

# 2007 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 2007**

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# Program Overview

*The Clinical Research Program (CRP) is a scientific, inter-disciplinary research program whose mission 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 education in clinical research methods and practice which targets the clinical researcher 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. In FY07 the CRP staff grew to 34 full-time, affiliated, and part-time staff from various disciplines, including epidemiologists, biostatisticians, application developers, project directors, 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 on 70 funded projects with CHB investigators and other institutional Programs.
- Fifty-two peer reviewed publications which were co-authored by CRP staff.
- Successful implementation or completion of 3 multi-site clinical research protocols for the Glaser Pediatric Research Network.
- A 120% increase in faculty department support.
- Expansion of educational offerings for Clinical Research, including a new Do-It-Yourself Data Management course.
- Successful integration of a new team within ISD, the clinical research informatics team (CRIT).
- Successful staff hiring of 4 faculty biostatisticians, 2 master's level biostatisticians, and 1 data manager, and an expansion of core services.

## **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 FY07 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**

The Clinical Research Executive Committee (CREC) continued to support several of its strategic initiatives including recruitment of clinical research faculty, growth in clinical research infrastructure, and education and faculty career development. Specifically in FY07, the CREC approved the allocation of funds from the Clinical General Research Endowment as follows: \$1.4 million was allocated for new clinical research faculty recruits, \$1.2 million was allocated to expand financial support for clinical research infrastructure including support for regulatory affairs personnel, research phlebotomy services at Waltham, the MRI core, and clinical research informatics electronic data capture tools, and \$430,000 was provided for education and faculty development including support to the Clinical Research Education Core, the Fellowship Training Program and four junior faculty clinical research development awards, each award totaling \$50,000 per year for two years.

## **2. PROGRAM ORGANIZATION**

The Clinical Research Informatics Teams was successfully integrated within the Information Systems Department under the joint leadership of Dan Nigrin, Danny Shaw, and Stavroula Osganian. This integration has led to several key enterprise-wide initiatives including the purchase of a new web-based, electronic data capture tool for clinical trials, a web-based, human subject volunteer registry, and approaches to improve investigator access to our clinical data warehouse. Many of these initiatives are expected to be completed in the next year in an effort to better serve the clinical research investigators.

## **3. PROGRAM UTILIZATION AND GROWTH**

In FY07 the CRP supported 253 investigator requests for assistance from 179 researchers in the institution. The Program has maintained significant funding from collaborative projects and CHB investigators, with 70 projects funding CRP staff in FY07 and totaling approximately \$1.1 million in funding from grants, departments, and programs.

## **4. PROGRAM COMMUNICATIONS**

In FY07 the CRP developed and distributed 3 issues of its 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 frequently asked statistical questions and answers.

## **5. BIOSTATISTICS CORE**

The Biostatistics Core includes seven doctoral level biostatisticians, all holding faculty appointments at Harvard Medical School through CHB departments and divisions, as well as four Master's-level biostatisticians and an administrative specialist. Capsule biographies are provided on page 17.

The mission of the Core is to provide biostatistical collaboration and consultation to CHB clinical researchers on the design, conduct, analysis and reporting of research projects. Core staff also conduct research on statistical methodology and contribute heavily to the CRP educational offerings.

Funding for the Biostatistics Core comes from federal and private research grants, departmental support, and CRP program funds.

The Biostatistics Core was directed for the first part of FY07 by Dr. Kelly Zou, who departed in June for a position in Europe. Dr. Osganian currently also serves as acting Director of the Core while a national search is currently underway for a new Director of Biostatistics.

### **a. Research Collaborations**

The primary activity of the Biostatistics Core is collaboration and consultation with CHB investigators, leading to involvement in clinical research protocols, grant proposals, randomization and other study operations, data collection, analysis, presentation, and publication in the biomedical literature. A full list of recent publications by CRP staff is provided in Appendix B. Highlights of FY07 follow.

- A study comparing the ability of three commonly employed definitions of hypotension to predict early brain injury in preterm infants was published in *Pediatrics* (Dr. Leslie Kalish, with investigators from the Department of Neurology).
- A randomized trial comparing low-fat to low-glycemic load diet for weight loss in obese young adults was published in *JAMA* (Dr. Henry Feldman, with investigators from the Division of Endocrinology).
- A Phase I double-blind, placebo-controlled crossover trial was completed to evaluate the tolerability of methylphenidate for reducing seizures in patients with both epilepsy and attention deficit hyperactivity disorder (Mr. Peter Forbes and Dr. Alka Indurkha, with investigators from the Department of Psychiatry).
- An analysis of risk factors for liver disease associated with parenteral nutrition in patients undergoing surgical therapy for necrotizing enterocolitis was conducted on registry data collected by the Glaser Pediatric Research Network (Dr. Kalish and Mr. Paul Mitchell, with investigators from the Division of Gastroenterology and Nutrition).
- A study of disordered weight-control behavior in early adolescents, as affected by a school-based, group-randomized intervention promoting healthful nutrition and physical activity, was published in *Archives of Pediatrics and Adolescent Medicine* (Dr. Feldman, with investigators from the Division of Adolescent and Young Adult Medicine).
- Evaluation of an oral health intervention promoting prevention of early childhood caries, implemented at the Primary Care Clinic of CHB, was presented at the American Academy of Pediatric Dentistry and received a citation for excellence (Dr. Indurkha, with investigators from the Department of Dentistry and Department of Medicine).
- A survey of environmental obstacles to dental care in children with special needs was completed (Ms. Jing Zhou, with investigators from the Department of Dentistry).

