

2006

Annual Report

of the
Clinical Research Program

SUBMITTED BY
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Children's Hospital Boston

**ANNUAL REPORT OF THE
CLINICAL RESEARCH PROGRAM
FY 2006**

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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 32 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.
- Forty-nine publications that were co-authored by CRP staff.
- 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.
- Organization of a new team within ISD, the clinical research information team (CRIT).
- 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 FY06 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

In spring of 2006, Dr. Osganian presented the 5-year clinical research strategic plan of the Clinical Research Executive Committee to the Research Subcommittee of the Board of Trustees. The plan was enthusiastically approved by the Board research subcommittee. The plan outlined several key recommendations that included support for the recruitment of clinical research investigators, support for clinical research infrastructure and pilot projects, growth in space, metrics to monitor the clinical research enterprise, and alternative sources of extramural support for clinical research as well as a 5-year financial plan to support the recommendations. The CREC also identified six research themes for which to prioritize institutional resources and growth: These included Interventions During Fetal Life; Clinical Neurosciences, Inflammation and Immunity; Tissue Engineering, Cell Therapy and Transplantation; Childhood Obesity; and Blood Development and Oncology. The CREC will be focusing on developing a plan for its implementation in the next fiscal year.

Other FY2006 activities included a \$20,000 commitment to support the educational activities of the Fellowship Training Program which is under the leadership of Dr. Jordan Kreidberg, and a commitment of \$302,000 per year for 2 years to the General Clinical Research Center, under the leadership of Dr. Richard Grand, to provide additional support for the implementation of CHB investigators' clinical research projects.

2. PROGRAM ORGANIZATION

Having recognized the need to develop innovative and efficient clinical research informatics solutions for the clinical research enterprise, the Clinical Research Program established a formal relationship with the Information Systems Department (ISD). The CRP applications development team was re-organized as the Clinical Research Information Technology (CRIT) Team within ISD's Knowledge Management Group, under the direction of Danny Shaw, and it has a direct reporting relationship within ISD and indirect reporting relationship within the CRP. This new integrated structure will allow the clinical research community to benefit from enterprise-wide technological initiatives and resources within ISD while still servicing the database needs of individual investigators. Team leader of the CRIT is Jason Rightmyer, MS.

3. PROGRAM UTILIZATION AND GROWTH

The CRP continues to support over 300 investigator requests for assistance from approximately 150 researchers in the institution. The Program has maintained significant funding from collaborative projects and CHB investigators, with 83 projects funding CRP staff in F06 and totaling approximately \$1.2 million in funding from grants, Departments and programs. Furthermore, forty-nine publications were co-authored by CRP staff.

4. PROGRAM COMMUNICATIONS

In 2006 the CRP developed and distributed two issues of its first quarterly newsletter, *Clinical Research News*. Distribution totaled 600 and included the hospital administration, Department and Division Chiefs, the Clinical Research Executive Committee, Basic Science leadership, and investigators throughout CHB. *Clinical Research News* combines spotlight articles about innovative clinical research being conducted at CHB, news from the Clinical Research Executive Committee, the GCRC and the Office of Faculty Development, as well as regular educational columns (which provide advice and guidance on the writing of research proposals for the CHB community), data management and study coordination tips, and in-depth statistical forums.

5. BIOSTATISTICS CORE

Under the direction of Dr. David Wypij, Core staff in FY2006 included Parul Aneja, MS, Carl de Moor, PhD, Henry Feldman, PhD, Peter Forbes, MA, Dionne Graham, PhD, Sion Harris, PhD, Patrick Johnston, MMATH, Leslie Kalish, ScD, and Clarissa Valim, MD, ScD.

a. Collaboration and Manuscript Preparation

CRP biostatisticians have worked in new and continued collaborations with Children's Hospital clinical investigators. FY2006 highlights include the following:

- Within the Stem Cell Program and Division of Hematology/Oncology, a new method for estimating stem cell frequency in zebra fish, a prominent animal model for studying the genetics of blood formation (with Dr. Henry Feldman);
- Analysis of a large retrospective clinical database to evaluate the utility of lymphocyte proliferation assays as a screening tool for detecting abnormalities in T-cell number and function (with Dr. Henry Feldman);
- Methodological studies of ultrasound and x-ray methods for measuring bone density and strength in young women with anorexia nervosa (with Dr. Henry Feldman);
- Identification of risk factors for the development of asthma in infants hospitalized with RSV (with Dr. Dionne Graham);
- Development of nomograms predicting the rate of resolution of vesico-ureteral reflux (with Dr. Dionne Graham);
- Variations in length of stay and hospital charges for cystic fibrosis patients (with Dr. Dionne Graham);
- Multi-site study assessing the prevalence of positive screens for substance abuse among adolescent primary care patients (with Drs. Sion Harris and Carl de Moor);
- A national survey of physicians assessing physician practices and knowledge regarding drug-testing of adolescent in ambulatory medicine (with Dr. Sion Harris);
- Use of alloplastic materials in rhinoplasty surgery via a meta-analysis (with Mr. Patrick Johnston);
- Effect of trainees on length of stay in a Pediatric Emergency Department (with Mr. Patrick Johnston);
- Impact of *Burkholderia dolosa* on lung function and survival in cystic fibrosis (with Dr. Leslie Kalish);
- Pulse-inversion ultrasound imaging of testicular ischemia (with Dr. Leslie Kalish);
- Association between financial ties to industry and the reporting of non-FDA-approved uses of industry products (with Dr. Leslie Kalish);

- Assessment of sedation adverse events (with Dr. Clarissa Valim);
- Evaluation of the efficacy of a fish oil based parenteral nutrition solution to reverse parenteral nutrition associated liver disease (with Dr. Clarissa Valim).

A full list of recent publications is included in Appendix B.

b. New Funded Grant Applications

CRP biostatisticians worked closely with various CHB clinical investigators on the development of protocols and grant applications for federal, foundation and other non-federal awards. New NIH grants that supported CRP biostatisticians include those of Dr. Alison Field on weight cycling and mortality in women (with Ms. Parul Aneja), Dr. Catherine Gordon on effects of adrenal and gonadal hormone replacement in young women with anorexia nervosa (with Dr. Henry Feldman), Dr. David Ludwig on reducing sugar-sweetened beverage consumption in overweight adolescents (with Dr. Feldman and Ms. Tracy Antonelli), Dr. Ludwig on popular diets, metabolism, and CVD risk (with Dr. Feldman), Dr. Lori Pbert on school nurse delivered smoking cessation intervention for adolescents (with Dr. Stavroula Osganian), Dr. Stephen Porter on health literacy and information management in ADHD: designing an optimal record (with Dr. Feldman), Dr. Terrie Taylor on redefining cerebral malaria (with Drs. David Wypij and Clarissa Valim), and Dr. Rachel Rosen on the accuracy of multi-channel intraluminal impedance to detect airway inflammation in children and on the effect of non-acid reflux on respiratory diseases (both with Dr. Clarissa Valim).

A full list of federal and non-federal grants that CRP staff have collaborated on is included in Collaborative Projects on page 37.

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. Additionally, Dr. Dionne Graham and Mr. Peter Forbes taught “Introduction to Biostatistics with SPSS” twice in FY2006 to faculty, fellows, and clinical researchers, and Dr. Henry Feldman taught a short course on Statistical Power for Clinical Studies. Besides teaching courses, CRP biostatisticians have made numerous presentations to hospital seminar series and at national meetings. Dr. Feldman presented at an American Heart Association seminar series on the epidemiology and prevention of cardiovascular diseases and also presented a biostatistics lecture series with consultation and work-in-progress seminars at the Department of Epidemiology, University of Alabama at Birmingham School of Public Health. Dr. David Wypij taught courses in biostatistics at Harvard School of Public Health. Dr. Wypij also presented at biostatistics short courses in Italy and with Dr. Clarissa Valim in Africa. The Biostatistics Core is planning to increase education opportunities at Children’s Hospital in the coming year.

A full list of teaching accomplishments that CRP biostatisticians have performed are described in Education and Training on page 25 and Staff Accomplishments on page 45.

d. Funding from Departments/Divisions

To best support Departments and Divisions at Children’s Hospital who require ongoing biostatistical assistance, the CRP Biostatistics Core has sought out additional collaborative relationships with several Departments and Divisions throughout the hospital.

In FY2006, in addition to continued support from Division of Adolescent Medicine, Psychiatry, and Program for Patient Safety and Quality, new department funding of CRP Biostatistics Core staff came from the Departments of Cardiology, Emergency, Division of Gastroenterology/Nutrition, and Division of General Pediatrics. Additional Departments and Divisions are expected to share funding of CRP biostatisticians from internal funds and research grants.

The CRP Biostatistics Core staff affiliated with each specific clinical Department/Programs includes: Adolescent/Young Adult Medicine (Ms. Parul Aneja), Psychiatry (Dr. Carl de Moor) Trauma Program (Mr. Peter Forbes), Program for Patient Safety and Quality (Dr. Dionne Graham), General Pediatrics (Dr. Sion Harris), Emergency Medicine (Mr. Patrick Johnston), Hematology/Oncology and Infectious Disease (Dr. Leslie Kalish), Division of Gastroenterology/Nutrition (Dr. Clarissa Valim), and Cardiology (Dr. David Wypij, Dr. Dionne Graham). In FY2007, the Core will further its expansion by recruiting biostatisticians affiliated with the Departments of Neurology, Surgery, and the Genomics Program.

e. New Hires

The CRP Biostatistics Core continued to grow in FY2006 with the addition of a new staff member, Mr. Patrick Johnston. Growth in CRP biostatistics staff has primarily come from collaborative efforts with various Departments and Divisions in the hospital, including Departmental and Program funds, and grant funding with CHB clinical investigators.

6. PROJECT AND DATA MANAGEMENT CORE

Under the direction of Dr. Carl de Moor, the Project and Data Management Core staff in FY 2006 included Susan McDermott, RN, MPH, Maggie McCarthy, MPH, Tracy Antonelli, MPH, Maureen Clark, MS, Aruna Jayashankar, MS, Sharon Wong, BS, Rajna Filip-Dhima, BS, and Harold Thurston, MA, MAT.

a. Study Coordinator Orientation and Coordinator Rounds Seminar Series

The DMC continued to host the bi-monthly Study Coordinator Orientation program for new clinical research assistants and study coordinators. With the change in staffing described below, Susan McDermott assumed the role as host and lead speaker for the Orientation as well as the bi-monthly Study Coordinator Rounds. The day long Study Coordinator Orientation program covers basic topics essential to the management of clinical research at CHB. The Coordinator Rounds offers CHB research staff a bi-monthly forum to discuss common logistic challenges and review important updates in the field of clinical research.

b. Development of Curriculum for Project/Data Management Course

Tracy Antonelli, MPH, developed the curriculum for this hands-on course to serve as a practical guide for new clinical investigators. The 3 session course in Project and Data Management aims to orient new investigators to those standards and regulations pertaining to the implementation of clinical research. Topics incorporated into the curriculum include a review of the ICH Good Clinical Practice standards and the principles and practices for development of study timelines, case report forms, and a study manual of operations. The target audience for the course is junior faculty, fellows, nurse investigators and others who develop and implement clinical research at CHB.

c. 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 18 new research projects.

d. DM Staff Skill Development

In the late winter of 2005, three assigned staff members of the DMC began an on-line course of study in SAS. The aim of this staff development initiative was to improve individual as well as team capabilities in data management and data file manipulation and to improve efficiencies when data are transferred between data management and biostatistical staff. The staff development initiative continued through FY06 and continues in FY07.

e. New Survey Scanning Capabilities

In 2006 the CRP purchased a new survey scanner, the OpScan iNSIGHT4U, which will allow DMC staff to design, print and scan custom-made surveys. The optical mark read (OMR) scanner permits scanning of 2,200 forms per hour. DMC staff will be trained on the software this coming year.

f. Development and Distribution of the Subject Recruitment SOP

In the spring of 2006, DMC staff developed a new Research Practice Guideline, "Guidelines for Recruitment." The new Guidelines describe relevant policies, standards and proven strategies for recruitment of subjects into clinical research studies with an aim to improve subject recruitment practices for CHB clinical research studies overall. The Guidelines include several examples and templates of recruitment tools including flyers, brochures, and publication advertisements.

g. Staffing Changes

The DMC added three staff members in fiscal year 2006. Tracy Antonelli, MPH, was hired as a Project Director in February 2006. Ms. Antonelli works as Project Manager of the BASH II study. She also provides project management and data management advice to CHB Investigators requesting assistance from the CRP.

Susan McDermott, RN, MPH, joined the DMC in August of 2006 as Team Leader of the Project Management and Data Management Team. As such, she provides direct leadership and supervision to the team and expert advice to CHB Investigators in the areas of project and data management. Ms. McDermott also serves as key speaker and host of the Study Coordinator Orientation and bi-monthly Study Coordinator Rounds.

Harold Thurston, MA, MAT, joined the DMC in March 2006 as Administrative Coordinator.

