faculty and Fellows; April 26, 2005.

Harvard Pediatric Health Services Research Fellowship Program Seminar Lecturer: Being Survey Savvy: Avoiding Common Errors in Survey Design; 75-minute presentation; 10 attendees: Faculty and Fellows; May 5, 2005.

MEI-CHIUNG SHIH, PhD

Presentations

Modified Haybittle-Peto group sequential tests for testing superiority and non-inferiority hypotheses in clinical trials; sponsored by The International Biometrics Society Western North American Region (WNAR) Annual Meeting; June 2005.

Estimation of genetic effect at a candidate gene for family-based association studies; sponsored by the Joint Statistical Meetings; August 2005.

External Teaching

Course Developer and Lecturer; Regression and Analysis of Variance in Experimental Research (BIO 211); Department of Biostatistics, Harvard School of Public Health; January-May 2005.

Program Resources

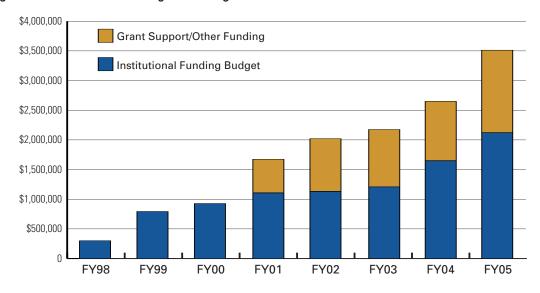
There has been a substantial institutional commitment to the Program, in terms of both space and operating budget, which has facilitated the growth and visibility of the Program. The Program presently occupies 2,715 square feet of office space located on the Fourth Floor of 333 Longwood Avenue with 14 offices, 18 cubicles, and 2 conference rooms.

Institutional and other sources of support for the Program are shown in Table 1. Institutional support for the Clinical Research Program (CRP) has increased substantially since the inception of the Program and now totals \$2.1 million. Equally exciting has been the rapid growth in funding from collaborative relationships with clinical investigators and CRP extramural funding, which now totals nearly \$1.4 million.

Table 1. CRP Funding for the period FY98 to FY05

Fiscal Year	Institutional Budget	Grant Support/Other Funding	Total	% Increase
FY98	\$299,871	_	\$299,871	
FY99	\$793,226	_	\$793,226	164%
FY00	\$927,204	_	\$927,204	17%
FY01	\$1,104,774	\$560,340	\$1,665,114	80%
FY02	\$1,130,346	\$885,225	\$2,015,571	21%
FY03	\$1,207,481	\$965,827	\$2,173,308	8%
FY04	\$1,646,804	\$996,664	\$2,643,468	21%
FY05	\$2,120,804	\$1,388,457	\$3,509,261	33%

Figure 1. Clinical Research Program funding



Appendices

Clinical Research Program 333 Longwood Ave., 4th floor

Phone: 617-355-2463 / Fax: 617-355-2312

crp@childrens.harvard.edu

APPENDIX A

Program Description and Request for Assistance Form

Mission

The mission of the Clinical Research Program is to enhance the quality of clinical research at Children's Hospital by providing to members of the research community scientific support, education, and collaborative assistance in the design, conduct, and analysis of clinical research. We also closely interact with the Children's Hospital General Clinical Research Center (GCRC) and provide some support to GCRC-funded studies.

CRP Personnel

Directors

Senior clinical researchers with extensive experience in conducting clinical research studies.

• Biostatisticians

Skilled in protocol and grant development, study design, and data analysis.

• Survey Epidemiologists

Skilled in the design and analysis of surveys.

• Clinical Research Specialists

Skilled in the design of case report forms and questionnaires, quality assurance procedures, and the development of manuals of operations.

• Applications Specialists

Skilled in data management system design, including database and Web application development.

Funding Sources

The CRP receives a portion of its support from the hospital as part of the institution's commitment to clinical research. A significant amount of funding also comes from federal, foundation, and other awards that are obtained by either our staff or the investigators with whom we collaborate. The CRP can offer a limited number of hours of support for consultation or advice at no cost to all clinical research investigators, but assistance that is more extensive will require a collaborative effort and funding. As we plan our role in your research, we will estimate your requirements and a realistic budget will be developed to formalize our collaboration. We also strongly encourage investigators to consider seeking GCRC support for their clinical studies wherever possible.

Resources

The CRP can provide support or guidance in the following areas.

- Grant Application or Study Protocol Development
- Study Design
- Sample Size and Power Calculations
- Analysis Methods
- Randomization
- Case Report Form and Survey Design

- Data Management and System Design
- Data Analyses
- Data Analyses Interpretation
- Manuscript Preparation
- Mentoring

Assistance Procedures

To be eligible for CRP assistance, you must have an appointment at Children's Hospital or be a Children's Hospital employee. For assistance with any aspect of study implementation or with data analyses, you must have a written study protocol with IRB approval to conduct the research.