- Measurement-error techniques were developed to impute length of intestine for infants with short-bowel syndrome, using historical autopsy data (Mr. Patrick Johnston, with investigators from the Division of Gastroenterology and Nutrition).
- A quality-improvement intervention study, aimed at reducing central line-associated bloodstream infections in the pediatric intensive care unit, was accepted for publication in *Pediatrics* (Dr. Dionne Graham, with investigators from the Department of Cardiology and Division of Infectious Diseases).
- A compassionate-care protocol, involving substitution of a fish oil-derived lipid solution for conventional parenteral nutrition following gastrointestinal surgery, proved effective in ameliorating liver dysfunction and was accepted for publication in *Pediatrics* (Dr. Clarissa Valim, with investigators from the Division of Gastroenterology and Nutrition and Department of Surgery).

#### **b. New Research Funding**

An important element of the CRP mission is to help investigators prepare grant-worthy and effective proposals for funding from NIH, other federal agencies, and medical foundations. The Biostatistics Core plays a crucial role in this aspect of the mission because statistical justification, well thought-out analytic plans, and adequately budgeted statistical effort are essential for a fundable proposal, but hard to achieve without expert assistance. The fruit of this activity, seeded by departmental and CRP funds, is federal and foundation grant support for CRP staff, which continued to grow in FY07.

A full list of federal and private research grants currently active at CRP is provided on page 41. The following new awards, received in FY07, involve substantial statistical effort from staff of the Biostatistics Core.

- **Do Condoms Protect from Non-viral Sexually Transmitted Infections?** National Institute of Allergy and Infectious Diseases. Dr. Indurkha, with P.I. Dr. Lydia Shrier, Division of Adolescent and Young Adult Medicine.
- **Continuous Monitoring for Cerebral Pressure-Passivity in Premature Infants.** National Institute of Child Health and Human Development. Dr. Matt Gregas, with P.I. Dr. Adré du Plessis, Department of Neurology.
- **Glycemic Load and Infant Birth Weight in Pregnant, Glucose Intolerant Women.** Dr. Feldman, with P.I. Dr. David Ludwig, Division of Endocrinology.
- **Placebo-Controlled Study of Baclofen for Gastroesophageal Reflux Disease in Children with Cerebral Palsy.** National Institute of Diabetes and Digestive and Kidney Diseases. Mr. Mitchell, with P.I. Dr. Samuel Nurko, Division of Gastroenterology and Nutrition.
- **Clinical Hematology Research Career Development Program.** National Heart, Lung, and Blood Institute. Dr. Kalish, with P.I. Dr. Ellis Neufeld, Division of Hematology/Oncology.
- **A Six-Month Open-Label Study of Amiloride Solution for Inhalation and Tobramycin Solution for Inhalation for Eradication of *Burkholderia dolosa* in Patients with Cystic Fibrosis.** Cystic Fibrosis Foundation. Dr. Kalish, with P.I. Dr. Dawn Ericson, Division of Respiratory Diseases.
- **Endotoxin-related Innate Immunity in Patients Undergoing Hematopoietic Stem Cell Transplantation.** Dana Foundation. Dr. Kalish, with P.I. Dr. Ofer Levy, Division of Infectious Diseases.

- **Efficacy of Omega-3 Enriched Fat Emulsion and Prevention of Perenteral Nutrition-Induced Liver Injury in Infants.** March of Dimes Foundation. Dr. Valim and Ms. Zhou, with P.I. Dr. Mark Puder, Department of Surgery.

- **Oral Health Needs Assessment of Children with Special Health Care Needs in Massachusetts.** Delta Dental. Dr. Indurkhya and Ms. Zhou, with P.I. Dr. Linda Nelson, Department of Dentistry.

### c. Teaching Clinical Investigators

Biostatistics Core staff play a prominent role in the educational offerings of CRP. The twice-yearly *Introduction to Clinical Research*, a four-day overview for new Fellows and junior faculty, features seven hours of statistical material, including both a general orientation to the role of statistics in clinical research and specific material on the elements of study design and analytic technique. The introductory course generates demand for more advanced short courses, of which one is now well established and three more are in development. Dr. Graham and Mr. Forbes teach *Introduction to Biostatistics* with SPSS twice yearly, combining six lectures on elementary descriptive and inferential statistics with companion computer laboratory sessions. Even allowing enrollment of 50 per offering, this course has been consistently over-subscribed in its two-year history. Dr. Feldman has developed a single-session course on *Statistical Power and How to Get It: Sample Size for Clinical Research*, aimed at investigators preparing research proposals, and in FY07 added a computer laboratory session. In the coming year Dr. Indurkhya will initiate a short course on analysis of discrete data titled *Beyond Chi-Squares: Drawing Inferences from Tables*.