7. CLINICAL RESEARCH INFORMATION TECHNOLOGY

The Clinical Research Information Technology (CRIT) staff serves to support and enhance the clinical research enterprise, support the investigator community and improve Clinical Research Program (CRP) operations.

a. New Relationship With Information Services Department (ISD)

The CRP applications development team officially joined the ISD in 2006. The team was renamed Clinical Research Information Technology and integrates closely the domain knowledge of the CRP with the technical expertise of the ISD. The CRIT is responsible primarily for sharing technical skills and resources, enhancing collaboration, and improving the efficiency of clinical research applications development. Led by Jason Rightmyer, the unit serves to champion innovative informatics solutions and expand IT services to the entire clinical research community.

b. New Budget Tracking Software for the CRP/GCRC

The CRIT worked closely with the CRP administrative team to design, program and deploy a new Web-based budget tracking software application. This application facilitates authoring and managing project budgets across multiple funding mechanisms. The software also provides a variety of reports to ensure accurate tracking of staff and funding commitments for strategic planning.

c. Replacement of Randomization Software Application

The CRP employs scientific software to support various randomization techniques. Over the past year, the CRP Biostatistics Core and CRIT team have worked collaboratively to develop new Web-based software that facilitates creating randomizations. This new software not only generates treatment

assignments and subject identification numbers, but also produces ready-made study materials. These materials include subject logs, study labels and data sets, which may be employed directly in study operations.

d. New IT Service for Survey Research

In 2006, the CRIT added electronic survey capabilities to its solutions platform. The CRIT now offers researchers access to Web-based software to quickly develop, deploy and manage interactive surveys through the Internet. The application software is easy to use and requires no programming experience. Furthermore, the product provides a variety of mechanisms to ensure safe and secure access to surveys and respondent data.

e. Upgrade of CRP and GCRC Web Sites with Content Management

In early 2006, the CRIT replaced the outdated CRP and GCRC Web sites. These new sites are supported by a content management system that enables administrative staff to update content without Web programming support. This new content management software benefits survey research teams too. The software allows the CRIT to quickly create and deploy study-specific Web sites that complement online surveys.

f. New GCRC Protocol Review Process

The General Clinical Research Center (GCRC) implemented a new electronic protocol review process using online collaborative application software. Mr. Joseph Rezuke worked closely with GCRC protocol reviewers to architect the solution using Microsoft SharePoint Services. The solution has benefited the GCRC administrative staff tremendously and now all protocols are reviewed and revised centrally on the hospital network.

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

The CRIT developed and deployed several new large-scale data management systems in 2006. Specifically, the applications development team implemented systems for use in Orthopedics, Hematology, Endocrinology and Urology. The CRIT now supports over 20 clinical data management systems in the field and anticipates adding several more in the upcoming year.

8. EDUCATION CORE

Under the direction of Dr. Jenifer Lightdale, the major activities and accomplishments of the Education Core in 2006 included:

a. Teaching Across the Entire Research Community at Children's Hospital Boston

The Education Core is responsible for the planning, organization and implementation of all CRP sponsored seminars and courses. Our aim is to provide a comprehensive educational plan with course offerings from a basic to advanced curriculum for clinical research. Accordingly, the Education Core works closely with both the Data Management Core (DMC) and the Biostatistics Core to meet the research educational needs of study coordinators, nurses, medical students, fellows, junior faculty and more senior faculty involved in clinical research across the hospital. The Education Core is continuing to build our curriculum by adding 1-2 new courses a year. In FY2006, Dr. Henry Feldman taught a 3-session advanced biostatistics course entitled: "(Study) Power and How to Get It." Additionally, we began to develop two new courses entitled: "Data Management" and "Bias and Confounding" for FY2007.

b. Accreditation from Harvard Medical School Continuing Medical Education (CME)

In FY2006, the Education Core applied for and received approval to offer a total of 16 Category I HMS CME credits to attendants of Introduction to Clinical Research. All physicians who attended the course were provided with an appropriate certificate.

c. Conducting of a Needs Assessment Survey for Fellows' Research Education

To better assess the clinical research needs of fellows in different Departments and Divisions across Children's Hospital, the Education Core conducted an electronic survey of all Fellowship Directors and Programmatic Chiefs at Children's in FY2006. We received a 60% response rate to our survey, with most (70%) directors/chiefs reporting that their individual fellowship training program was required to provide education about conducting clinical research. Almost all (94%) reported that at least some of their fellows performed clinical research during their fellowship, mostly during their second and third years of training. 62% of fellowship directors / program chiefs stated that they felt Children's Hospital Boston could do more to contribute to their fellows' knowledge about conducting and interpreting clinical research.

d. Establishment of a Career Development Award (K-series) Lending Library

To provide examples of successful Career Development Awards for prospective grant applicants to use as models during their own grant writing process, the Education Core solicited, compiled and has made available a lending library of K-awards. All principal investigators who have contributed their grants to the library have graciously agreed to let other investigators at Children's Hospital use them (often in conjunction with reviewer comments), as they prepare their own submissions. It is hoped that such collaboration and "virtual" mentoring will strengthen the nascent clinical research community at Children's.

e. New Hires

In FY06 the Education Core hired Kristi Lawrence, BA, as Education Coordinator. Ms. Lawrence provided administrative support to all faculty and students involved in courses directed and organized by the CRP. She provided an infrastructure by which to best coordinate and successfully implement a growing clinical research education curriculum at Children's.

8. GLASER PEDIATRIC RESEARCH NETWORK

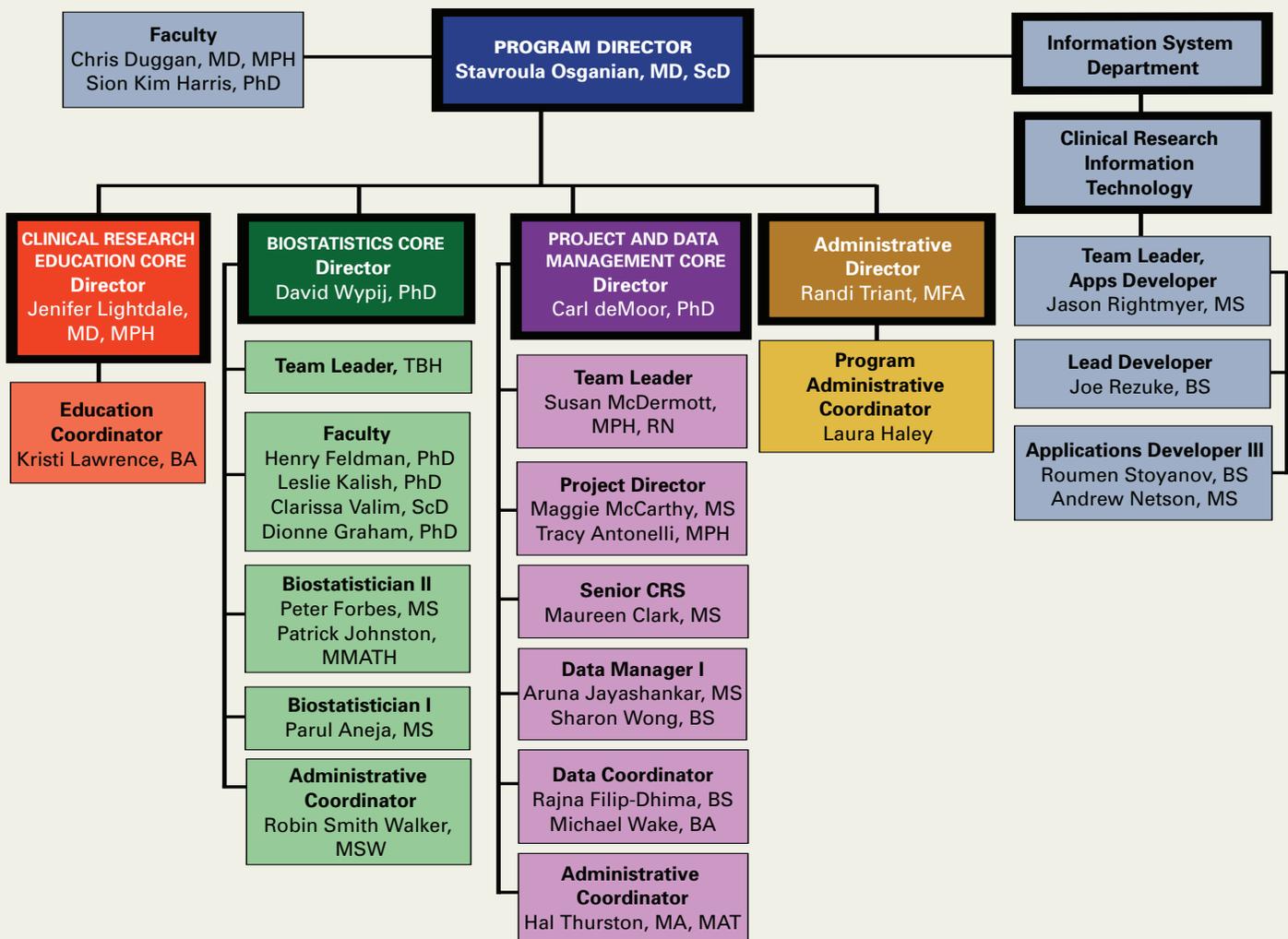
The Program continues to serve as the Design, Analysis, and Coordinating Center for the Glaser Pediatric Research Network, providing biostatistical support and data management for current studies and education for the Glaser fellows. The Core contract between CRP and GPRN covers review of developing studies and conduct of training seminars for the fellows. Three additional contracts were in operation in 2006 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 one-year follow-up evaluation period, and submitted the findings for publication.
- A trial of metformin in obese adolescents published baseline data and completed the one-year intervention period.
- A registry for clinical data on necrotizing enterocolitis in newborns enrolled an additional 150 patients, nearing 400 total.

Program Organizational Structure

The Program included in 2006 28 full-time and 4 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. Her present research includes a trial of metformin for weight loss in obese adolescents and a school nurse-delivered smoking cessation intervention for adolescent smokers.

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 multicenter research network for cutting edge pediatric studies based at Children's Hospital Boston as well as Stanford, UCSE, 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 on 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), the Adolescent Patient-Provider Interaction Scale (APPIS), the State-Behavioral Scale (a sedation assessment tool for use with critically ill infants and children), the Active Where instrument which assesses the influence of environmental factors on youth physical activity, and a survey for teen pregnancy prevention coalition members to assess functioning and capacity for action, 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 is the recipient of the 2006 Young Professional Award from the American Public Health Association, Maternal and Child Health Section.

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.

In July 2006, Dr. Wypij left the CRP to join the Department of Cardiology at CHB. We thank him for his dedicated service and leadership to the Biostatistics Core and outstanding teaching to the clinical research community.

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 multicenter 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, *Senior 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 in protocol development and data analysis. In addition, Dr. Valim is a statistician for the Division of GI/ Nutrition, Department of Medicine, and instructor at the Harvard Medical School. Additionally, she is a biostatistician of the NIH-funded Severe Malaria in African Children clinical research network. She has also been committed to teaching at CRP in the Introduction to Clinical Research course.

Dr. Valim's methodological research interests are currently in the area of survival and longitudinal methods and have focused on gastrointestinal diseases. More specifically, she is interested in survival

methods in studies when censoring occurs due to mortality related to the study outcome. In the area of longitudinal analysis, Dr. Valim is interested in predictive models with functional outcomes.

Dionne Graham Manning, PhD, Senior Biostatistician

Dr. Graham Manning 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 Manning'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, Senior 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.

Patrick Johnston, MS, Senior Biostatistician

Patrick Johnston joined the CRP in April 2006 and has since provided statistical support and collaboration to medical researchers in various departments. He has worked extensively on the necrotizing enterocolitis (NEC) study sponsored by the Glaser Pediatric Research Network and is the statistician for the Division of Emergency Medicine. Mr. Johnston is interested in many areas of applied and theoretical statistics, from Bayesian, likelihood, and frequentist approaches to inference, through parametric and semiparametric models, to solving practical problems in design and analysis by simulation. Prior to joining the CRP, Mr. Johnston worked for Abt Associates and GlaxoSmithKline on a broad variety of observational and randomized studies. Mr. Johnston was trained in statistics at the University of Waterloo, and also holds degrees in mathematics and economics.

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 B.Sc. 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 responsibilities include data handling, statistical graphics and statistical analysis. She primarily works with Adolescent Health on the analytic needs of post doctoral fellows and researchers.

Robin Walker, M.S.W., *Administrative Coordinator*

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).

PROJECT AND 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. In May 2006, Dr. de Moor left the CRP to relocate to Ohio. We thank him for his dedicated service to the Project and Data Management Core and contributions to the Biostatistics Core of the CRP.



Susan McDermott, RN, MPH, *Team Leader*

As a public health nurse and ANCC certified nurse practitioner, Ms. McDermott began her clinical research career in 1985 as Field Supervisor working in collaboration with the RAND Corporation on a large national study evaluating the impact of advanced practice nursing on patient care outcomes in underserved populations in the rural western US.

Between 1988 and 2006, Ms. McDermott worked as Project Director and Senior Research Specialist for the New England Research Institutes in Watertown, MA. At NERI, she worked on more than 20 NIH funded studies including R01s, P01s, SBIRs, and cooperative agreements, providing managerial, administrative, statistical, and data coordinating center services to large, multi-center clinical research studies and networks.