- For each request, complete the CRP Investigator **Request Request for Assistance form** and submit by interoffice mail or e-mail: *crp@childrens.harvard.edu*. We will respond within 10 business days to schedule an initial planning meeting.
- Along with your request form, send all pertinent background materials (including a draft of your research aims, draft protocol or grant proposal, guidelines for submission of the grant application, draft data forms, etc.). These materials should be sent to the CRP at least one week before your meeting.
- At the initial planning meeting, CRP staff will meet with you (and your mentor, if applicable) to assess your request. At the initial planning meeting we will begin to discuss feasibility and resources. This includes an evaluation of tasks to be performed, assignment of responsibilities, and the need for budgetary support.
- At a follow-up meeting, we will develop a mutually agreed-upon written plan of action and an
 estimate of costs, when needed.
- Work will proceed according to an agreed-upon timeframe.

Timeframes

Grant proposal applications as well as study protocols vary in complexity and length. Most National Institutes of Health (NIH) applications (R01's, K23's and other funding mechanisms) as well as applications to major foundations require significant time and effort to prepare. Most studies also require **6 to 12 months** of planning and development prior to the start of recruitment of subjects. Similarly, data analyses require sufficient time for data cleaning, statistical programming, interaction with the investigators, and writing and review of manuscripts. Furthermore, the CRP provides assistance to many investigators at any given time. Therefore, we ask that investigators adhere to the following timeframes when requesting assistance from the CRP.

- For grant applications, we recommend beginning to work with us at least 90 days before the submission deadline or due date and **require a minimum of 60 days**. We also **require** a complete first draft of the grant proposal or study protocol and preliminary budget a **minimum of 30 days** before the submission deadline or due date. If this timeframe is not met or we feel there is not adequate time to assist you, we may recommend delaying submission to the next cycle.
- For assistance with study implementation, we ask that you begin working with us at least
 6 months in advance of your anticipated start of recruitment.
- For assistance with data analyses, we recommend beginning to work with us **60 to 90 days** before any deadline, depending on the scope and complexity of the analyses.

CRP Contact Information

The CRP Offices are located on the 4th floor at 333 Longwood Avenue. We can be reached by phone at 617-355-2463 or by e-mail at crp@childrens.harvard.edu. Visit our website at http://web2.childrens.harvard.edu/clinresearch/core/index.html.

Clinical Research Program 333 Longwood Ave., 4th floor Phone: 617-355-2463 / Fax: 617-355-2312 crp@childrens.harvard.edu

CRP USE ONLY			
A. Form Received: _	/_	/_	Entered:
B. Intro. Meeting: _	/_	_/_	Staff:

Investigator Request for Assistance

Instructions: Please complete our Request for Assistance questionnaire to help us better assist you with your project. Submit this form via e-mail, fax, or interoffice mail (see above). A CRP staff member will contact you within the next week to schedule a meeting.

1. Principal Investigator:				
Last Name	First Name		CH ID#	
2. Title: Prof. Assoc. Prof. Other (specify):			Resident	Nurse
3. Department:	Divis	ion:		
4. Phone/Ext #				
5. Research Mentor (if applicable)				
6. Requestor: Check if same as nar	me of PI			
Last Name	First Name		CH ID#	
7. Project Title (same as title on IRB pr	otocol or grant applicati	on):		
8. What do you require assistance with a. Grant Proposal/Protocol Development Grant Proposal Development Study Protocol Development Study Design or Concept Develop Statistical Analysis Plan Power and Sample Size Determin Data Monitoring Plan (DSMP)/In c. Data Analysis/Interpretation Presentation Manuscript Statistical Analyses Interpretation of Results d. Other (Specify below)	pment ation	b. Study Implemen Case Report For Survey/Question Randomization Database Develo Data Manageme Assistance with	rm Development nnaire Design opment ent	
9. What is the deadline for completion	of work for this request	' (MM/DD/YYYY):	//	continued

10. What type of assistance are you requesting [see program description for explanation]? (check one) Collaboration (more extensive support, requires funding) Consultation (limited support/advice, no funding)
11. Funding Status a. Is your project currently funded?
12. Funding Sources NIH a. Name of Institute/Center: b. Type of funding mechanism (check one): K01 R03 R21 K01 K08 K23 K24 c. Is this a response to an announcement? Yes No i. If Yes, what is the type? RFA RFP PA
Other Federal Agency:
Foundation/Association: 1)
2)
☐ Industry Sponsor:
☐ Internal Award:
Department/Division/Program Funds:
Philanthropic funds
Other (specify):
13. Will this protocol utilize the GCRC or its resources?
14. Other Requests/Comments
NOTE: Make certain that you send all pertinent background materials (including a draft of your research aims, draft protocol or grant proposal, guidelines for submission of the grant application, draft data forms, etc.) to the CRP along with your request form at least one week before your meeting. This will lead to a much more productive first session. Thank you!

APPENDIX B

2005 Staff Publications

Almond, CS, AY Shin, EB Fortescue, RC Mannix, **D Wypij**, BA Binstadt, CN Duncan, DP Olson, AE Salerno, JW Newburger, DS Greenes (2005). "Hyponatremia among runners in the Boston Marathon." *N Engl J Med* 352(15):1550-1556.