Besides the CRP short-course program, members of the Biostatistics Core regularly deliver hospital seminars and conduct training at national meetings. In FY07 Drs. Graham, Kalish, and Feldman contributed to the Research Skills lecture series for the CHB Health Services Research Fellowship. Dr. Feldman served for his tenth year as faculty in the American Heart Association Ten-Day Seminar on Epidemiology and Prevention of Cardiovascular Diseases, a post-doctoral training course for preventive cardiology and related professions of which several CHB faculty are graduates. Dr. Indurkhya taught a semester course on *Biostatistical Applications Using SAS* at University of Massachusetts Medical School, Worcester, and conducted a tutorial titled *A Reviewer's Perspective on Career Development* at the 19th National Institutes of Mental Health Conference on Mental Health Services Research in Washington, D.C.

### d. Funding From Departments and Divisions

An important organizing principle of CRP is the integration of its faculty with CHB Departments and Divisions, so as to foster creative research collaborations between department-based investigators and CRP-based biostatisticians knowledgeable in the scientific and medical subject matter. FY07 saw substantial progress in this direction, with the hiring of four new faculty members tied to particular departments, establishment of two new ties for existing faculty, and launching of faculty searches for three additional departments. In each case the department or division supports a substantial fraction of a biostatistician's effort for their dedicated involvement in the department or division's research as well as to support and promote their academic and professional development. This helps to provide the biostatistician with scientific focus and methodological expertise, and continuity of collegial contact, leading to a facilitative environment for generating new ideas, securing new grant support, and publishing research findings. The following departmental affiliations are in place or planned.

Dr. Feldman, *Division of Endocrinology*.

Mr. Forbes, *Department of Psychiatry*.

Dr. Graham, *Department of Cardiology and Program for Patient Safety and Quality*.

Dr. Gregas, *Department of Neurology.*  
Dr. Guo, *Division of Genetics and Program in Genomics.*  
Dr. Indurkha, *Division of Adolescent and Young Adult Medicine and Department of Psychiatry.*  
Mr. Johnston, *Division of Emergency Medicine and Department of Otolaryngology.*  
Dr. Kalish, *Division of Hematology/Oncology.*  
Mr. Mitchell, *Division of Gastroenterology and Nutrition.*  
Dr. Valim, *Department of Surgery.*  
Ms. Zhou, *Department of Surgery and Program for Patient Safety and Quality.*  
Faculty search in progress, *Division of Gastroenterology and Nutrition.*  
Faculty search in progress, *Department of Urology.*

#### **e. New Staff**

The Biostatistics Core grew substantially in FY07 with the addition of four faculty and two Master's-level statisticians. This expansion, continuing over several years now, was made possible by the increased interest of departments and divisions in supporting an identified member of the CRP for collaborative work in a particular area. Dr. Kelly Zou came from the Department of Radiology at Brigham and Women's Hospital where she served as Associate Professor of Radiology and Principal Statistician, with expertise in ROC curves; Dr. Alka Indurkha from University of Massachusetts Medical School with expertise in community-based intervention and prevention research with children and adolescents; Dr. Matt Gregas from Harvard School of Public Health and University of Minnesota with a background in analysis of neuronal signals; and Dr. Chao-Yu Guo from Boston University with expertise in statistical genetics as applied to epidemiological studies. Ms. Jing Zhou came from Brown University Medical School with experience in obesity and surgical research, while Mr. Paul Mitchell came from New England Research Institutes with skills and experience in multi-site community trials and clinical trial networks.

## **6. PROJECT AND DATA MANAGEMENT CORE**

Under the direction of Team Leader, Susan McDermott, the Project and Data Management Core staff included Project Directors Maggie McCarthy and Tracy Antonelli; Epidemiologist Dr. Jui Haker; Research Data Managers Aruna Jayashankar, Sharon Wong, Rajna Filip-Dhima, and Handan Titiz; Data Coordinator Laura Boger; and Administrative Coordinator Harold Thurston.

#### **a. Project and Data Management Collaborations and Consultations**

The principle work of the PDMC is to provide hands-on support and/or expert consultation to CHB clinical investigators for best practice project and data management for planning and implementing clinical research studies at CHB. In FY07, PDMC team provided assistance on 65 projects, through the provision of simple advice to extensive hands-on efforts and deliverables.

#### **b. Development of a PDMC Toolbox**

In FY07, PDMC staff designed several project and data management templates and assembled them in a "PDMC Toolbox." The Toolbox is a compendium of templates and examples that can be used for easy reference for planning and implementing clinical research investigations. Use of documents in the Toolbox improves efficiencies for PDMC staff when assisting and advising study staff with planning and study start-ups. Templates are used by CRP staff and/or provided directly to CHB study staff during consultations for teams who chose to design their own tools. The Toolbox organizes in one place many templates already shared amongst CRP staff members such as Case Report Forms and Question by Question Specification Guides of commonly used question sets and formats such as



Eligibility Screening (inclusion/exclusion criteria), Baseline History and Physical Measurements (socio-demographics, vital signs, anthropometrics, etc.), and common lab tests, special studies and procedures. Other templates include CRP Subject ID Assignment Logs, examples of Randomization Schemes and the Randomization Protocol Checklist, Critical Tasks Timelines and all the CRP Research Practice Guidelines. Other management tools developed for internal use include a newly developed Virtual Queue for tracking the status of databases under development, SPSS Programming Guidelines and Handouts, examples of Measures by Visit Schedule, CRIT VISIO visual formats, and various database development progress tracking tools.