Since coming to Children's Hospital, Boston in August, 2006, Ms McDermott has served as Clinical Research Team Leader for the Project and Data Management Core of the Clinical Research Program. Her specialties include clinical research team management; proposal development for field methods and budgeting; on-time study start-up; complex field methods development, deployment, testing and monitoring; data collection tools development; research staff training; quality assurance planning; and development of quality control procedures for clinical research.

Maggie McCarthy, MS, MPH, 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.

Tracy Antonelli, MPH, Project Director

Ms. Antonelli joined the CRP in February 2006. Her responsibilities include managing all aspects of a multi-site NIH-funded trial with the Obesity Program, including study planning, development of case report forms and manuals of operation, data management system specifications, recruitment, and implementation of the protocol in the field. She is also developing clinical research courses, training materials, and SOPs that will be integral parts of the CRP's educational efforts.

Ms. Antonelli has a Master's Degree in Public Health from Boston University. She worked as an Associate Research Scientist at New England Research Institutes managing several multi-site NIH-funded studies. She also has several years of experience in the field where she directed and performed clinical research for a large private urology practice.

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 eleven 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.

Aruna Jayashankar, MS, Data Manager

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 such as 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, Data Manager

Ms. Wong has been working at the CRP since September 2001. Currently, a Data Manager in the Data Management Core, she was previously a Research Software Developer within the CRP. Ms. Wong provides consultation to/collaboration with Principal Investigators and their research teams in different areas of study implementation. Her responsibilities to these projects include various tasks relating to data management and database development for single and multi-site studies.

The majority of Ms. Wong's projects involve building SPSS Data Entry Builder databases and recently, Web-based surveys. In addition to database development, she creates database specifications, tests and debugs the databases/surveys, provides tutorials and supervision to research staff in building databases/surveys, and trains research staff (e.g., data entry). She is also teaching and reviewing CRP DMC staff-built SPSS Data Entry Builder databases, and testing and debugging SciRUS databases. Her data management-related responsibilities include developing study logs and case report forms; running randomization; coordinating study data; performing data entry and data cleaning; performing quality assurance checks; and investigating any missing and/or conflicting data. She is also learning and using SAS to clean data in existing databases.

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, Ms. Filip-Dhima 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. Ms. Filip-Dhima 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.

Recently, Ms. Filip-Dhima has been more involved with some of the studies as she is assisting biostatisticians on the preparation of the data for analysis using SAS. In addition, she programs databases using SPSS data builder, as well as creates case report forms for some of the studies she is working on.

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.

Harold Thurston, MA, MAT, *Administrative Coordinator*

Mr. Thurston joined the CRP in March, 2006; he provides overall administrative support for the Project and Data Management Core and Clinical Research Information Technology Group (CRIT). He has spent his professional life working in the private public health research sector, most recently as the Executive Assistant to the Vice President of Communications and Media for New England Research Institutes, and as a patient information specialist at Caritas St. Elizabeth Medical Center, Boston. Mr. Thurston holds a Master of Arts with a concentration in Design & Environmental Analysis and a Master of Arts in Teaching with a concentration in Program and Curriculum Development from Cornell University.

CLINICAL RESEARCH INFORMATICS TECHNOLOGY

Jason Rightmyer, MS, *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). In FY2006 Mr. Rezuke developed a new Web-based budget tracking software application for the CRP.

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. Mr. Stoyanov works closely with the Program for Patient Safety and Quality

(PPSQ). He has developed a number of solutions for the PPSQ including SEAMA, a case management tool for investigative operations of safety events reported at Children's Hospital Boston. Mr. Stoyanov is also responsible for all software development initiatives of the Glaser Pediatric Research Network (GPRN). He has implemented and supported several Web-based data management systems for national multi-site clinical trials and longitudinal studies for the GPRN.

ADMINISTRATION CORE



Randi Triant, MFA, *Administrative Director*

Ms. Triant joined the CRP in January of 2006 as Administrative Director. She has over twenty-four years of administrative and management experience, particularly in public health research. Prior to joining the CRP she was the Vice President of Communications and Media for New England Research Institutes. She also served as Principal Investigator or Project Director of fourteen NIH-funded SBIR grants, developing and evaluating multi-media programs and hand-held devices.

Laura Haley, *Program Administrative Coordinator*

Ms. Haley joined the CRP in July 2003; she provides direct administrative support to the Director as well as general Program administration. She has over ten years of administrative experience, primarily in the private sector, in industries as varied as software development, manufacturing, marketing, and telecommunications.

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 at 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 Quality (KO8 HS013675) to investigate means of improving patient safety for children receiving procedural sedation and analgesia.

Kristi Lawrence, BA, *Administrative Associate IV*

Ms. Lawrence started in the CRP as Education Coordinator in February 2006. Prior to that she had been an administrative assistant in the Emergency Department.

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 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 FY06, the CRP worked on 330 clinical research projects (Table 1). The majority of these projects (n=247) did not provide funding for CRP staff. Eighty-three (25%) of these projects funded the CRP staff for a total of \$1,215,694.

Table 1. FY06 CRP projects by funding status

	Funding Status		Total
	No CRP funds received in FY06	Any CRP funds received in FY06	
No. of Projects	247	83	330
Total CRP FY06 costs	0	\$1,215,694	\$1,215,694

*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 83 projects during FY06 and the amount of support provided to each area. Data Management Services include the combined service areas of Clinical Study Management, Database Programming, and Data Entry.

Table 2. Direct costs by service area for 83 projects funding CPR in FY06

Service areas	No. of Projects requiring funded services*	FY06 CRP Funding (% of total dollars)
PI	13	\$155,330 (13%)
Biostatistics	66	\$630,551 (52%)
Clinical Study Management	28	\$173,507 (14%)
Database Programming	19	\$203,318 (17%)
Data entry	18	\$52,988 (4%)
Total	83	\$1,215,694 (100%)

*A single project often funds several service areas.

Figure 1. CRP Direct Costs by Service Area

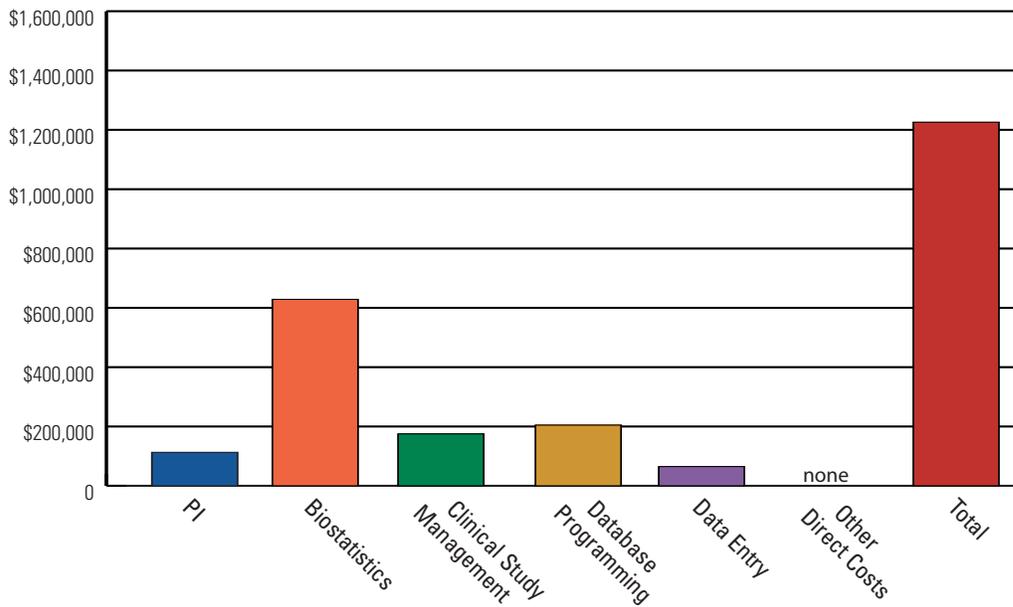


Table 2 presents the distribution of funding sources for the 83 projects providing financial support to the CRP. NIH and Foundations were the primary sources of funding for these projects (58% and 29% of funded projects, respectively). Among the 34 NIH funded projects, 18 were funded by R01 mechanisms, 2 were R03, 2 were R21, 3 were K23, and 9 were other funding mechanisms (K23, R37, M01, P50, etc.).

More than half (n=48) of the 83 funded projects were from collaborations with researchers from the Department of Medicine. The remainder was from various departments in the Hospital including Cardiology (n=3), Radiology (n=4), Surgery (n=2), Laboratory Medicine (n=1), Otolaryngology (n=3), Neurology (n=3), Psychiatry (n=2), Anesthesia (n=3), and Urology (n=3). The Clinical Research Program faculty were PIs on five of the 83 projects. The rank of the PI for the funded projects was also variable: Professor (12%), Associate Professor (10%), Assistant Professor (23%), Fellow (5%), Instructor (33%), Nurse (3%), and Other (3%).

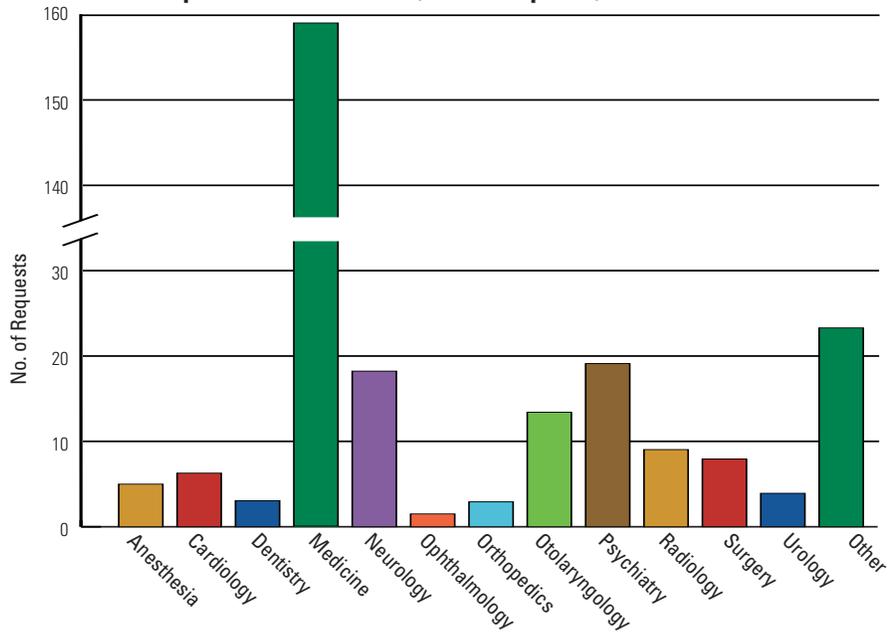
Table 3. Funding sources for 83 projects funding CPR in FY06

	No. of Projects	FY06 CRP Funding (% of total dollars)	
NIH	34	\$705,538	(58%)
Other Federal	8	\$78,924	(6%)
Foundation	22	\$353,266	(29%)
Industry	6	\$44,909	(4%)
Departmental	7	\$21,021	(2%)
Other	6	\$12,036	(1%)
Total	83	\$1,215,694	(100%)

NEW REQUESTS FOR ASSISTANCE IN FY06

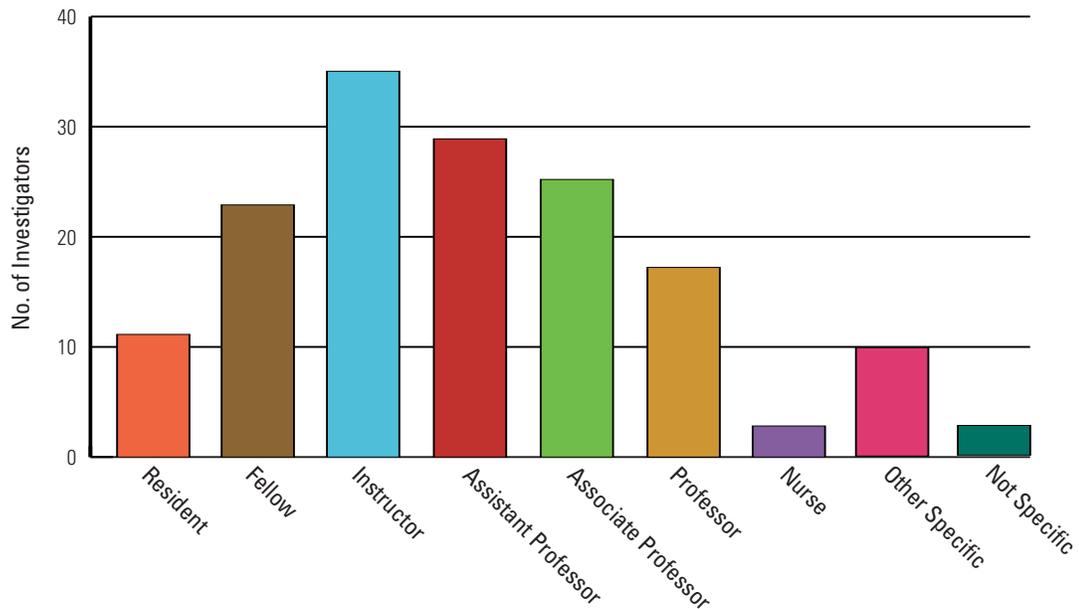
During FY06, the CRP received 272 new requests for assistance from 156 Children's Hospital faculty or staff. The distribution of requests according to hospital department is shown in Figure 2. The majority of requests were from Investigators with appointments in Medicine (n=159) and within the Divisions of Emergency Medicine (n=13), Endocrinology (n=19), Adolescent Medicine (n=23), Hematology/Oncology (n=14), GI/Nutrition (n=33), General Pediatrics (n=8), Infectious Diseases (n=11), and Pulmonary (n=7).