Bolon, MK, AD Arnold, **HA Feldman**, DA Goldmann, SB Wright (2005). "An antibiotic order form intervention does not improve or reduce vancomycin use." *Pediatr Infect Dis J* 24(12):1053-1058.

Bolon, MK, AD Arnold, **HA Feldman**, DH Rehkopf, EF Strong, DA Goldmann, SB Wright (2005). "Evaluating vancomycin use at a pediatric hospital: new approaches and insights." *Infect Control Hosp Epidemiol* 26(1):47-55.

Cheifetz, AT, **SK Osganian**, EN Allred, HL Needleman (2005). "Prevalence of bruxism and associated correlates in children as reported by parents." *J Dent Child* (Chic) 72(2):67-73.

Curley, MA, PL Hibberd, LD Fineman, **D Wypij**, **MC Shih**, JE Thompson, MJ Grant, FE Barr, NZ Cvijanovich, L Sorce, PM Luckett, MA Matthay, JH Arnold (2005). "Effect of prone positioning on clinical outcomes in children with acute lung injury: a randomized controlled trial." *JAMA* 294(2): 229-237.

de Moor, **CH**, H Meijer, S Lissenden (2005). "Mechanisms of translational control by the 3' UTR in development and differentiation." *Semin Cell Dev Biol* 16(1):49-58.

Ebbeling, CB, MM Leidig, KB Sinclair, LG Seger-Shippee, **HA Feldman**, DS Ludwig (2005). "Effects of an ad libitum low-glycemic load diet on cardiovascular disease risk factors in obese young adults." *Am J Clin Nutr* 81(5):976-982.

Fligor, BJ, MW Neault, CH Mullen, **HA Feldman**, DT Jones (2005). "Factors associated with sensorineural hearing loss among survivors of extracorporeal membrane oxygenation therapy." *Pediatrics* 115(6):1519-1528.

Hansen, A, **P Forbes**, R Buck (2005). "Potential substitution of cord blood for infant blood in the neonatal sepsis evaluation." *Biol Neonate* 88(1):12-18.

Homer, CJ, **P Forbes**, L Horvitz, LE Peterson, **D Wypij**, P Heinrich (2005). "Impact of a quality improvement program on care and outcomes for children with asthma." *Arch Pediatr Adolesc Med* 159(5):464-469.

Hutchinson LM, EL Chang, CM Becker, **MC Shih**, M Brice, WC DeWolf, SM Gaston, BR Zetter (2005). "Use of Thymosin \(\mathbb{B} 15 \) as a urinary biomarker in human prostate cancer." *Prostate* 64:116-127.

Hutchinson LM, EL Chang, CM Becker, N Ushiyama, D Behonick, **MC Shih**, WC DeWolf, SM Gaston, BR Zetter (2005). "Development of a sensitive and specific enzyme-linked immunosorbent assay for Thymosin £15, a urinary biomarker of human prostate cancer." *Clinical Biochemistry* 38:558-571.

Kussman, BD, **D Wypij**, JA DiNardo, J Newburger, RA Jonas, J Bartlett, E McGrath, PC Laussen (2005). "An evaluation of bilateral monitoring of cerebral oxygen saturation during pediatric cardiac surgery." *Anesth Analg* 101(5):1294-1300.

Missinou, MA, CH Olola, S Issifou, PB Matsiegui, AA Adegnika, S Borrmann, D Wypij, TE Taylor, PG Kremsner (2005). "Short report: Piloting paperless data entry for clinical research in Africa." Am J Trop Med Hyg 72(3):301-303.

Mooney, DP, C Downard, S Johnson, CC Atkinson, PW Forbes, GT Taylor (2005). "Physiology after pediatric splenic injury." J Trauma 58(1):108-111.

Mrakotsky, C, A Bousvaros, L Chriki, E Kenney, P Forbes, E Szigethy, D Waber, R Grand (2005) "Impact of acute steroid treatment on memory, executive function, and mood in pediatric inflammatory bowel disease:154." Journal of Pediatric Gastroenterology & Nutrition. 41(4):540-541.

Newton, CR, C Valim, S Krishna, **D Wypij**, C Olola, T Agbenyega, TE Taylor (2005). "The prognostic value of measures of acid/base balance in pediatric falciparum malaria, compared with other clinical and laboratory parameters." Clin Infect Dis 41(7):948-957.

Parsons SK, MC Shih, DK Mayer, SE Barlow, SE Supran, SL Levy, S Greenfield, SH Kaplan (2005). "Preliminary psychometric evaluation of the Child Health Ratings Inventories (CHRI) and Disease-Specific Impairment Inventory-HSCT (DSII-HSCT) in parents and children." Quality of Life Research 14:1613-1625.

Randolph, AG, PW Forbes, RG Gedeit, JH Arnold, RC Wetzel, PM Luckett, ME O'Neil, ST Venkataraman, KL Meert, IM Cheifetz, PN Cox, JH Hanson (2005). "Cumulative fluid intake minus output is not associated with ventilator weaning duration or extubation outcomes in children." Pediatr Crit Care Med 6(6):642-647.