#### **c. Refinement of PDMC Service Definitions**

With an aim to improve tracking PDMC service metrics, Ms. McDermott developed PDMC service definitions to standardize systems and improve compliance for counting and tracking PDMC services requested and provided. The service definitions were useful in the design of a new CRP Intake Database developed by CRP Administrative Director Randi Triant and CRIT Team Leader, Jason Rightmyer.

#### **d. CRP Randomization Procedure**

The CRP Randomization Procedure was enhanced in FY07 to simplify the procedure for Investigators and standardize implementation across CRP project and data managers. Major changes include addition of a Randomization Checklist for Investigators, elimination of randomization envelopes for most blinded studies, standardization of an invisible link between the master study database and the blinded randomization assignment log. The Procedures are available to CHB Investigators as a Research Practice Guideline on the CRP web page.

#### **e. Support of and Development of SPSS Databases**

The CRP commitment to SPSS database development continued throughout the year.

Development of Databases: The DMC provided support and hands-on database development for 49 new research projects.

Development and implementation of training curriculum: CRP Data Manager Ms. Jayashankar, developed a 2-session curriculum and delivered training to 3 investigators and 2 CRP staff members for programming databases in SPSS Data Entry Builder. 'After training' tutorial support was provided by CRP Data Managers and Coordinators. The training resulted in 4 functioning databases (included in the number above). The handouts have been distributed to other investigators as appropriate. The curriculum and handouts are currently being refined for a repeat training in FY08.

#### **f. Do-It-Yourself Data Management Course**

Ms. Antonelli served as Course Director for the Do-It-Yourself Data Management Course sponsored by the CRP Education Core. The 3-session, hands-on course serves as a practical guide for new clinical investigators preparing for study start-up. The 3-session course aims to orient new investigators to best practice standards pertaining to the implementation of clinical research at CHB. Topics incorporated into the curriculum include an introduction to ICH Good Clinical Practice guidelines; preparing for an EQIP QC review; and 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. The curriculum is currently being expanded and repeat trainings are planned in FY08.

#### **g. Study Coordinator Orientation and Coordinator Rounds Seminar Series**

PDMC staff continued to direct the bi-monthly Study Coordinator Orientation program for new clinical research assistants and study coordinators sponsored by the CRP Clinical Research Education Core. The day long orientation aims to introduce new Study Coordinators to the basic elements of clinical research and to the clinical research staff, resources and services provided by various CHB departments. Team Leader Susan McDermott serves as Director and lead speaker for the Orientations. The program was revamped in FY07 to minimize redundancies and add topics of increasing importance to CHB clinical research coordinators, e.g. Good Clinical Practice.

The Coordinator Rounds offers CHB research staff a bi-monthly forum to discuss common logistic challenges, exchange proven operational strategies, and review important updates in the field of clinical research. The hour long forum allows a more in depth discussion of topics than is possible in the Orientation program. A list of the topics presented in FY07 appears in Appendix C.

#### **h. Increasing PDMC Staff Knowledge of FDA Regulations Pertaining to Project and Data Management of CHB Clinical Research Regulated by FDA**

PDMC staff organized an electronic compendium of web links to relevant federal regulations and guidelines. The links are organized in an Excel spreadsheet and stored in the PDMC Toolbox and on the CRP internal share drive. The table is organized such that the links can easily be bookmarked as internet favorite sites by PDMC staff.

Ms. McDermott joined the Clinical Research Education Core Staff in planning for in-service training in federal regulations for PDMC staff members. Plans were completed in FY07 for participation in a Brigham and Woman's FDA Day, scheduled for January 11, 2008.

#### **i. New Staff Hires**

Laura Boger, BA, joined the CRP in October 2006 as a Data Coordinator. Jui Haker, MD, MPH, serves as Epidemiologist and Project Director in the PDMC. She joined the CRP in January 2007. Ms Handan Titiz joined the CRP in September 2007 as a Data Manager.

Biographical information of these and all PDMC staff appears on page 20.

### **7. CLINICAL RESEARCH INFORMATION TECHNOLOGY**

This section highlights the major activities and accomplishments of the Clinical Research Information Technology (CRIT) staff, which serves to support and enhance the clinical research enterprise, support the investigator community and improve Clinical Research Program (CRP) operations.

#### **a. Evaluated and Acquired New Enterprise Electronic Data Capture (EDC) Software for Clinical Research**

The CRIT in partnership with the CRP established a search committee to investigate and recommend a new clinical data management system (CDMS) and EDC solution for the clinical research enterprise. The committee selected Phase Forward InForm™ ITM (Integrated Trial Management), an industry standard solutions platform for developing and supporting research databases. The technology and its related services will be available in 2008.

Phase Forward's InForm™ ITM software application is a web-based EDC and CDMS used by research teams to facilitate study data collection, monitoring and analysis. The product supports enhanced reporting and integration capabilities as well as features to comply with FDA requirements. InForm™

is based on open data standards (CDISC ODM, XML, etc.) and is designed to facilitate the integration of disparate clinical or bioinformatics services.

The InForm™ application software employs Microsoft and Oracle technologies to deliver secure web services and data storage. The software licensing and related IT services (network hosting, data storage, backup and security) will be provided at no cost to CHB clinical investigators. However, staff effort related to database development, documentation and implementation may be subject to cost recovery and direct billing hospital policies.