Figure 2. FY06 CRP Requests for Assistance (N=272 Requests)



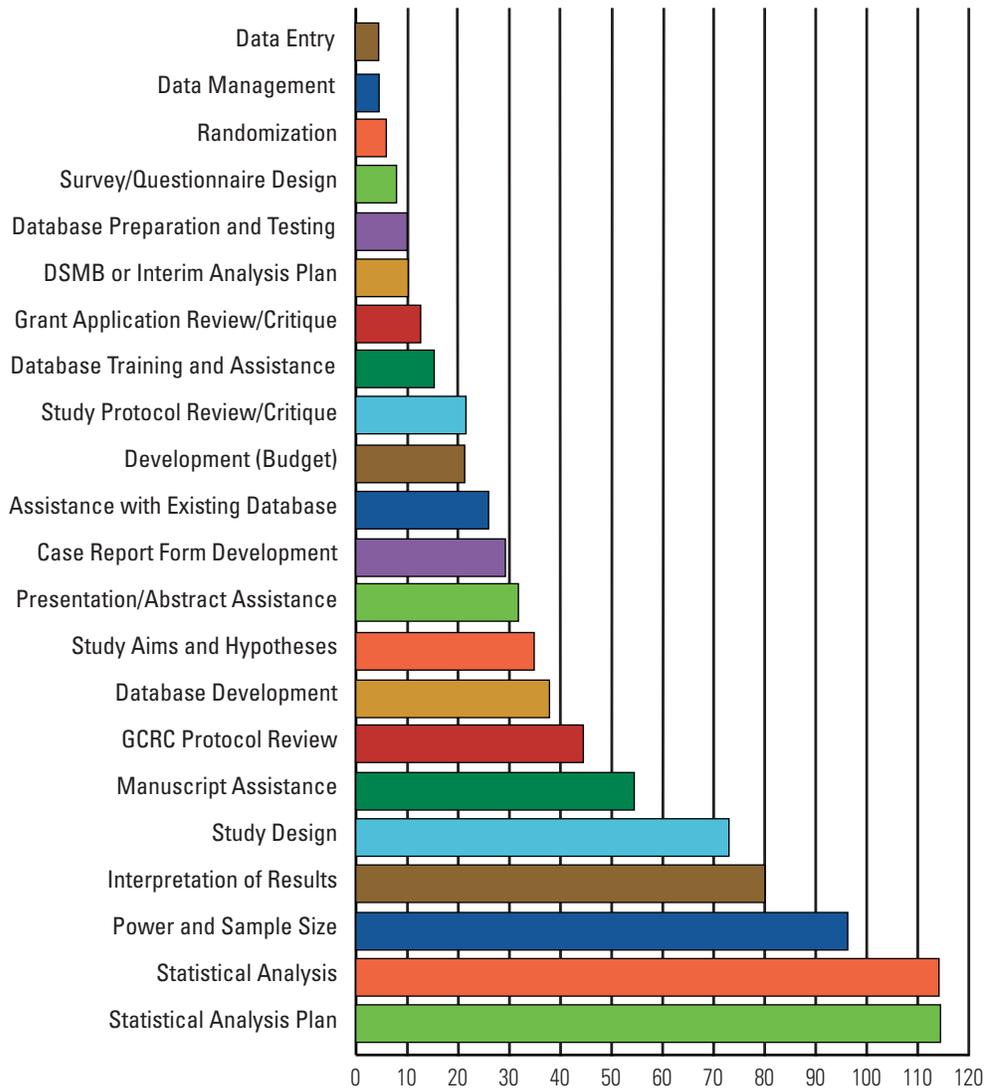
As shown in Figure 3, investigators requesting assistance were somewhat more likely to be at the rank of, Instructor (n=35), Assistant Professor (n=29), Associate Professor (n=25) or Fellow (n=23), as compared to Professor (n=17) or Resident (n=11).

Figure 3. Rank of Investigators Requesting CRP Assistance (N=156 Investigators)



As shown in Figure 4, the majority of requests were for consultation on design and analysis including estimation of sample size and power (n=96), development of a statistical analysis plan (n=114), study design (n=72), or analyses of data (n=114). Approximately 46 requests were related to study implementation, including case report form or survey design and/or database assistance.

Figure 4. Services Requested (N=272 Requests)



More than a third (n=102) of the 272 new requests for CRP resources had funding to support the project and almost one-quarter (n=71) were applying for funding. Among the 102 funded projects, NIH (n=33), foundations (n=23) and department funds (n=25) were the primary funding sources. Among those investigators submitting grant proposals for funding, the majority (n=52) were first submissions, whereas the remainder were mainly resubmissions (n=16) or non-competing renewals (n=3).

Among the 71 new requests applying for funding, 38 are applying to NIH, 17 to foundations, 3 to other federal, 3 to department funds, 3 to Internal Award, 1 to industry, and 6 to other mechanisms for funding. For the 38 applying to NIH, the mechanisms for funding were 14 for R01s, 3 for R03s, 9 for R21s, 9 for various K awards, 2 for other mechanisms, and 1 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 **Introduction to Clinical Research, Orientation for New Study Coordinators, Coordinator Rounds, Introduction to Biostatistics, and (Statistical) Power and How to Get It**, which are described below. Agendas for the courses are located in Appendix C.

A. INTRODUCTION TO CLINICAL RESEARCH

1. Description

As part of the charter mission of the CRP at Children's Hospital Boston, the *Introduction to Clinical Research* course has been offered biannually since the inception of the program in 1998. The timing, content and format of this course are appropriate for faculty, fellows, nurse investigators and others at Children's Hospital Boston who may want to develop a grant proposal or clinical research project.

The major components of *Introduction to Clinical Research* course include:

- Study Design
- Research Ethics
- Clinical Trials
- Data Management
- Biostatistics
- Grant Writing

The course provides participants with a knowledge base so that they may be better prepared to develop and conduct their research. Upon completion of the course, participants gain a better understanding of how to:

- Develop a research question and hypotheses.
- Select a study design that makes it possible to answer the proposed study hypotheses.
- Understand the potential biases associated with the various study designs.
- Understand the basic statistical analysis methods and how they address a research question.
- Interpret the results of statistical tests and data analyses.
- Be aware of the logistics involved in implementing a clinical research study.
- Protect human subjects, confidentiality of data, and ethical issues in pediatric research.
- Understand the content of a NIH grant proposal and the application process.
- Understand the data and safety monitoring requirements for clinical trials.
- Understand how to evaluate and interpret the performance of a screening or diagnostic test.

- Be aware of investigators' obligations to meet Good Clinical Practices (GCP) guidelines for clinical research studies.
- Understand approaches to improve the quality of scientific review and presentations.
- Use the resources available for the conduct of clinical research at Children's Hospital.

2. Overall Evaluation

The following table summarizes participants overall evaluation of the *Introduction to Clinical Research* sessions that were offered in 2006.

Overall Course Evaluation*	
Level of the presentation was appropriate	3.5
Sufficient time for questions	3.4
Contact with faculty	3.1
The slides were clear	3.7
The syllabus is a useful reference	3.6

*Score Range: 1 (Strongly Disagree) to 4 (Strongly Agree)

B. ORIENTATION FOR NEW STUDY COORDINATORS

1. Description

This one day *Orientation* for new study coordinators and research assistants provides information about conducting clinical research at Children's Hospital Boston. The *Orientation* covers the most relevant clinical research topics for study coordinators and research assistants. To facilitate group discussions and allow ample time for questions, registration in the *Orientation* is limited to 10 people per session.

Topics covered include:

- Overview of Study Coordinator Responsibilities
- CHB resources for conducting clinical research: CRP & GCRC
- Good clinical practices for clinical research professionals
- The IRB
- Human Subject Protocols
- Obtaining informed consent/assent
- Introduction to the Clinical Trials Office
- Introduction to the Office of Sponsored Projects
- Study implementation and data management
- Study data and documents
- Organization of study materials

2. Overall Evaluation

The following table summarizes participants' overall evaluation for the 2006 *Orientation for New Study Coordinators* sessions.

	Orientation Objectives Met*
Satisfaction with the Orientation overall	3.5
Orientation met expectations	3.5
Orientation provided information that can be useful in clinical research role	3.7
Would recommend Orientation to others	3.7

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

C. COORDINATOR ROUNDS

1. Description

The CRP offers a seminar series entitled *Coordinator Rounds* for clinical research staff featuring topics pertinent to conducting clinical research at CHB. The seminar series complements the *Orientation for New Study Coordinators* by exploring issues related to coordinator responsibilities in greater depth. After surveying our participants, the *Coordinator Rounds* were switched to a bimonthly schedule in 2006. Topics and speakers for the 2006 *Coordinator Rounds* are listed below:

Date	Topic	Speaker(s)
1/11	Clinical Research Billing: Update and Open Forum	Kristine Jordan, John Counts, Beth Brennan & Kathleen Theisen
2/8	Database Management Systems	Jason Rightmyer
3/8	CHAMPS Lecture	CHAMPS Team
4/12	Patients Guide to Medical Research	CRP
5/10	Genetics Research	Stephanie Brewster & Ingrid Holm
10/18	Clinical Trials Office	Jesse Wheeler, Kelley Madden, John Counts, Beth Brennan, Tracy Lewis & Kristine Jordan
12/13	Introduction to Patents	Patrick Taylor

D. INTRODUCTION TO BIOSTATISTICS

1. Description

Introduced in 2006, this six-lecture course and its companion computer labs cover the basic principles of biostatistics and the SPSS program. The course is designed for junior faculty, fellows, nurse investigators, study coordinators and others who desire further knowledge of introductory biostatistics. Participants are encouraged to attend *Introduction to Clinical Research* or *Orientation for New Study Coordinators*, prior to taking this course. The lectures are taught by Dionne Graham, PhD and the SPSS computer labs are led by Peter Forbes, MA, both of the CRP.

Topics include:

- Data Summaries
- Graphical Methods
- Confidence Intervals

- Comparing Means
- Comparing proportions
- Nonparametric tests
- Managing your data
- Statistical analysis with SPSS

Course participants become better prepared to analyze their data, interact with statisticians, and interpret scientific literature. Upon completion of the course, participants gain an understanding of how to:

- Summarize data and present results in graphical and tabular forms.
- Calculate and interpret confidence intervals.
- Compare means between two or more groups using t-tests and ANOVA.
- Compare proportions between two or more groups using the Chi-square test.
- Perform non-parametric tests.
- Interpret p-values.
- Choose the appropriate statistical test.
- Evaluate and interpret the performance of a screening or diagnostic test.
- Create and import datasets in SPSS.
- Perform data cleaning and create new variables in SPSS.
- Use SPSS to perform the statistical methods presented during lecture.

2. Overall Evaluation

95.5% of participants agreed that the lectures were useful.

86.4% of participants thought that the content of the SPSS labs was useful.

E. (STATISTICAL) POWER AND HOW TO GET IT

1. Description

Introduced in 2006 and taught by Dr. Henry Feldman, this mini-course explores more advanced concepts of statistical precision, power, and detectable effect, using case studies and exercises to illustrate their applications to the design of clinical research. The course is designed for faculty, fellows and others planning to be investigators in clinical studies. Previous courses in biostatistics (such as the CRP's *Introduction to Biostatistics*) are recommended. The three sessions include:

- Review of key concepts: precision, standard error, inferential error
- Definition of power and detectable effect
- Relation to sample size, study design, Type I and Type II error
- Catalogue of formulas for various study designs
- Take-home exercise: real life design scenarios
- In-class presentation and discussion

The course provides participants with a working knowledge of the rationale and trade-offs for choice of sample size in clinical research. Students become better prepared to design studies, interact with statisticians, win research grants, evaluate protocols, and interpret their own and others' findings. Upon completion of the course, participants are able to:

- Interpret confidence intervals, p-values, and estimates of power and detectable effect.
- Use pilot data or data from literature to design a new study.
- Choose among alternative designs to answer a scientific question.
- Choose among alternative outcome measures.
- Justify the proposed sample size for a research grant.
- Evaluate a proposed clinical protocol.
- Collaborate with biostatistician colleagues.

F. CAREER DEVELOPMENT BLOCK

1. Description

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. CRP faculty continue to participate quarterly in CDB activities. 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's Hospital, Boston Improving quality of health care at all levels.