Rhodes, ET, JI Wolfsdorf, DD Cuthbertson, HA Feldman, DS Ludwig (2005). "Effect of low-dose insulin treatment on body weight and physical development in children and adolescents at risk for type 1 diabetes." Diabetes Care 28(8):1948-1953.

Sandora TJ, EM Taveras, MC Shih, EA Resnick, GM Lee, D Ross-Degman, DA Goldmann (2005). "A randomized controlled trial of a multifaceted intervention including alcohol-based hand sanitizer and hand hygiene education to reduce illness transmission in the home." Pediatrics 116:587-594.

Saunders, AC, HA Feldman, CE Correia, DA Weinstein (2005). "Clinical evaluation of a portable lactate meter in type I glycogen storage disease." J Inherit Metab Dis 28(5):695-701.

Shrier LA, MC Shih, WR Beardslee (2005). "Affect and sexual behavior in adolescents: A review of the literature and comparison of momentary sampling with diary and retrospective self-report methods of measurement." Pediatrics 115:e573-581.

Terry KL, I De Vivo, L Titus-Ernstoff, MC Shih, DW Cramer (2005). "Androgen receptor cytosine, adenine, guanine repeats, and haplotypes in relation to ovarian cancer risk." Cancer Research 65:5974-5981.

Waltzman, ML, M Baskin, D Wypij, D Mooney, D Jones, G Fleisher (2005). "A randomized clinical trial of the management of esophageal coins in children." Pediatrics 116(3):614-619.

2004 Staff Publications

Agrawal, D, **HA Feldman**, B Krauss, ML Waltzman (2004). "Bispectral index monitoring quantifies depth of sedation during emergency department procedural sedation and analgesia in children." *Ann Emerg Med* 43(2):247-255.

Alangari AA, FJ Twarog, **MC Shih**, LC Schneider (2004). "Clinical features and anaphylaxis in children with cold urtecaria." *Pediatrics* 113:e313-317.

Asmuth, DM, MP Busch, ME Laycock, BA Mohr, **LA Kalish**, CM van der Horst (2004). "Hepatitis B and C viral load changes following initiation of highly active antiretroviral therapy (HAART) in patients with advanced HIV infection." *Antiviral Res* 63(2):123-131.

Bartlett, JM, **D Wypij**, DC Bellinger, LA Rappaport, LJ Heffner, RA Jonas, JW Newburger (2004). "Effect of prenatal diagnosis on outcomes in D-transposition of the great arteries." *Pediatrics* 113(4):e335-340.

Bassin, EB, MA Mittleman, **D Wypij**, K Joshipura, CW Douglass (2004). "Problems in exposure assessment of fluoride in drinking water." *J Public Health Dent* 64(1):45-49.

Callahan, ST, ER Woods, SB Austin, **SK Harris** (2004). "Young adults in Massachusetts: who is at risk of being uninsured?" *J Adolesc Health* 35(5):425 e19-27.

Carmack Taylor, CL, MA Smith, **C de Moor**, AL Dunn, C Pettaway, R Sellin, C Charnsangavej, MC Hansen, ER Gritz (2004). "Quality of life intervention for prostate cancer patients: design and baseline characteristics of the active for life after cancer trial." *Control Clin Trials* 25(3):265-285.

Chung, S, N Schamban, **D Wypij**, R Cleveland, SA Schutzman (2004). "Skull radiograph interpretation of children younger than two years: how good are pediatric emergency physicians?" *Ann Emerg Med* 43(6):718-722.

Cinciripini, P, D Wetter, G Tomlinson, J Tsoh, **C De Moor**, L Cinciripini, J. Minna (2004). "The effects of the DRD2 polymorphism on smoking cessation and negative affect: evidence for a pharmacogenetic effect on mood." *Nicotine Tob Res* 6(2):229-239.

de Ferranti, S, K Gauvreau, PR Hickey, RA Jonas, **D Wypij**, A du Plessis, DC Bellinger, K Kuban, JW Newburger, PC Laussen (2004). "Intraoperative hyperglycemia during infant cardiac surgery is not associated with adverse neurodevelopmental outcomes at 1, 4, and 8 years." *Anesthesiology* 100(6):1345-1352.

Ebbeling, CB, KB Sinclair, MA Pereira, E Garcia-Lago, **HA Feldman**, DS Ludwig (2004). "Compensation for energy intake from fast food among overweight and lean adolescents." *JAMA* 291(23):2828-2833.

Goff, DC, Jr., P Mitchell, J Finnegan, D Pandey, V Bittner, **H Feldman**, H Meischke, RJ Goldberg, RV Luepker, JM Raczynski, L Cooper, C Mann (2004). "Knowledge of heart attack symptoms in 20 US communities. Results from the Rapid Early Action for Coronary Treatment Community Trial." *Prev Med* 38(1):85-93.

Gordon, CM, KC DePeter, **HA Feldman**, E Grace, SJ Emans (2004). "Prevalence of vitamin D deficiency among healthy adolescents." *Arch Pediatr Adolesc Med* 158(6):531-537.