**b. Fostered New Relationships Within the Information Services Department (ISD)**

The CRIT engaged in several new ISD initiatives in 2007. After officially joining the ISD in 2006, the team immediately established close relationships with the Business Intelligence (BI) and Document Management teams. Specifically, the CRIT worked directly with the BI team to train on Business Objects technology, which includes CHQuery and the clinical data warehouse (CDW).

Furthermore, the CRIT worked closely with the Document Management team to support the use of Microsoft Sharepoint technologies in clinical research. Sharepoint benefits research teams by enhancing communications, document sharing and project management. Additional CHB services, training and collaboration are planned for 2008.

**c. Enhanced Software Applications to Support Clinical Research**

The CRIT released several new versions of its software in 2007. Specifically, the team released version 1.5 of its data management system framework. Enhancements included support for SQL Server 2005 as well as features to improve multi-site data coordination and CDISC compliance.

The CRIT also released version 1.2 of its randomization software product. The software is used by the CRP to generate randomization schemes and materials for clinical trials research. Enhancements included revised reports, support for SQL Server 2005 and Microsoft.NET 2.0, as well as improved algorithms for allocation assignments.

The CRIT established a new web service architecture strategy in 2007. This new architecture is based on a platform of modular, reusable web-based programs, which connect common research-related functions. These functions include Active Directory lookup, randomization, z-score calculation, and data validation.

**d. Enhanced Administrative Applications for the CRP/GCRC**

The CRIT worked closely with the CRP administrative team to revise and redesign two of its administrative software applications. Specifically, the team added features and reports to the CRP web-based budget tracking software. In addition, the team revamped the CRP intake database with new technologies and functionality. This new system will facilitate the CRP transition to a paperless administrative process, which includes online request submissions and automated email workflow in the next year.

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

The CRIT in close collaboration with the CRP Project and Data Management Core developed and deployed many new large-scale data management systems in 2007. Specifically, the CRIT implemented six new systems for use in Emergency Medicine, Urology, Radiology, and Adolescent Medicine. The CRIT now provides ongoing support to over 25 large-scale systems in the field.

## 8. CLINICAL RESEARCH EDUCATION CORE

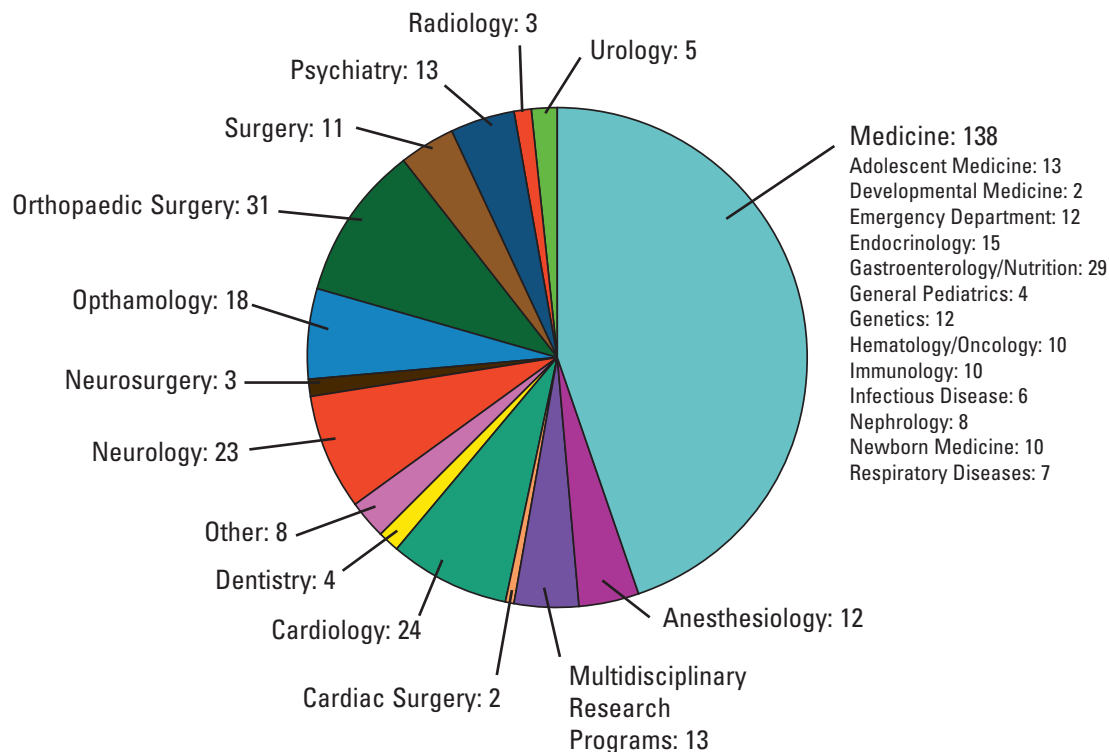
The Clinical Research Education Core is responsible for the planning, organization and implementation of all CRP sponsored seminars and courses. Our aim is to provide a comprehensive educational plan with course offerings that cover basic to advanced curriculum for clinical research. Accordingly, the Clinical Research Education Core works closely with both the Project and Data Management and Biostatistics Cores of the CRP to meet the research educational needs of study coordinators, nurses, medical students, fellows, junior faculty, as well as senior faculty involved in clinical research across the hospital.