Clinical Research Program Spotlights

A. COLLABORATIONS WITH CHB INVESTIGATORS

1. Biostatistics Departmental Affiliated Model

The key mission of the Clinical Research Program is to enhance the quality of the clinical research performed at Children's Hospital. In order to better serve the hospital departments with large clinical research components as well as to enhance the collaborative efforts of CRP biostatisticians, the CRP is moving toward a model where each staff member is affiliated with a particular department, which, for PhD level biostatisticians, includes academic appointment within the department. In return for partial salary support, CRP biostatisticians provide the same range of biostatistical expertise available in short-term billing arrangements; however, the continuity provided by the departmental affiliation fosters true collaborative spirit among the investigators and biostatisticians, allowing the biostatisticians to deepen their understanding of the clinical questions as well as furthering the statistical knowledge of clinicians. Such interactions lead to improved quality of clinical research and innovations in statistical methodology. During FY06, all CRP PhD biostatisticians held academic appointments within Children's Hospital and Harvard Medical School. They were: Carl de Moor, Adolescent Medicine and Psychiatry; Henry Feldman, Endocrinology; Dionne Graham, Cardiology; Sion Harris, General Pediatrics; Leslie Kalish, Infectious Disease; Clarissa Valim, Gastroenterology/Nutrition; and David Wypij, Cardiology. Similarly, all Master's-prepared biostatisticians were also affiliated with departments: Parul Aneja, Adolescent/Young Adult Medicine; Peter Forbes, Trauma Program; and Patrick Johnston, Emergency Medicine.

As an example of collaboration resulting from departmental affiliation, Dr. Graham, since joining the Department of Cardiology in July 2006, has been working with Drs. Seda Tierney, Doff McElhinney, and Tal Geva on a retrospective study to identify echocardiographic predictors of progressive congenital mitral stenosis. She has also collaborated with Drs. Brian Soriano and Gerald Marx on a study comparing the assessment of ventricular function by magnetic resonance imaging with that of three-dimensional echocardiography, a novel technique. Additionally, she serves on the Data Safety and Monitoring Board of a randomized trial led by Dr. John Costello, "Pilot study of the effects of nesiritide on hemodynamics and urine output following cardiopulmonary bypass in infants."

2. Innovative CHB Research on Health Informatics Kiosks

Over the past five years, the CRP has collaborated on several Health Information Technology (HIT) projects with Dr. Stephen Porter, a researcher and faculty member in the Informatics program at Children's Hospital Boston. This partnership has yielded grant funding for a K08 as well as two R01s.

For example, an HIT product developed by Dr. Porter, the *Asthma Kiosk*, collects asthma-specific knowledge from parents at the time of an Emergency Department (ED) visit. The system maps parents' report of children's symptoms, current medications, and care needs to national guidelines for optimal control of pediatric asthma. The kiosk then generates a message to parents about how the ED can meet their child's specific needs and a message to providers with an "action list" for optimizing asthma care. Dr. Henry Feldman and Mr. Peter Forbes from the CRP collaborated on the evaluation of the *Asthma*

Kiosk, which was shown to generate a more complete and correct list of medications than is commonly documented by ED nurses and physicians. Impact of the kiosk on parents' experience with care and on guideline-appropriate prescribing was published in *Pediatrics* earlier this year.

Currently, Dr. Leslie Kalish and Mr. Forbes from the CRP are also collaborating with Dr. Porter on the evaluation of a next generation system called ParentLink. ParentLink expands the *Asthma Kiosk* to a wider range of disease conditions common to pediatric patients in the ED setting.

The working hypotheses for this collaborative HIT approach are that it will gather comprehensive, relevant information about the patient and lead to fewer medical errors and better adherence to treatment guidelines. The approach promotes both 'informed patients' and 'proactive providers.'

This project addresses two unsolved aspects of systems-based engineering that relate to quality and safety in health care: (1) how to gather accurate patient-produced data at the beginning of a health care visit, and (2) how to integrate these data with evidence-based guidelines to deliver safe and effective clinical decision-making. Data analysis is currently underway.

3. Pulse-Inversion US Imaging of Testicular Ischemia

Testicular torsion often presents clinically as acute scrotal pain requiring immediate surgical intervention to avoid serious long term injury. However, the symptoms of testicular torsion may arise from other conditions, for which surgery is not required. Therefore, it is important to make an accurate diagnosis in a timely fashion, typically based in part on ultrasound evidence of reduced blood flow or perfusion to one testis. Color Doppler ultrasonography is currently the imaging test of choice in the workup of these patients, but it can be unreliable because of small testicular size and lack of patient cooperation in small children. Dr. Leslie Kalish, collaborated with Dr. Harriet Paltiel from the Department of Radiology on a study evaluating pulse inversion (PI) imaging to see if this method is better able to assess testicular perfusion than conventional ultrasound. Thirty four rabbits were imaged using PI at baseline and at three increasing levels of unilateral spermatic cord occlusion, as a model of ischemia that might be caused by testicular torsion. Conventional ultrasound was also performed, as well as a "gold standard" method of measuring perfusion using radio-labeled microspheres. Two expert ultrasound readers, blinded to experimental conditions, viewed movie clips of the images of perfusion and made qualitative judgments of the relative perfusion in the left vs. right sides. Relative perfusion was also measured by several different automated quantitative methods using the quantitative PI data. The quantitative and qualitative methods of assessing relative perfusion were compared against the gold standard. Identification of the testis with less perfusion was better with the quantitative methods than with the qualitative assessment of images by the readers. This work was published in *Radiology* (2006; 239:718 729) and *Physics in Medicine and Biology* (2006; 51:3419 3432).

4. Association between Financial Ties to Industry and the Reporting of Non-FDA-Approved Uses of Industry Products

In recent years, there has been increased concern with the possible conflicts of interest that may arise when a scientific investigator has financial ties to industry. Dr. Stephen Brown in the Department of Radiology came to the CRP for help with the analysis and interpretation of a study addressing this topic. To conduct the study, he took advantage of the fact that when abstracts are submitted for consideration of presentation at the Radiological Society of North America (RSNA) annual meeting, the authors are asked to disclose their financial ties to industry and also to indicate whether the abstract reports on the use of a non FDA approved product. Using the 1549 abstracts of scientific papers presented at the 2003 RSNA annual meeting, each abstract was classified by whether or not

a non FDA approved product was reported on and whether or not any author had financial ties (e.g., employment, grant support, consultant, and stock holder). The analysis, directed by Dr. Leslie Kalish from the CRP, found that when the abstract disclosed at least one author with financial ties to the company whose product was reported on (17% of all abstracts), the abstract was about twice as likely to report on a non FDA approved use of a commercial product than abstracts without such financial ties (32% vs 15%, $p < .001$). While this association could be explained by a variety of factors, the finding raises the possibility that corporate relationships may influence the selection of research topics and the direction of radiological research. The study was published in *Radiology* (2006;239:839-855) along with an accompanying editorial.

5. Preliminary Validation of the Pediatric Withdrawal Assessment Tool (WAT-1)

Iatrogenic withdrawal is a common side effect of analgesia and sedative therapy in the intensive care unit setting (ICU) and occurs when patients who have received psychoactive drugs such as opioids, benzodiazepines, or hypnotics for several days are weaned too abruptly from these medications. Although iatrogenic withdrawal has been observed for over 20 years in infants and children receiving intensive care, there are no validated measures on which to base diagnosis or treatment. Dr. Sion Kim Harris, a measurement specialist in the CRP, has been working with Dr. Martha A.Q. Curley in Critical Care Nursing at CHB and Dr. Linda S. Franck at the Institute of Child Health, University College London, to evaluate the psychometric properties of a new withdrawal assessment tool (WAT- version 1) in a population of pediatric patients at high risk for iatrogenic withdrawal symptoms. This evaluation was conducted as part of a two-center pilot study (Curley, PI) evaluating a sedation management protocol in 245 pediatric patients, 2-weeks to 18 years of age, supported on mechanical ventilation for acute respiratory failure. 121 (55%) were identified to be at-risk for withdrawal (>5 days of scheduled intermittent/continuous opioid administration) and WAT-1 forms were completed for 88 of them (73%) Q12 hours from the start of opioid weaning until 72 hours after the last opioid dose. 19 symptoms associated with iatrogenic withdrawal were assessed during a pre-stimulus, stimulated and post-stimulus observation period. Inter-rater reliability was established, and validity was evaluated by comparing WAT-1 ratings to nursing clinical judgment of withdrawal using a 10-point numeric rating scale (NRS), and to clinical variables such as number of days on medication, amount of medication received prior to weaning, and length of weaning. A manuscript is currently in preparation.

B. COLLABORATIONS WITH EXTERNAL INVESTIGATORS AND INSTITUTIONS

1. The NIH MRI Study of Normal Brain Development

Peter Forbes of the CRP has worked collaboratively with the Dr. Deborah Waber and the Department of Psychiatry on an analysis of the neuropsychological tests given for the National Institutes of Health (NIH) Magnetic Resonance Imaging Study of Normal Brain Development. This is a landmark study in which structural and metabolic brain development and behavior are followed longitudinally from birth to young adulthood in a population-based sample of healthy children. The purpose of the study is to collect a representative sample of normal, healthy infants and children for a magnetic resonance imaging study that will serve two purposes: 1) to provide the largest normative database to date of the developing human brain for comparison with brain scan studies of children with neurological, developmental, and psychiatric disorders; and 2) to provide longitudinal data for investigating brain maturation in relationship to behavioral and cognitive development in a normal sample. Such data will allow a greater understanding of deviations in brain structural development associated with pediatric brain disorders. The study involves six different sites in the United States and Canada. The findings from the neuropsychological testing are themselves of interest, independent of the imaging data, since they portray the neuropsychological status of this healthy, diverse and representative sample of U.S.

children as a point of reference for both developmental and clinical studies. The neuropsychological assessment protocol for children aged 6 to 18 years was described and normative data were presented for participants in that age range among 385 subjects. The effect of age on the raw measures was modeled with cubic regression splines. For many measures, raw score performance improved steeply from 6 to 10 years, decelerating during adolescence. Sex differences were documented for Block Design (male advantage), Verbal learning, Pegboard and Coding (female advantage). Household income predicted IQ and achievement, as well as externalizing problems and social competence, but not the other cognitive or behavioral measures. Performance of this healthy sample was generally better than published norms. This linked imaging-clinical/behavioral database will be an invaluable public resource for researchers for many years to come.

2. The Severe Malaria in African Children Network: Redefining Cerebral Malaria

The Severe Malaria in African Children (SMAC) was the first network dedicated to study clinical malaria. SMAC is led by Dr. Terrie Taylor from Michigan State University and includes investigators from five African countries and from Europe. The network is now entering in its second NIH-funding cycle and has performed studies aiming to assess prognosis factors of severity of malaria, including use of acidosis measures and malaria pigmented cells as predictors of death. One of the goals of SMAC has been to support randomized trials involving treatment or prevention of less frequent forms of pediatric severe malaria. Besides the current NIH-funded study, the network will start hosting the first randomized trials. Additionally, SMAC plays a fundamental role in making feasible studies to assess endpoints of severe malaria for vaccine studies. The current NIH-funded study aims to assess a new, more accurate diagnosis method of cerebral malaria based on optical fundus examination. Training and Reliability studies have been performed during the last year and the SMAC sites are launching the study now.

3. The Active Where? Project

Emerging evidence from studies have linked environmental factors to physical inactivity and patterns of overweight in youth. Given the role that physical inactivity plays in overweight, increasing our knowledge of the impact of the school and neighborhood environment in a child's ability to participate in physical activity may enhance our understanding of the factors that contribute to the disparities in childhood obesity. A new comprehensive survey tool was developed collaboratively by researchers at Children's Hospital Boston (Nefertiti Durant and Sion Kim Harris), Cincinnati Children's Hospital Medical Center (Brian Saelens), and San Diego State University (Jacqueline Kerr, Greg Norman, and Jim Sallis) to assess environmental factors related to childhood and adolescent overweight, obesity, and weight-related behaviors such as physical activity and diet. Both youth and parent-report versions were developed and administered to youth and parents in Boston, Cincinnati, and San Diego. A sub-sample of parents and youth returned 1-week later to complete a re-test. The tool's internal consistency, test-retest reliability and construct validity are currently being evaluated, and manuscripts are in preparation.

C. GLASER PEDIATRIC RESEARCH NETWORK

1. Synopsis

Since September, 2002 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. The core grant for these activities was renewed in 2005 for a three-year term, with Dr. David Wypij succeeded by Dr. Henry Feldman in 2006 as Principal Investigator. Additional contracts are let by GPRN as it develops new multi-site studies. Three of these were active in 2006, with Drs. Feldman, Osganian, and Kalish as PI.

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 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, September, 2006

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

2. Core Functions

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 biweekly teleconferences of 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. The Glaser Fellows began their training by attending the three-day CRP course, Introduction to Clinical Research, providing an opportunity for intensive methodological orientation at the start of their first Fellowship year. Following up the course, Dr. Feldman organizes a monthly Work-in-Progress seminar via telephone, at which the Fellows present and jointly critique each other's protocols, manuscripts, and grant applications.