Hoelscher, DM, **HA Feldman**, CC Johnson, LA Lytle, SK Osganian, GS Parcel, SH Kelder, EJ Stone, PR Nader (2004). "School-based health education programs can be maintained over time: results from the CATCH Institutionalization study." *Prev Med* 38(5):594-606.

Kalish, **LA**, B Buczynski, P Connell, A Gemmel, C Goertz, EA Macklin, M Pian-Smith, S Stevens, J Thompson, P Valaskatgis, PM Wayne, RM Zusman (2004). "Stop Hypertension with the Acupuncture Research Program (SHARP): clinical trial design and screening results." *Control Clin Trials* 25(1): 76-103.

Knight JR, Sherritt L, Gates EA, **Harris SK** (2004). "Should the CRAFFT substance abuse screening test be shortened?" *Journal of Clinical Outcomes Management*. 11(1):19-25.

Lai TL, **MC Shih** (2004). "Power, sample size and adaptation considerations in the design of group sequential clinical trials." *Biometrika* 91:507-528.

Levy, S, L Sherritt, **SK Harris**, EC Gates, DW Holder, JW Kulig, JR Knight (2004). "Test-retest reliability of adolescents' self-report of substance use." *Alcohol Clin Exp Res* 28(8):1236-1241.

McAdam, AJ, ME Hasenbein, **HA Feldman**, SE Cole, JT Offermann, AM Riley, TA Lieu (2004). "Human metapneumovirus in children tested at a tertiary-care hospital." *J Infect Dis* 190(1):20-26.

McElhinney, DB, SD Colan, AM Moran, **D Wypij**, M Lin, JA Majzoub, EC Crawford, JM Bartlett, EA McGrath, JW Newburger (2004). "Recombinant human growth hormone treatment for dilated cardiomyopathy in children." *Pediatrics* 114(4):e452-458.

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2005 Staff Abstracts

Curley, MAQ, **SK Harris** "State Behavioral Scale: A sedation instrument for ventilated infants and young children." Poster at 2005 American Thoracic Society International Conference, May 2005.

Knight, JR, S Van Hook, T Brooks, P Carey, P Kossack, J Kulig, **SK Harris** "The 'Six T's': Barriers to screening teens for substance abuse in primary care." Poster at 2005 Pediatric Academic Societies Annual Meeting, May 2005.

Lee PDK, RH Lustig, **HA Feldman**, Glaser Pediatric Research Network. "Insulin-like growth factor binding protein 1 (IGFBP-1) predicts insulin sensitivity and area-under-the-curve insulin (AUC) in obese, non-diabetic adolescents." Endocrine Society 87th Annual Meeting, San Diego, CA, 2005.

Levy, S, **SK Harris**, L Sherritt, M Angulo, J Knight "Drug testing of adolescents in ambulatory medicine: physician practices and knowledge." Oral presentation at 2005 Association for Medical Education and Research in Substance Abuse National Conference, October 2005.

Levy, S, **SK Harris**, L Sherritt, M Angulo, J Knight "Drug testing of adolescents in ambulatory medicine: what are the indications for testing, and what do physicians do with the results?" Poster at 2005 Association for Medical Education and Research in Substance Abuse National Conference, October 2005.

Levy, S, **SK Harris**, L Sherritt, M Angulo, J Knight "Primary care physicians' urine drug testing knowledge and practices." Poster at 2005 Pediatric Academic Societies Annual Meeting, May 2005.

Lightdale JR, **HA Feldman**, AR Newburg, V Turbini, LA Heard, K Donovan, JA DiNardo, VL Fox. "A randomized double-blind controlled trial of microstream capnography to reduce oxygen desaturation during gastrointestinal procedures with conscious sedation." *Gastrointest Endosc*, 2005; 61:AB81.

Oyeku SO, **HA Feldman**, K Ryan, S Muret-Wagstaff, EJ Neufeld. "Clinician knowledge and confidence about newborn screening for sickle cell disease: randomized assessment of educational strategies." National Sickle Cell Disease Program 28th Annual Meeting, Cincinnati, OH, 2005.

Oyeku SO, **HA Feldman**, K Ryan, S Muret-Wagstaff, EJ Neufeld. "Primary care provider knowledge and confidence about newborn screening for sickle cell disease." Pediatric Academic Societies Annual Meeting, Washington, DC, 2005.

Paltiel HJ, **LA Kalish**, F Frauscher, P O'Kane, R Susaeta, LF Filho, P Dunning. "Pulse inversion imaging of testicular ischemia: qualitative analysis of perfusion in a rabbit model." 2005 American Institute of Ultrasound in Medicine Annual Convention, Orlando, FL, June 2005.

Paltiel HJ, **LA Kalish**, R Susaeta, F Frauscher, P O'Kane, LF Filho. "Pulse inversion imaging of testicular ischemia: quantitative and qualitative analysis of perfusion in a rabbit model." Society for Pediatric Radiology 48th Annual Meeting, New Orleans, LA, May 2005.