### a. Lessons Learned, Challenges, and Goals for the Future

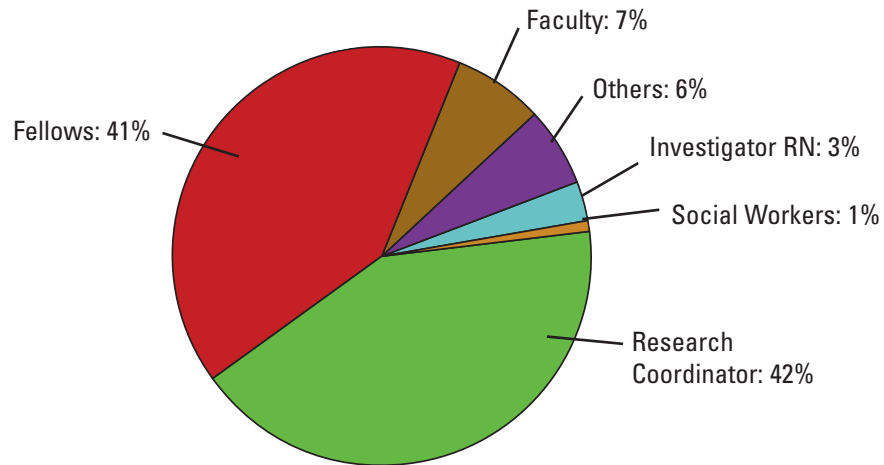
Under the direction of Dr. Jenifer Lightdale, the Clinical Research Education Core provides considerable educational opportunities for CHB staff and faculty involved in clinical research. Over the past several years, we have prioritized the following:

**Demand:** There is strong demand for the CRP courses from clinical research faculty and staff representing most CHB departments and divisions (Figure 1). While we specifically aim to meet the needs of fellow trainees and study coordinators, course attendees also represent the spectrum of the CHB Clinical Research Community (Figure 2). Demand for spaces in the CRP courses is often larger than capacity, and we generally reach targeted enrollment within a week or two of opening a course for registration (Table 1). In order to meet increasing demand for the CRP courses, we have chosen larger venues and increased the frequency of our course offerings.

**Figure 1. CRP Course Attendees by Department 2006–2007**



**Figure 2. CRP Course Attendees by CHB Role 2007**



**Table 1. CRP Course Attendance by Year 2005–2007**

Course	2005	2006	2007
Introduction to Clinical Research	103	100	108
Orientation for New Study Coordinators	69	60	73
Coordinator Rounds	—	75	120
Introduction to Biostatistics with SPSS	—	62	79
Power and How to Get It	—	42	30
Do-It-Yourself Data Management	—	—	5

**Table 2. CRP Course Offerings by Year 2004–2008**

CRP Course	2004	2005	2006	2007	2008
Introduction to Clinical Research	***	***	***	***	***
Orientation for New Study Coordinators	***	***	***	***	***
Coordinator Rounds	***	***	***	***	***
Introduction to Biostatistics with SPSS			***	***	***
Power and How to Get It			***	***	***
Do-It-Yourself Data Management				***	***
Beyond Chi-Squares: Drawing Inferences from Tables					***
Biostatistics and Clinical Tests					***
Statistics for Small Sample Size Studies					***

\*\*\* course offered

**Curriculum:** The Clinical Research Education Core is continuing to build upon our curriculum by adding 1-2 new courses a year (Table 2). The need for introductory and more advanced biostatistics courses continues, as well as for courses in data management. In April 2007, we introduced *Do-It-Yourself Data Management* a course designed to teach junior investigators and fellows the fundamentals of study organization and data management. In early 2008, we will be introducing three short advanced biostatistics courses.

**Faculty:** The faculty from the CRP and other CHB departments continue to apportion their valuable time in order to enthusiastically participate in CRP courses. In 2007, the CREC formally recognized their invaluable contributions to the CRP education program by providing funds for “course appropriate” faculty honorariums.

**Interaction:** Course participants, particularly junior faculty and fellows, continue to seek increased interaction with course faculty. As a result, we introduced course lunches with the *Introduction to Clinical Research* faculty in March 2007. Many of our other courses offer similar informal opportunities for student-faculty interaction. We will continue to promote interaction and foster collaboration within the CHB investigative community through the CRP’s educational offerings.

**E-Learning:** The Clinical Research Education Core recognizes the growing demand for web-based on-demand learning opportunities. As such, we are working to make more courses available for on-demand viewing using Adobe Breeze software. We successfully piloted our use of Breeze by recording and webcasting the CHB Responsible Conduct of Research training in June 2007. Over the past year, we have transitioned to an online registration and web-based evaluation system for all CRP courses.

## **9. GLASER PEDIATRIC RESEARCH NETWORK**

The Program continues to serve as the Design, Analysis, and Coordinating Center for the Glaser Pediatric Research Network. Three contracts were in operation in 2007 for coordination and statistical analysis of GPRN-funded research:

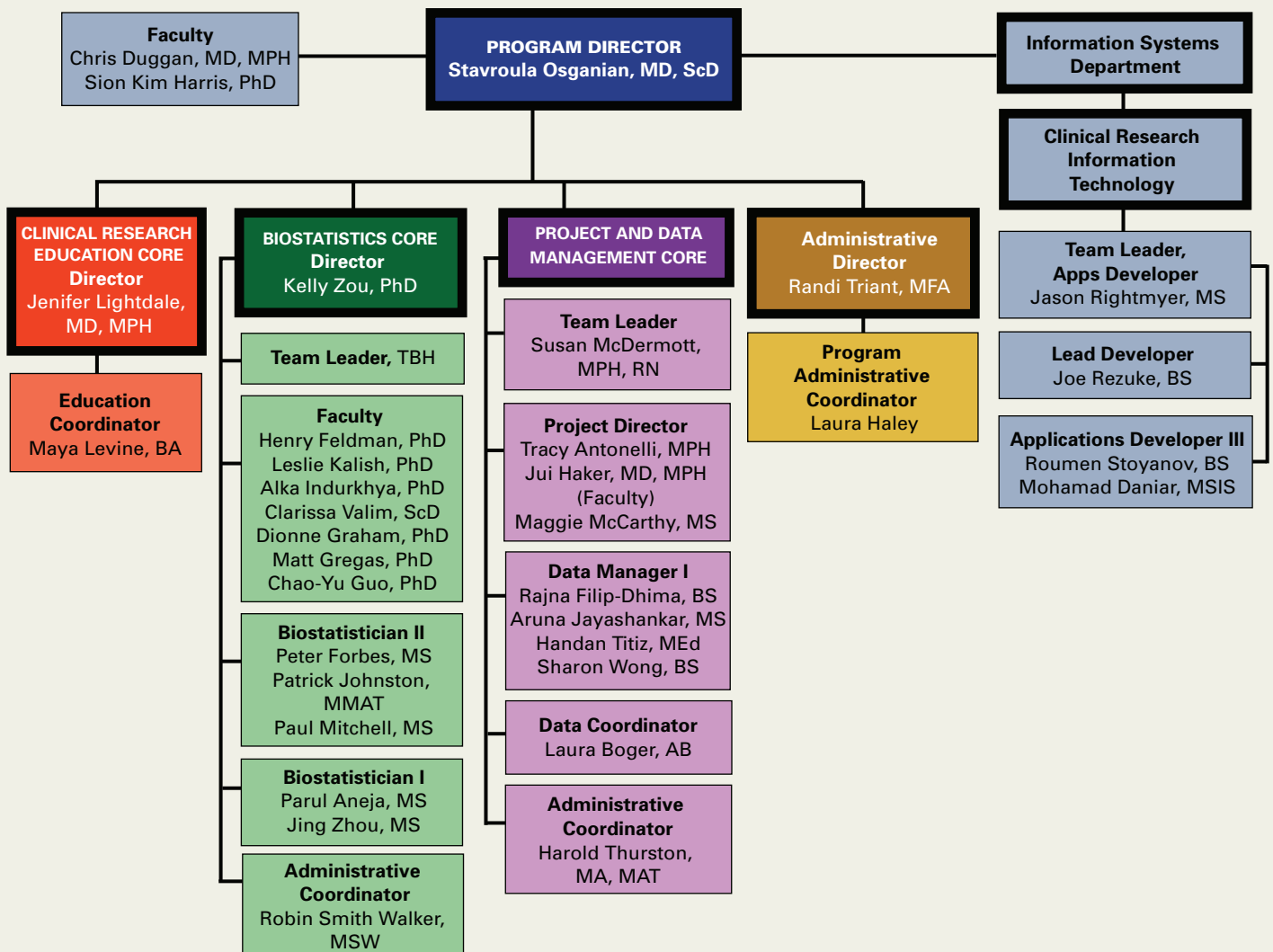
- A registry for clinical data on necrotizing enterocolitis in newborns enrolled its 500th patient, presented preliminary findings, and initiated an expanded protocol with biologic samples added to data collection.
- A trial of metformin in obese adolescents completed all data collection and presented its principal findings at a national meeting.
- A multi-site Phase I/II trial of rituximab in children with chronic immune thrombocytopenic purpura, for which GPRN provided 5 of 10 sites, published its primary findings and submitted one-year follow-up results for publication.

An additional Core contract provides statistical support and data management for current studies and education for the network’s Fellowship program.

# Program Organizational Structure

In FY 07 the Program included 28 full-time, 3 affiliated, and 3 part-time staff organized into three major cores: the Biostatistics Core, the Project and 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 Project and 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.

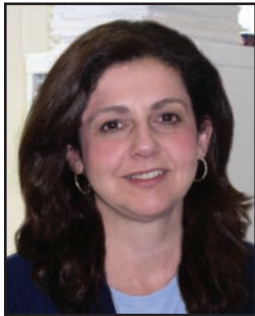
## A. ORGANIZATIONAL CHART



## **B. STAFF ROLES AND BIOGRAPHIES**

Staff publications can be found in Appendix B.

### **PROGRAM DIRECTOR**



#### **Stavroula Osganian, MD, ScD, MPH, *Program Director***

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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. Her present research includes a trial of metformin for weight loss in obese adolescents, a school nurse delivered smoking cessation intervention for adolescent smokers, and a school nurse delivered obesity intervention in adolescents. 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***

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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. Dr. Duggan has been a member of several large multi-center clinical trial groups, including the Glaser Pediatric Research Network. He is an Associate Professor of Pediatrics at Harvard Medical School, an Associate 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***

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Dr. Harris has over 15 years of experience in survey design, implementation, and analysis and she provides consultation throughout Children's Hospital Boston in the design and implementation of surveys. Dr. Harris also has extensive experience in public health epidemiology, psychometric evaluation of measures, clinical and community-based adolescent health research, program evaluation, and qualitative research methods. She has collaborated in the development and/or psychometric evaluation of numerous instruments for use in adolescent health research. She is currently an investigator in the CHB Center for Adolescent Substance Abuse Research, and holds joint faculty appointments in the Divisions of Adolescent/Young Adult Medicine, and Developmental Medicine.