3. Research Coordination Contracts

Finally and most substantially, CRP has served the Glaser network since 2002 as data coordinating center for its multi-site studies, each via separate contract. As of fall 2006, agreements were in effect for two clinical trials and one registry project, listed in Table 2. More than a dozen CRP staff have taken part in 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, September 2006

Title	CRP role, key personnel	Start	Enrollment (% of final)
Multi-center trial of metformin for treatment of obesity in adolescents	<i>Coordinating Center:</i> S. Osganian (PI) H. Feldman (Biostatistician) M. McCarthy (Coordinator)	Dec. 2002	97 baseline studies, 77 randomized (100%)
Multi-center neonatal surgical database: necrotizing enterocolitis	<i>Coordinating Center:</i> L. Kalish (PI) M. McCarthy (Coordinator)	Dec. 2002	390 enrolled 320 completed follow-up
Multi-center open-label Phase I/II trial of rituximab for chronic, severe idiopathic thrombocytopenic purpura in children and adolescents	<i>Coordinating Center:</i> H. Feldman (PI/Biostatistician) M. McCarthy (Coordinator)	May 2003	36 (100%)
Multi-center randomized trial of alendronate treatment for children receiving high doses of steroids	<i>Advisory:</i> D. Wypij	July 2002	26 (100%)
Pharmacokinetics of doxorubicin	<i>Advisory:</i> D. Wypij	Jan., 2003	22 (100%)
Palliative care and quality of life: children's, parents', and physicians' perceptions	<i>Advisory:</i> L. Kalish	Aug., 2004	45 (90%)

4. Highlights of 2006

In 2006 GPRN significantly advanced its research activities with intensive participation and leadership from CRP. Drs. Kalish, Feldman, and Osganian each continued to act 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. Study details are provided in Table 2 above. Highlights include the following:

- 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 one-year follow-up evaluation period and prepared the findings for publication. The initial findings were published in 2006 in the journal *Blood*.
- The drug-treatment trial of obese adolescents completed its primary 12-month evaluation period with better-than-expected retention of participants. Several abstracts from baseline data were presented at national meetings.
- The registry of necrotizing enterocolitis surpassed enrollment of 350 infants and undertook an analysis of the role of feeding in pathogenesis of the disease.

A development of uncertain significance in 2006 was the decision of the Elizabeth Glaser Pediatric AIDS Foundation to limit its support of GPRN to completion of ongoing projects. GPRN has already obtained supplementary funding from Gerber Foundation and is investigating other potential sources of support including the National Institute for Child Health and Human Development.

In sum, our involvement with GPRN has given CRP a rewarding experience and a worthy track record in coordinating clinical research on the national level. Should GPRN succeed in sustaining its support from new sources and developing new initiatives, we expect CRP to continue this productive collaboration.

D. GENERAL CLINICAL RESEARCH CENTER

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.

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. As Director of Biostatistics for the GCRC, Dr. Kalish coordinates this review. 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, statistical power and sample size, adverse events reporting procedures, and data and safety monitoring plans. Written statistical reviews are provided to the investigators and to the primary scientific reviewers for the GCRC Scientific Advisory Committee. These reviews are also available to the IRB. Forty nine written reviews were completed during Fiscal Year 2006. If the biostatistical review calls for revisions or clarifications, 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 the GCRC manage the scientific review process for newly proposed studies, tracking laboratory specimens, administrative management support, and database development for research projects. During the past year a new Protocol Review Process System was implemented which automates many steps in the administration of the Scientific Review process. Included in its capabilities are managing 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.

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) **07/01/04-06/30/06**
NIH/NIMH **\$62,733**

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**
NIH/NCI **\$194,125**

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 NR05336 (Curley) **3/01/01-02/28/06**
NIH/NINR **\$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) **09/01/03-08/31/06**
NIH/NICHD **\$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) **04/01/04-06/30/06**
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 (Add Health).

R01 DK059570 (Field) **04/01/02-03/31/07**
NIH/NIDDK **\$299,776**
The Development of Eating Disorders in Males and Females

The goal of this project is to follow 9,039 girls and 7,834 boys through their transition from childhood to late adolescence and early adulthood to assess whether personal factors, peer influences, family influences, and media influences predict the development and course of purging, binge eating, and eating disorders of at least subsyndromal severity.

R21-DK073130A (Field) **01/15/06-12/31/07**
NIH/NIDDK **\$54,742**
Weight Cycling and Mortality in Women

This project assesses the relationship between weight cycling and mortality among 77,021 middle-aged and older women in the Nurses' Health Study. The goals are: (1) to evaluate whether independent of net weight gain during adulthood, which is known to increase risk of death, weight cycling is associated with an increased risk of mortality; (2) to assess the association of weight cycling due to intentional weight losses, as well as cycling due to unintentional weight losses; (3) to assess whether weight variability, which includes both intentional and unintentional weight losses and gains, increases mortality risk.

R01 MH65877 (Galler/CHB subcontract: Waber) **05/01/04-06/01/06**
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) **06/01/06-08/31/10**
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 5U01DK067767 (Jonas) **09/01/05-08/31/07**
NIH/NIDDK **\$20,690**
PEDS-C Trial

This is a Phase II randomized, blinded placebo trial to compare safety and efficacy of PEG-2a plus placebo versus PEG-2a plus riavirin in children chronically infected with Hepatitis C virus.

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) **09/30/04-08/31/09**
NIH/NIDA **\$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) **06/01/04-03/31/09**
NIH/NIDA **\$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.

R01 EB01998 (Levine/CHB subcontract: Estroff) **07/01/03-05/31/08**
NIH/BIDMC **\$203,029**

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) **4/01/02-2/28/06**
NIH/NIDDK **\$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) **4/01/02-2/28/06**
NIH/NIDDK **\$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.

R01 DK063554-03 (Ludwig) **03/01/06-02/28/10**
NIH/NIDDK **\$244,441**

Reducing Sugar-Sweetened Beverage Consumption in Overweight Adolescents

This project is a long-term, large-scale, multi-site randomized study partnering with 6 high schools in the greater Boston area. This study has been designed to demonstrate whether or not an intervention

focused exclusively on sugar-sweetened beverage consumption is efficacious in the prevention and treatment of obesity in children.

5 R01 DK072428-02 (Ludwig)
NIH/NIDDK

09/15/05-07/31/09
\$345,392

Popular Diets, Metabolism, and CVD Risk

A three-period, randomized, crossover feeding trial in obese adults following weight loss, designed to evaluate the impact on resting energy expenditure of three prevalent diets: low fat, low glycemic index, and very low carbohydrate (Atkins-type).

M01 RR02172 (Mandell)
NIH/NCRR

04/01/04-03/31/09
\$2,076,155

General Clinical Research Center

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

P50 HL074734 (Newburger)
NIH/NHLBI

02/15/04-06/30/06
\$3,116,544

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)
NIH/NHLBI

07/01/04-06/30/06
\$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 CA114556 (Pbert/CHB subcontract: Osganian)
NIH/NCI

03/08/06-02/28/10
\$23,061

School Nurse Delivered Smoking Cessation Intervention for Adolescents

The overall aim of the project is to conduct a randomized controlled school-based trial (RCT) to evaluate the effectiveness of a promising four-session school nurse-delivered smoking cessation intervention in an ethnically diverse student population and with longer-term follow-up than in the pilot project.

R01 HL68922 (Platt)
NIH/NHLBI

09/30/01-07/31/06
\$657,435

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) **10/01/04-03/31/07**
DHHS/AHRQ **\$233,613**
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.

R01 LM009256-01 (Porter) **09/01/06-08/31/09**
NIH/NLM **\$380,142**
Health Literacy and Information Management in ADHD: Designing an Optimal Record

The goal of this project is to develop and evaluate an electronic data-entry tool for parents of children with ADHD, enabling the parents to provide data essential to the child’s treatment regardless of their own level of medical knowledge. The study will include a formative phase for instrument development, a retrospective examination of health literacy and documented ADHD care, and a prospective trial assessing the utility of the instrument.

FD-R-002202 (Rufo) **10/01/02-03/31/06**
FDA **\$149,736**
Clostrimazole 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) **04/01/05-03/31/08**
NIH/NIMH **\$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.

R01 MH65877 (Waber) **05/01/04-05/31/06**
NIH/NIMH **\$47,648**
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.

2 U01 AI45955 (Taylor/CHB subcontract: Wypij) **09/30/05-09/30/10**
NIH/NIAID **\$27,869**
Redefining Cerebral Malaria

This study aims to assess new criteria to diagnose cerebral malaria and sequestration — ocular fundus finding and brain smear. More specifically, the study aims to assess the accuracy of ocular fundus finding to diagnose cerebral malaria and evaluate the prognostic significance of ocular fundus to predict death in patients with clinical cerebral malaria. Additionally, the accuracy of brain smear as a

predictor of cerebral sequestration will be investigated. The study will be carried out within the Severe Malaria in African Children (SMAC) Network, which includes five sites in East and West Africa.

B. NIH CAREER DEVELOPMENT GRANTS

K08 HS013675 (Lightdale) **06/01/03-05/31/07**
DHHS/AHRQ **\$116,500**
Improving Safety of Pediatric Sedation

Mentored Clinical Scientist Development Award, goals of which 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) **07/01/04-06/30/09**
NIH/NHLBI **\$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.

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

(Feldman) **09/01/02-08/31/08**
Glaser Pediatric Research Network **\$156,890**
*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) **12/01/02-02/28/08**
Glaser Pediatric Research Network **\$113,577**
*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) **12/01/02-2/28/07**
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.

<p>(Moss/CHB subcontract: Jaksic/DACC: Kalish) Glaser Pediatric Research Network <i>Necrotizing Enterocolitis (NEC) Surgical Database</i></p>	<p>12/01/02-05/31/07 \$97,123</p>
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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

<p>(Peterson/ CHB Subcontract: Austin) International Nutrition Foundation <i>Massachusetts Healthy Choices Evaluation</i></p>	<p>07/01/05-10/31/08 \$21,115</p>
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Scientific oversight, study design, statistical analysis, and interpretation of data for evaluation of a program in Massachusetts middle schools promoting cardiovascular health through increased physical activity, increased fruit and vegetable consumption, and limited TV and computer time.

<p>(Bennett) St. Giles Foundation <i>Genetic Modifiers of Childhood Chronic Immune Thrombocytopenic Purpura (ITP)</i></p>	<p>07/07/04-09/30/07 \$125,000</p>
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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.

<p>(Curley) Gustavus and Louise Pfeiffer Research Foundation <i>Sedation Management in Pediatric Patients Supported on Mechanical Ventilation</i></p>	<p>05/01/04-05/31/06 \$50,200</p>
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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.

<p>(Duggan) Mass Vitamin Litigation Fund <i>Body Composition in Cancer Patients Undergoing Stem Cell Transplantation</i></p>	<p>02/01/03-01/31/06 \$42,884</p>
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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.

<p>(Grand) Crohn's & Colitis Foundation of America <i>Use of Intranasally Administered Calcitonin in the Treatment of Osteopenia and Osteoporosis in Children, Adolescents, and Young Adults with IBD: A Pilot Study</i></p>	<p>01/01/03-06/30/07 \$99,456</p>
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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.

(Harris) **1/1/06-12/31/06**
Aerosmith Foundation **\$11,864**
Substance Use and HIV Risk Reduction through Science-Based Drug Abuse Education: A High School Pilot Study

This project involves a collaboration between CHB and science teachers at two Boston high schools to evaluate how receipt of science-based drug abuse education through a science class unit entitled "The Brain: Understanding Neurobiology Through the Study of Addiction," developed by NIH's Office of Science Education (OSE) and the National Institute of Drug Abuse (NIDA), affects high school students' substance use knowledge, attitudes, perceived risk of harm, and behavior.

045222 (Knight) **5/1/02-10/31/05**
Robert Wood Johnson Foundation **\$70,850**
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.

047191 (Mooney) **10/01/04-10/31/07**
Robert Wood Johnson Foundation **\$8,472**
Injury Free Coalition for Kids of Boston

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) **04/01/04-09/30/06**
Aerosmith Foundation **\$3,780**
Depression and HIV Risk with Heterosexual Partnerships

The goal of this project is to determine effect of depression on the HIV risk for a heterosexual couple.

E. INDUSTRY

(Laufer) **05/01/03-06/30/06**
Personal Products Worldwide **\$29,477**
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, M.D., SC.D.

External Teaching

Small Group Leader; sponsored by Harvard School of Public Health, Clinical Effectiveness Program; Summer 2006.

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; 2003-2006.

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

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.

Data and Safety Monitoring Board: Reducing Risk Factors in Peripheral Arterial Disease. Northwestern University, Chicago, Ill., and University of Massachusetts, Worcester.

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. 23-Aug. 4, 2006.

LESLIE KALISH, SCD

National Committee

Member of the Data and Safety Monitoring Board for “Program to Reduce Incontinence by Diet and Exercise (PRIDE),” sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases, 2004-present.

SION HARRIS, PHD

External Presentations

Boston Arts Academy; The Teen Brain: What’s Going On In There?; 60-minute presentation; 50 attendees: 11th grade biology students: June 14, 2006.

Massachusetts Health Sciences Library Network/North Atlantic Health Sciences Library, Inc.; Being Survey Savvy: Design and Implementation Tips for More Effective Surveys; 120-minute presentation; 44 attendees: University and medical librarians; June 23, 2006.