Paltiel HJ, **LA Kalish**, R Susaeta, LF Filho. "Pulse inversion imaging of testicular ischemia: quantitative analysis of perfusion in a rabbit model". 2005 American Institute of Ultrasound in Medicine Annual Convention. Orlando, FL, June 2005.

Porter SC, **PW Forbes**, **HA Feldman**, DA Goldmann. "Impact of patient-centered decision support on quality of asthma care in the emergency department." Pediatric Academic Societies Annual Meeting, Washington, DC, 2005.

Stone KD, **HA Feldman**, *C* Huisman, FA Bonilla. "Interpretation of in vitro T-cell proliferation data: optimization for the identification of patients with primary immunodeficiencies." *J Allergy Clin Immunol*, 2005; 115(S1):S157.

2004 Staff Abstracts

Brett-Fleegler, MB, RJ Vinci, DL Weiner, **SK Harris**, **MC Shih**, ME Kleinman. "Evaluation of a simulator-based tool for the assessment of resuscitation competency of pediatric residents." Poster at 2004 Pediatric Academic Societies Annual Meeting, May 2004.

Brown SD, JC Daly, **LA Kalish**. "Analysis of financial disclosures of scientific papers presented at RSNA 2003: characterization of the financial relationships with industry and their association with the reporting of non-FDA approved uses of industry products." Radiological Society of North America, 90th Scientific Assembly and Annual Meeting, Chicago, IL, November 28 – December 3, 2004.

Curley, M, M Hunsberger, **SK Harris** "Family-Centered Care Scale: A measure of mutuality within pediatric nurse-parent relationships." Poster at 2004 National Congress on the State of the Science in Nursing Research, October 2004.

Ebbeling CB, KB Sinclair, MA Pereira, E Garcia-Lago, **HA Feldman**, DS Ludwig. "Effects of fast food on total energy intake in obese and nonobese adolescents." *Obes Res*, 2004; 12:171.

Ebbeling CB, MM Leidig, KB Sinclair, LG Seger-Shippee, **HA Feldman**, DS Ludwig. "Effects of a reduced glycemic load diet on cardiovascular disease risk factors in obese young women." *Obes Res*, 2004; 12(Suppl):A44.

Fligor BJ, MW Neault, **HA Feldman**, CL Nulton, CH Mullen, DT Jones. "Factors associated with sensorineural hearing loss in graduates of ECMO therapy." American Academy of Audiology 16th Annual Meeting, Salt Lake City, Utah, 2004.

Gordon CM, E Binello, **HA Feldman**, MS LeBoff, ME Wohl, CJ Rosen, AA Colin. "Role of dehydroepiandrosterone and vitamin D in the bone loss of cystic fibrosis." *J Bone Miner Res*, 2004; 19(S1):S305.

Hanson E, **L Kalish**, E Bunce, C Curtis, S McDaniel, J Petry, J Ware. "Use of complementary and alternative medicine by children with an autism spectrum disorder." Society for Developmental and Behavioral Pediatrics Annual Meeting, Chicago, IL, September 30–October 4, 2004.

Levy H, RA Sebro, BA Raby, **L Kalish**, W Robinson, C Gerard, ME Wohl, G Pier, J Celedon, EK Silverman, ST Weiss. "Biomarkers of lung disease and cystic fibrosis." 100th International Conference of the American Thoracic Society. Orlando, FL, May 2004.

Loud KJ, **HA Feldman**, KC DePeter, AA Pettinato, CM Gordon. "Quantitative ultrasound measurements of bone in healthy American adolescents." *J Bone Miner Res*, 2004; 19(S1):S376.

Rhodes ET, JI Wolfsdorf, **HA Feldman**, DS Ludwig. DPT-1 Study Group. "Effect of low-dose insulin treatment on body weight and adiposity in children at risk of Type 1 diabetes mellitus." *Diabetes*, 2004; 53(S2):A415.

Ross, W, E Chan, **S Harris**, L Rappaport. "Pediatric experience with psychiatric collaboration." Plenary presentation at 2004 Society for Developmental Behavioral Pediatrics Annual Meeting, October 2004.

APPENDIX C

Course Agendas

A. Introduction to Clinical Research

Introduction to Clinical Research Agenda

	Tuesday, January 18, 2005
8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 9:00	Introduction and Overview Voula Osganian, MD, ScD David Wypij, PhD
9:00 – 10:15	Data Analysis I: Descriptive Statistics David Wypij, PhD
10:15 – 10:30	BREAK
10:30 – 11:00	Data Analysis II: Precision and Accuracy of Measurement David Wypij, PhD
11:00 – 11:30	Study Data and Documents: What to File and Where Eunice Newbert, MPH
11:30 – 11:45	The General Clinical Research Center (GCRC) Richard Grand, MD Kristine Jordan
11:45 – 12:45	LUNCH
12:45 – 1:00	Overview of Research Administration: Organization and Resources Carleen Brunelli, PhD, MBA
1:00 – 1:30	Scientific Presentations Jonathan Finkelstein, MD
1:30 – 2:15	Designing Surveys and Questionnaires Sion Kim-Harris, PhD
2:15 – 3:00	Operational Issues in Conducting Clinical Research Christopher Duggan, MD