Honors

2006 Young Professional Award, Maternal and Child Health Section, American Public Health Association.

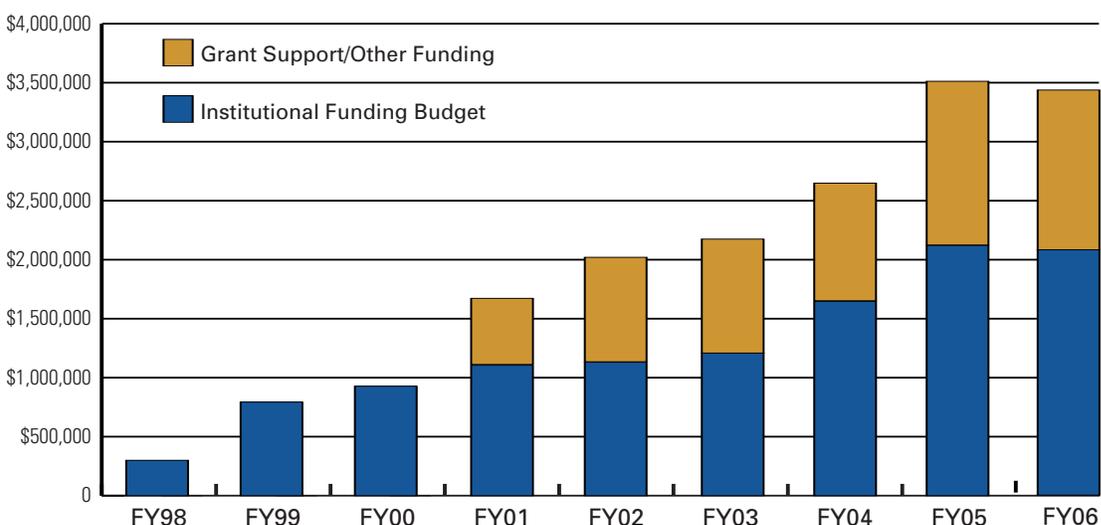
Program Resources

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 fourteen offices, eighteen cubicles, and two conference rooms.

Institutional and other sources of support for the Program are shown in Table 1 below. 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 over \$1.3 million.

Table 1. CRP Funding for the period FY98 to FY06

Fiscal Year	Institutional Budget	Grant Support/Other Funding	Total	% Change
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%
FY06	\$2,119,070	\$1,326,735	\$3,445,805	-2%



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>.

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. Asst. Prof. Instructor Fellow Resident Nurse

Other (specify): _____

3. Department: _____ Division: _____

4. Phone/Ext # _____

5. Research Mentor (if applicable) _____

6. Requestor: Check if same as name of PI

Last Name _____ First Name _____ CH ID# _____

7. Project Title (same as title on IRB protocol or grant application):

8. What do you require assistance with...? (check all that apply)

a. Grant Proposal/Protocol Development

- Grant Proposal Development
- Study Protocol Development
- Study Design or Concept Development
- Statistical Analysis Plan
- Power and Sample Size Determination
- Data Monitoring Plan (DSMP)/Interim Analysis Plan

b. Study Implementation

- Case Report Form Development
- Survey/Questionnaire Design
- Randomization
- Database Development
- Data Management
- Assistance with existing database

c. Data Analysis/Interpretation

- Presentation
- Manuscript
- Statistical Analyses
- Interpretation of Results

d. Other (Specify below)

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? Yes No
b. Are you presently applying for funding? Yes No; Skip to Q. 12
c. If Yes, what type of application is it? New Submission Resubmission

12. Funding Sources

- NIH
a. Name of Institute/Center: _____
b. Type of funding mechanism (check one): R01 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? Yes No

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

2006 Staff Publications

Agus MS, Javid PJ, Piper HG, **Wypij D, Duggan CP**, Ryan DP, Jaksic T (2006) "The effect of insulin infusion upon protein metabolism in neonates on extracorporeal life support." *Ann Surg* 244(4): 536-544.

Angelone DF, Wessels MR, Coughlin M, Suter EE, Valentini P, **Kalish LA**, Levy O (2006) "Innate immunity of the human newborn is polarized toward a high ratio of IL-6/TNF-alpha production in vitro and in vivo." *Pediatr Res* 60(2):205-9.

Bassan H, Benson CB, Limperopoulos C, **Feldman HA**, Ringer SA, Veracruz E, Stewart JE, Soul JS, Disalvo DN, Volpe JJ, du Plessis AJ (2006) "Ultrasonographic features and severity scoring of periventricular hemorrhagic infarction in relation to risk factors and outcome." *Pediatrics* 117(6): 2111-2118.

Bassan H, **Feldman HA**, Limperopoulos C, Benson CB, Ringer SA, Veracruz E, Soul JS, Volpe JJ, du Plessis AJ (2006). "Periventricular hemorrhagic infarction: risk factors and neonatal outcome." *Pediatr Neurol* 35(2):85-92.

Bennett, CM, Rogers ZR, **Kinnamon DD**, Bussel JB, Mahoney DH, Abshire TC, Sawaf H, Moore TB, Loh ML, Glader BE, McCarthy MC, Mueller BU, Olson TA, Lorenzana AN, Mentzer WC, Buchanan GR, **Feldman HA**, Neufeld EJ (2006). "Prospective phase 1/2 study of rituximab in childhood and adolescent chronic immune thrombocytopenic purpura." *Blood* 107(7):2639-2642.

Bourgeois FT, **Valim C**, Wei JC, McAdam AJ, Mandl KD (2006) "Influenza and other respiratory virus-related emergency department visits among young children." *Pediatrics* 118(1):e1-8.

Brown SD, Daly JC, **Kalish LA, McDaniel SA** (2006) "Financial disclosures of scientific papers presented at the 2003 RSNA Annual Meeting: association with reporting of non-Food and Drug Administration-approved uses of industry products." *Radiology* 239(3):849-855.

Curley MA, **Harris SK**, Fraser KA, Johnson RA, Arnold JH (2006) "State Behavioral Scale: a sedation assessment instrument for infants and young children supported on mechanical ventilation." *Pediatr Crit Care Med* 7(2):107-114.

Duggan C, Piper H, Javid PJ, **Valim C**, Collier S, Kim HB, Jaksic T (2006) "Growth and nutritional status in infants with short-bowel syndrome after the serial transverse enteroplasty procedure." *Clin Gastroenterol Hepatol* 4(10):1237-1241.

Ebbeling CB, **Feldman HA, Osganian SK**, Chomitz VR, Ellenbogen SJ, Ludwig DS (2006) "Effects of decreasing sugar-sweetened beverage consumption on body weight in adolescents: a randomized, controlled pilot study." *Pediatrics* 117(3):673-680.

Fine AM, Goldmann DA, **Forbes PW, Harris SK**, Mandl KD (2006). "Incorporating vaccine-preventable disease surveillance into the National Health Information Network: leveraging children's hospitals." *Pediatrics* 118(4):1431-1438.

Fineman, LD, LaBrecque MA, **Shih MC**, Curley MA (2006). "Prone positioning can be safely performed in critically ill infants and children." *Pediatr Crit Care Med* 7(5):413-422.

Guinan EC, **Kalish LA**, Berry WS, **McDaniel S**, Lehmann LE, Diller LR (2006) "A novel pattern of transaminase elevation associated with autologous transplant for neuroblastoma." *Pediatr Transplant* 10(6):669-676.

Gura KM, **Duggan CP**, Collier SB, Jennings RW, Folkman J, Bistrain BR, Puder M (2006) "Reversal of parenteral nutrition-associated liver disease in two infants with short bowel syndrome using parenteral fish oil: implications for future management." *Pediatrics* 118(1):e197-201.

Gurian, EA, **Kinnamon DD**, Henry JJ, Waisbren SE (2006). "Expanded newborn screening for biochemical disorders: the effect of a false-positive result." *Pediatrics* 117(6):1915-1921.

Heuschkel R, **Duggan C** (2006) "Enteral feeding: gastric versus post-pyloric" In: Rose BD, editor. *Up To Date in Gastroenterology and Hepatology*, Wellesley, MA: Up To Date

Horn, MH, **Kinnamon DD**, Ferraro N, Curley MA (2006). "Smaller mandibular size in infants with a history of an apparent life-threatening event." *J Pediatr* 149(4):499-504.

Kalish LA, Waltz DA, Dovey M, Potter-Bynoe G, McAdam AJ, Lipuma JJ, Gerard C, Goldmann D (2006) "Impact of *Burkholderia dolosa* on lung function and survival in cystic fibrosis." *Am J Respir Crit Care Med* 173(4):421-425.

Kelleher DK, Laussen P, **Teixeira-Pinto A**, **Duggan C** (2006) "Growth and correlates of nutritional status among infants with hypoplastic left heart syndrome (HLHS) after stage 1 Norwood procedure." *Nutrition* 22(3):237-244.

Lai, TL, **Shih MC**, Wong SP (2006). "A new approach to modeling covariate effects and individualization in population pharmacokinetics-pharmacodynamics." *J Pharmacokinet Pharmacodyn* 33(1): 49-74.

Lai, TL, **Shih MC**, Zhu G (2006). "Modified Haybittle-Peto group sequential designs for testing superiority and non-inferiority hypotheses in clinical trials." *Stat Med* 25(7):1149-1167.

Le Bovidge JS, Stone KD, Twarog FJ, Raiselis SW, **Kalish LA**, Bailey EP, Schneider LC (2006) "Development of a preliminary questionnaire to assess parental response to children's food allergies." *Ann Allergy Asthma Immunol* 96(3):472-477.

Lee, RS, Cendron M, **Kinnamon DD**, Nguyen HT (2006). "Antenatal hydronephrosis as a predictor of postnatal outcome: a meta-analysis." *Pediatrics* 118(2):586-593.

Leung Lai, T, **Shih MC**, Wong SP (2006). "Flexible modeling via a hybrid estimation scheme in generalized mixed models for longitudinal data." *Biometrics* 62(1):159-167.

Levy S, **Harris SK**, Sherritt L, Angulo M, Knight JR (2006) "Drug testing of adolescents in general medical clinics, in school and at home: physician attitudes and practices." *J Adolesc Health* 38(4): 336-342.

Levy S, **Harris SK**, Sherritt L, Angulo M, Knight JR (2006) "Drug testing of adolescents in ambulatory medicine: ph Levy S, Harris SK, Sherritt L, Angulo M, Knight JR. The authors reply. *Journal of Adolescent Health*. 2006;39(2):155.ysician practices and knowledge." *Arch Pediatr Adolesc Med* 160(2):146-150.

Lightdale JR, Goldmann DA, **Feldman HA**, Newburg AR, DiNardo JA, Fox VL (2006) "Microstream capnography improves patient monitoring during moderate sedation: a randomized, controlled trial." *Pediatrics* 117(6):e1170-1178

Lutsey PL, Steffen LM, **Feldman HA**, Hoelscher DH, Webber LS, Luepker RV, Lytle LA, Zive M, **Osganian SK** (2006) "Serum homocysteine is related to food intake in adolescents: the Child and Adolescent Trial for Cardiovascular Health." *Am J Clin Nutr* 83(6):1380-1386.

Macklin EA, Wayne PM, **Kalish LA**, Valaskatgis P, Thompson J, Pian-Smith MC, Zhang Q, Stevens S, Goertz C, Prineas RJ, Buczynski B, Zusman RM (2006) "Stop Hypertension with the Acupuncture Research Program (SHARP): results of a randomized, controlled clinical trial." *Hypertension* 48(5): 838-845.

Modi BP, Langer M, **Duggan C**, Kim HB, Jaksic T (2006) "Serial transverse enteroplasty for management of refractory D-lactic acidosis in short-bowel syndrome." *J Pediatr Gastroenterol Nutr* 43(3):395-397.

Mooney DP, Rothstein DH, **Forbes PW**. (2006) "Variation in the management of pediatric splenic injuries in the United States." *J Trauma* 61(2):330-333; discussion 333.

Muthayya S, Dwarkanath P, Mhaskar M, Mhaskar R, Thomas A, **Duggan C**, Fawzi WW, Bhat S, Vaz M, Kurpad A (2006) "The relationship of neonatal serum vitamin B12 status with birth weight." *Asia Pac J Clin Nutr* 15:538-543.

Muthayya S, Kurpad AV, **Duggan CP**, Bosch RJ, Dwarkanath P, Mhaskar A, Mhaskar R, Thomas A, Vaz M, Bhat S, Fawzi WW (2006) "Low maternal vitamin B12 status is associated with intrauterine growth retardation in urban South Indians." *Eur J Clin Nutr* 60:791-801

O'Rourke JM, Kalish LA, **McDaniel S**, Lyons B (2006) "The effects of exposure to environmental tobacco smoke on pulmonary function in children undergoing anesthesia for minor surgery." *Paediatr Anaesth* 16(5):560-567.

Paltiel HJ, **Kalish LA**, Susaeta RA, Frauscher F, O'Kane PL, Freitas-Filho LG (2006) "Pulse-inversion US imaging of testicular ischemia: quantitative and qualitative analyses in a rabbit model." *Radiology* 239(3):718-729.