Introduction to Clinical Research Agenda

Wednesday, January 19, 2005

	,, Julius y 15, 2000
8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 9:45	Data Analysis III: Comparing Two Groups Henry Feldman, PhD
9:45 – 10:00	BREAK
10:00 – 11:15	Human Subjects, Institutional Review Board, and HIPAA Susan Kornetsky, MPH
11:15 – 12:00	Clinical Trials: Design and Monitoring Jane Newburger, MD
12:00 – 1:00	LUNCH
1:00 – 2:00	Writing for Scientific Publication Jean Emans, MD
2:00 – 3:00	Observational Study Designs Voula Osganian, MD, ScD
	Thursday, January 20, 2005
8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 9:45	Statistical Issues in Study Design David Wypij, PhD
9:45 – 10:30	Bias and Confounding Clarissa Valim, MD, ScD
10:30 - 10:45	BREAK
10:45 – 12:00	Data Analysis IV: Correlation and Regression Henry Feldman, PhD
12:00 – 1:00	LUNCH
1:00 – 1:45	Evaluating the Performance of a Test Carl de Moor, PhD
1:45 – 2:15	Writing a Grant and Applying for Funding Voula Osganian, MD ScD
2:15 – 2:45	The NIH Scientific Review Voula Osganian, MD, ScD
2:45 – 3:00	Wrap-up Voula Osganian, MD, ScD David Wypij, PhD

Introduction to Clinical Research Agenda

Tuesday, July 19, 2005

	January Grand Control of the Control
8:00 – 8:30	CONTINENTAL BREAKFAST
8:30 – 8:45	Introduction and Overview Voula Osganian, MD, ScD David Wypij, PhD
8:45 – 10:00	Human Subjects, Institutional Review Board, and HIPAA Susan Kornetsky, MPH
10:00 – 10:45	Data Analysis I: Descriptive Statistics and Inference David Wypij, PhD
10:45 – 11:00	BREAK
11:00 – 11:30	Data Analysis II: Precision and Accuracy of Measurement David Wypij, PhD
11:30 – 12:30	Observational Study Designs Voula Osganian, MD, ScD
	Wednesday, July 20, 2005
8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 9:30	Writing for Scientific Publication Jean Emans, MD
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9:30 – 10:30	Clinical Trials: Design and Monitoring Jane Newburger, MD
9:30 – 10:30 10:30 – 10:45	e e
	Jane Newburger, MD

Introduction to Clinical Research Agenda

Thursday, July 21, 2005

8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 8:45	Overview of Research Administration: Organization and Resources Carleen Brunelli, PhD, MBA
8:45 – 9:45	Bias and Confounding Clarissa Valim, MD, ScD
9:45 – 10:30	Data Analysis III: Comparing Two Groups Henry Feldman, PhD
10:30 - 10:45	BREAK
10:45 – 11:30	Data Analysis IV: Correlation and Regression Henry Feldman, PhD
11:30 – 12:30	Evaluating the Performance of a Test Carl de Moor, PhD
	Friday, July 22, 2005
8:00 - 8:30	CONTINENTAL BREAKFAST
8:30 – 9:15	Scientific Presentations Jonathan Finkelstein, MD
9:15 – 9:45	Study Data and Documents: What to File and Where Eunice Newbert, MPH
9:45 – 10:30	Operational Issues in Conducting Clinical Research Christopher Duggan, MD
10:30 - 10:45	BREAK
10:45 – 11:00	The General Clinical Research Center (GCRC) Richard Grand, MD Kristine Jordan
10:00 – 10:45	Writing a Grant and Applying for Funding Voula Osganian, MD, ScD
10:45 – 12:15	The NIH Scientific Review Voula Osganian, MD, ScD
12:15 – 12:30	The CRP Course Wrap-up Voula Osganian, MD, ScD David Wypij, PhD

B. Biostatistics Seminar Series

Biostatistics Seminar Series Schedule

December 20, 2004

Individual and population penalized regression splines for accelerated longitudinal designs — Jaroslaw Harezlak

Jan 11, 2005

Analysis of data from complex sample designs using SAS, with examples from H-CUP datasets — Peter Forbes

March 24, 2005

A specification test for the mixing distribution in a generalized linear mixed model: joint work with Brent Coull

- Eric Tchetgen

April 12, 2005

Sample-size calculation for a simple pretest-posttest design: change-scores and ANCOVA reconciled — Henry Feldman