Pappa, HM, Gordon CM, Saslowsky TM, Zholudev A, Horr B, **Shih MC**, Grand RJ (2006). "Vitamin D status in children and young adults with inflammatory bowel disease." *Pediatrics* 118(5):1950-1961.

Parsons, SK, **Shih MC**, Duhamel KN, Ostroff J, Mayer DK, Austin J, Martini DR, Williams SE, Mee L, Sexson S, Kaplan SH, Redd WH, Manne S (2006). "Maternal perspectives on children's health-related quality of life during the first year after pediatric hematopoietic stem cell transplant." *J Pediatr Psychol* 31(10):1100-1115.

- Pbert L, **Osganian SK**, Gorak D, Druker S, Reed G, O'Neill KM, Sheetz A (2006) "A school nurse-delivered adolescent smoking cessation intervention: a randomized controlled trial." *Prev Med* 43(4):312-320.
- Pettinato AA, Loud KJ, Bristol SK, **Feldman HA**, Gordon CM (2006) "Effects of nutrition, puberty, and gender on bone ultrasound measurements in adolescents and young adults." *J Adolesc Health* 39(6):828-834.
- Porter SC, **Forbes P**, **Feldman HA**, Goldmann DA (2006) "Impact of patient-centered decision support on quality of asthma care in the emergency department." *Pediatrics* 117(1):e33-42.
- Reaves L, Steffen LM, Dwyer JT, Webber LS, Lytle LA, **Feldman HA**, Hoelscher DM, Zive MM, **Osganian SK** (2006) "Vitamin supplement intake is related to dietary intake and physical activity: The Child and Adolescent Trial for Cardiovascular Health (CATCH)." *J Am Diet Assoc* 06(12):2018-2023.
- Recklitis, CJ, Parsons SK, **Shih MC**, Mertens A, Robison LL, Zeltzer L (2006). "Factor structure of the brief symptom inventory—18 in adult survivors of childhood cancer: results from the childhood cancer survivor study." *Psychol Assess* 18(1):22-32.
- Taveras, EM, Sandora TJ, **Shih MC**, Ross-Degnan D, Goldmann DA, Gillman MW (2006). "The association of television and video viewing with fast food intake by preschool-age children." *Obesity* (Silver Spring) 14(11):2034-2041.
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APPENDIX C

Course Agendas

INTRODUCTION TO CLINICAL RESEARCH AGENDA

Tuesday, March 14, 2006

8:00 – 8:30	CONTINENTAL BREAKFAST
8:30 – 8:45	<i>Introduction and Overview</i> Voula Osganian, MD, ScD David Wypij, PhD
8:45 – 9:00	<i>Overview of Research Administration: Organization and Resources</i> Carleen Brunelli, PhD, MBA
9:00 – 9:45	<i>Data Analysis I: Descriptive Statistics and Inference</i> David Wypij, PhD
9:45 – 10:00	BREAK
10:00 – 10:30	<i>Data Analysis II: Precision and Accuracy of Measurement</i> David Wypij, PhD
10:30 – 10:45	<i>The General Clinical Research Center (GCRC)</i> Richard Grand, MD Kristine Jordan
10:45 – 11:30	<i>Observational Study Designs</i> Voula Osganian, MD, ScD
11:30 – 12:15	<i>Designing Surveys and Questionnaires</i> Sion Kim-Harris, PhD

Wednesday, March 15, 2006

8:00 – 8:30	CONTINENTAL BREAKFAST
8:30 – 9:30	<i>Writing for Scientific Publication</i> S. Jean Emans, MD
9:30 – 10:15	<i>Clinical Trials: Design and Monitoring</i> Jane Newburger, MD
10:15 – 10:30	BREAK
10:30 – 11:15	<i>Statistical Issues in Study Design</i> David Wypij, PhD
11:15 – 12:30	<i>Human Subjects, Institutional Review Board and HIPAA</i> Susan Kornetsky, MPH

Thursday, March 16, 2006

- 8:00 – 8:30 CONTINENTAL BREAKFAST
- 8:30 – 9:30 ***Bias and Confounding***
Clarissa Valim, MD, ScD
- 9:30 – 10:15 ***Data Analysis III: Comparing Two Groups***
Henry Feldman, PhD
- 10:15 – 10:30 BREAK
- 10:30 – 11:15 ***Data Analysis IV: Correlation and Regression***
Henry Feldman, PhD
- 11:15 – 12:00 ***Evaluating the Performance of a Test***
Carl de Moor, PhD

Friday, March 17, 2006

- 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 – 10:15 ***Operational Issues in Conducting Clinical Research***
Christopher Duggan, MD
- 10:15 – 10:30 BREAK
- 10:30 – 11:15 ***Writing a Grant and Applying for Funding***
Voula Osganian, MD ScD
- 11:15 – 11:45 ***The NIH Scientific Review***
Voula Osganian, MD, ScD
- 11:45 – 12:00 ***The CRP Course Wrap-up***
Voula Osganian, MD, ScD
David Wypij, PhD

INTRODUCTION TO CLINICAL RESEARCH AGENDA

Monday, October 9, 2006

DESIGN AND ANALYSIS

- 8:00 – 8:15 **Introduction and Overview**
Jenifer Lightdale, MD, MPH
- 8:15 – 8:45 **Operational Issues in Conducting Clinical Research**
Christopher Duggan, MD, MPH
- 8:45 – 9:45 **Observational Study Designs**
Voula Osganian, MD, ScD
- 9:45 – 10:00 BREAK
- 10:00 – 10:45 **Designing Surveys and Questionnaires**
Erinn Rhodes, MD, MPH
- 10:45 – 11:45 **Introduction to Statistics**
Henry Feldman, PhD

Tuesday, October 10, 2006

GRANTS AND MANUSCRIPTS

- 8:30 – 9:15 **Writing a Grant and Applying for Funding**
Voula Osganian, MD, ScD
- 9:15 – 9:30 **Overview of Research Administration: Organization and Resources**
Carleen Brunelli, PhD, MBA
- 9:30 – 9:45 BREAK
- 9:45 – 10:15 **The NIH Scientific Review**
Voula Osganian, MD, ScD
- 10:15 – 10:45 **The General Clinical Research Center**
Kristine Jordan
Richard Grand, MD
- 10:45 – 11:00 BREAK
- 11:00 – 12:00 **Writing Scientific Publication**
S. Jean Emans, MD

Thursday, October 11, 2006

INSTITUTIONAL APPROVAL AND STUDY IMPLEMENTATION

- 8:30 – 9:45 **Human Subjects, Institutional Review Board and HIPPA**
Susan Kornetsky, MPH
- 9:45 – 10:00 **BREAK**
- 10:00 – 10:30 **Informed Consent**
Eunice Newbert, MPH
- 10:30 – 11:15 **CRFs and Data Management**
Susan McDermott, MPH, RN, CS
- 11:15 – 11:30 **BREAK**
- 11:30 – 12:30 **Good Measures and Good Tests**
Clarissa Valim, MD, ScD

Friday, October 13, 2006

DESIGN AND ANALYSIS

- 8:00 – 9:15 **Introduction to Statistics**
Dionne Graham, PhD
- 9:15 – 9:30 **BREAK**
- 9:30 – 10:15 **Clinical Trials: Design and Monitoring**
Jane Newburger, MD
- 10:15 – 11:00 **Scientific Presentations**
Jonathan Finkelstein, MD, MPH
- 11:00 – 11:15 **BREAK**
- 11:15 – 12:15 **Introduction to Regression**
Henry Feldman, PhD
- 12:15 – 12:30 **The CRP Course Wrap-Up**
Jenifer Lightdale, MD, MPH

2006 NEW STUDY COORDINATOR ORIENTATION AGENDA

2/22, 6/28, 7/26, 8/23, 10/25, & 11/29

8:15 – 8:30	CONTINENTAL BREAKFAST
8:30 - 8:45	Welcome and Overview
8:45 - 9:05	Overview of Responsibilities of Study Coordinators Study Coordinator's Central Role in Clinical Research
9:05 - 9:30	Human Subject Protections – IRB Issues: Before the Research Begins Introduction/Why are we here? Training Requirements Protocol Submissions
9:30 - 10:00	IRB 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	Obtaining Informed Consent/Assent — A Practical Approach
11:00 - 12:00	Informed Consent/Assent and Subject Recruitment Writing Informed Consent/Assent Research Subject Recruitment Communication/Shared Responsibility
12:00 - 1:00	LUNCH
1:00 - 1:15	Resources 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 - 1:45	Study Implementation and Data Management Study Start-up Manual of Operations, CRF Completion, and Quality Control Source Documentation
1:45 – 2:00	Study Data and Documents — Regulations and Policies Storage of Study Documents and Informed Consent Documents Study Close-out and Document Retention
2:00 - 2:45	The Study Binder and Files Organizing Study Documents
2:45 - 2:50	Introduction to the Clinical Trials Office
2:50 – 3:00	Introduction to Clinical Research Financial Management Funded Research Patient Care Costs
3:00 – 3:15	Wrap-up, Review, Questions

2006 COORDINATOR ROUNDS

Wednesdays, 12:00 – 1:00pm

Date	Topic	Speaker(s)
1/11	Clinical Research Billing: Update and Open Forum	Kristine Jordan, John Counts, Beth Brennan & Kathleen Theisen
2/8	Database Management Systems	Jason Rightmyer
3/8	CHAMPS Lecture	CHAMPS Team
4/12	Patients Guide to Medical Research	CRP
5/10	Genetics Research	Stephanie Brewster & Ingrid Holm
10/18	Clinical Trials Office	Jesse Wheeler, Kelley Madden, John Counts, Beth Brennan, Tracy Lewis & Kristine Jordan
12/13	Introduction to Patents	Patrick Taylor

INTRODUCTION TO BIOSTATISTICS LECTURE AGENDA

Dionne Graham, PhD

March/April 2006

MARCH 6

Lecture 1: *Summary Statistics and Graphical Methods*

- Data Types
- Graphical Display: Bar Charts, Histograms, Boxplots
- Summary Statistics: Measures of Central Tendency, Measures of Spread

MARCH 13

Lecture 2: *Estimating the Mean*

- Normal Distribution
- Principles of Estimation
- Estimating the Mean
- Confidence Intervals for the Mean

MARCH 20

Lecture 3: *Hypothesis Testing & Comparing Two Means*

- Inference Overview
- Introduction to Hypothesis Testing
- Comparing Two Means: Paired t-test, Two sample t-test
- Interpreting p-values

MARCH 27

Lecture 4: *Comparing k-Means, Non-Parametric Tests, Correlation*

- Comparing Three or More Means: ANOVA
- Nonparametric Tests: Wilcoxon rank sum; Kruskal Wallis
- Correlation

APRIL 3

Lecture 5: *Estimating and Testing Proportions*

- Estimating a Proportion
- Confidence Intervals for Proportions
- Comparing Two or More Proportions: Chi-squared test, Fisher's exact test

APRIL 10

Lecture 6: *Odds Ratios and Diagnostic Tests*

- Odds Ratios
- Sensitivity and Specificity of Diagnostic Tests
- Course Wrap-Up

SPSS COMPUTER LAB AGENDA

Peter Forbes, MA

March/April 2006

MARCH 9

Lab 1: *Introduction to the SPSS Interface*

- Opening an existing SPSS database
- Graphical data analysis
- Descriptive statistics
- Creating a new data set from “scratch”
- Introduction to SPSS syntax

MARCH 16

Lab 2: *Descriptive statistics and data set basics*

- Confidence intervals for the mean
- Descriptive analysis by group
- The split file command
- Subsetting data with filters
- Computing new variables
- The IF statement
- Recoding variables

MARCH 23

Lab 3: *T-tests and more SPSS tools*

- One sample t-test
- Two sample t-test
- Paired t-test
- Defining and using variable ‘sets’

MARCH 30

Lab 4: *Anova and nonparametric tests*

- ANOVA
- Wilcoxon and KW tests
- Correlation

APRIL 6

Lab 5: *Tests for proportions*

- One sample test for proportions
- Crosstabs
- Chi squared test
- Fisher’s exact test
- Reading data from other formats

APRIL 13

Lab 6: *More tests for proportions and final topics*

- Odds ratios
- Sensitivity and specificity
- Data cleaning
- Understanding and using date variables
- Exporting SPSS output to Word or PowerPoint

POWER AND HOW TO GET IT: SAMPLE SIZE FOR CLINICAL STUDIES

Lectures: Henry Feldman, PhD

Lab: Parul Aneja, MS

Lectures: Thursday, May 18 and Thursday, May 25

2:00 – 4:00pm

Lectures: December 5 and December 1

Lab: December 8, 2006

2:00 – 4:00pm

LECTURE 1

- Review of key concepts: precision, standard error, inferential error
- Definition of power and detectable effect
- Relation to sample size, study design, Type I & Type II error
- Catalogue of formulas for various study designs

LECTURE 2

- Take-home exercise: Real-life design scenarios
- In-class presentation and discussion

LAB

- Introduction to Power and Samples Size program
- Examples: Continuous and Binary variables