May 17, 2005

Models for correlated non-commensurate outcomes

— Armando Teixeira-Pinto

June 21, 2005

Shrinkage and regression: from Stein's paradox to the lasso

— Daniel Kinnamon

September 13, 2005

Evaluating experimental designs for estimating amino acid requirements

- Les Kalish

C. New Study Coordinator Orientation

New Study Coordinator Orientation Agenda 8:30 - 8:45WELCOME AND OVERVIEW 8:45 - 9:05Overview of Responsibilities of Study Coordinators Study Coordinator's Central Role in Clinical Research 9:05 - 9:30Human Subject Protections — IRB Issues: Before the Research Begins • Introduction/Why are we here? • Training Requirements • Protocol Submissions 9:30 - 10:00IRB Issues — During the Research • Continuing Renewals • 3 Year Re-writes • Amendments/Revisions • Adverse Events • Violations/Deviations 10:00 - 10:15**BREAK** 10:15 - 11:00 Informed Consent/Assent and Subject Recruitment • Writing Informed Consent/Assent Research Subject Recruitment Communication/Shared Responsibility 11:00 - 12:00Obtaining Informed Consent/Assent — A Practical Approach 12:00 - 1:00**LUNCH** 1:00 - 1:15Resources for Conducting Clinical Research • Introduction to the Clinical Research Program (CRP) • Introduction to the General Clinical Research Center (GCRC) Good Clinical Practices for Clinical Research Professionals 1:15 - 1:35Study Implementation and Data Management • Study Start-up • Manual of Operations, CRF Completion, and Quality Control • Source Documentation 1:35 - 1:50Study Data and Documents — Regulations and Policies Storage of Study • Documents and Informed Consent Documents Study Close-out and Document Retention 1:50 - 2:30The Study Binder and Files Organizing Study Documents 2:30 - 2:45Introduction to Clinical Research Financial Management • Funded Research • Patient Care Costs 2:45 - 2:50Training Requirements, References, Resources 2:50 - 3:00Wrap-up, Review, Questions

Topics for Coordinators Rounds

Wednesdays 12:00 – 1:00 PM

Date	Topic	Speaker
4/13	Clinical Research at Children's	Carleen Brunelli
5/11	Preparing a Regulatory Binder/Study Filing System	Eunice Newbert
6/8	Obtaining Informed Consent/Assent	Kristi Thomas
7/27	HIPAA-Overview of HIPAA guidelines	
	and how it impacts clinical research	Susan Kornetsky
8/10	Strategies for Patient Recruitment	Carol Sweeney
9/14	Source Documentation	Vicky Turbini
10/12	IRB Submissions/Applications	Christina DiTomasso
11/9	Documenting Protocol Errors and Deviations	Eunice Newbert

D. Coordinating Clinical Research

Coordinating Clinical Research Schedule

November 15 – 17, 2004 8:30 am – 12:00 pm Conference Center at Harvard Medical School

November 15, 2004 Human Subject Protections

WELCOME AND COURSE OVERVIEW Maureen Clark and Amy Kroeplin
Human Subject Protection Responsibilities for Research Nurses/ Study Coordinators and IRB Staff Susan Kornetsky
 Before the Research Begins Training Requirements: Josh Fiedler Protocol Submissions: Christina Di Tomasso Developing/Writing Informed Consents: Christina Di Tomasso
BREAK
 During the Research Research Subject Recruitment: Sarah Mian Continuing Renewals: Josh Fiedler 3 Year Re-writes: Christina Di Tomasso Amendments/Revisions: Sarah Mian Adverse Events: Sarah Mian
After the Research • Working as a Research Team: Susan Kornetsky
Quality Improvement and Human Subject Protection Eunice Yim-Newbert
Obtaining Consent/Assent: Practical Techniques Kristi Thomas
Questions and Discussion

Coordinating Clinical Research Schedule

November 16, 2004 Clinical Research Study Implementation

8:30 – 9:00	 Resources for Conducting Clinical Research Introduction to the CRP: Stavroula Osganian Introduction to the GCRC: Meg McCabe and Kris Jordan
9:00 – 9:30	Designing Clinical Research Studies David Wypij
9:30 – 10:15	Study Implementation and Data ManagementOperationalizing the Study Protocol: Amy Kroeplin
	 Manual of Operations and Training Case Report Form Design and Completion: Amy Kroeplin Managing the Data: Data Management Software, Data Entry, Reports, and Error Resolution: Jason Rightmyer
10:15 – 10:30	BREAK
10:30 – 11:00	 Quality Control of Data Collection Carol Sweeney Internal Study Performance Monitoring and External Study Audits Source Documentation (What, Why and How)
	Study Closeout and Record Retention Carol Sweeney
11:00 - 11:30	Clinical Research Financial Management Kris Jordan
11:30 - 11:45	Training and Certification Resources Maureen Clark
11:45 – 12:00	Questions and Discussion

November 17, 2004 Clinical Trials: FDA Regulations and ICH Good Clinical Practice

This session will provide a general understanding of the drug development process and the US regulatory environment. You will be provided with commonly used clinical research definitions, abbreviations, acronyms and resources. The regulatory historical framework which is the underpinning of how clinical research is practiced today will be discussed and the Code of Federal Regulations emphasized. The organizational structure and the roles of the Food and Drug Administration will be enumerated. The definition, purpose, origin and importance of the International Conference on Harmonization (ICH) Good Clinical Practices will be discussed as well as the key elements of the phases of clinical research.

8:30 – 12:00 Regulatory Historical Framework

Code of Federal Regulations (ICH) Good Clinical Practices Terry Himmelmann PA, MA, CCRA