## BIostatISTICS CORE



BIostatISTICS CORE STAFF L TO R (BACK): PAUL MITCHELL, PATRICK JOHNSTON, HENRY FELDMAN, CHAO-YU GUO, LESLIE KALISH, MATT GREGAS. L TO R (FRONT): JING ZHOU, ROBIN WALKER, CLARISSA VALIM, DIONNE GRAHAM MANNING, PETER FORBES.

### **Henry A. Feldman, PhD, *Lead Biostatistician***

Henry Feldman joined CRP in 2001, having held research and teaching positions at New England Research Institutes, Harvard School of Public Health, and NIH. His publications span medicine, public health, and biological science, including clinical and community trials, epidemiologic surveys, human and animal physiology, cellular and molecular biology, and mathematical methods for study design and data analysis. Through an appointment in the Endocrinology Division, he collaborates with senior faculty as co-investigator on a variety of funded studies centering on obesity and bone health and actively counsels junior faculty and fellows on development of new protocols. Dr. Feldman takes regular part in CRP educational offerings and in 2007 received the A. Clifford Barger Award for Excellence in Mentoring from Harvard Medical School.

### **Peter Forbes, MA, *Senior Biostatistician***

Peter Forbes joined the CRP in 2000, following several years' experience in the Learning Disabilities Research Center in the Department of Psychiatry. His activities include data cleaning and data set creation, SAS programming, data reporting, data analysis, statistical graphics, and participation in the writing of grants and papers. He plays an important role in the CRP education program, conducting computer laboratories for the introductory biostatistics course. His areas of interest include statistical software and programming, data analysis, sample design, and survey research methods.

### **Dionne Graham Manning, PhD, *Senior Biostatistician***

Dionne Graham Manning joined the CRP in 2005, bringing a doctorate in biostatistics from Harvard University and a Master's degree in biomedical engineering from Johns Hopkins University. She devotes substantial effort to the Program for Patient Safety and Quality, assessing the efficacy of various safety and quality initiatives and developing measures for monitoring hospital performance. Dr. Graham Manning delivers a popular introductory biostatistics course under CRP auspices. Through an affiliation with the Department of Cardiology, she provides general statistical support to hospital researchers, from grant writing and protocol review to the design and analysis of clinical trials.

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**Matt Gregas, PhD, Senior Biostatistician**

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Matt Gregas joined the CRP in 2007 after completing a post-doc at the Harvard School of Public Health. Dr. Gregas received his doctorate from the School of Statistics, University of Minnesota in 2005 where he primarily developed methodology for the analysis of neuronal data. He is affiliated with the Department of Neurology where he works with faculty and fellows on grant proposals, protocol development, data analysis, and manuscript preparation. His projects include neonatal epilepsy, autism, and the effects of neonatal hypotension on the physiology of the infant brain. Dr. Gregas's methodological interests include nonparametric function estimation, functional data analysis, and changepoint estimation. This research has been motivated by his collaboration in neurological projects at Minnesota and Harvard.

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**Chao-Yu Guo, PhD, Senior Biostatistician**

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Chao-Yu Guo joined the CRP in 2007, coming from a faculty position at Boston University Department of Mathematics and Statistics. His research activities have been focused on various statistical methodologies for epidemiological research, longitudinal studies, and statistical genetics using the Framingham Heart Study data. He has special interests in family-based linkage and association studies and missing data patterns in genetic studies. Dr. Guo is affiliated with the Program in Genomics, Department of Medicine and is currently working on an autism project.

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**Alka Indurkha, PhD, Lead Biostatistician**

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Alka Indurkha joined CRP in 2007, bringing broad experience with biostatistics in clinical and health services research, epidemiology, and behavioral science from faculty positions at Michigan State University, Harvard School of Public Health, and University of Massachusetts Medical School. Her research interests include cost-effectiveness, barriers to care for children and adolescents, and community-based intervention and prevention. Through affiliations with the Department of Psychiatry and the Adolescent Medicine Division, she provides collaboration on study design, scale development, and data analysis to a wide panel of senior and junior faculty.

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**Patrick Johnston, MS, Senior Biostatistician**

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Patrick Johnston joined the CRP in 2006. He holds degrees in mathematics and economics and has wide interests in theoretical and applied statistics, from Bayesian, likelihood, and frequentist approaches to inference, through parametric and semiparametric models, to solving practical problems in design and analysis by simulation. He has devoted substantial effort to a study of necrotizing enterocolitis sponsored by the Glaser Pediatric Research Network and provides statistical support and collaboration to medical researchers in various departments, serving particularly as statistician for the Emergency Medicine Division.

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

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Dr. Kalish joined the CRP in 2003, having held leadership positions in multi-center studies at New England Research Institutes and Dana Farber Cancer Institute and having taught in the Biostatistics Department at Harvard School of Public Health. His professional focus is the design, coordination, and analysis of clinical trials and epidemiologic cohort studies. He has collaborated on clinical research in many areas, including HIV and other infectious diseases, transfusion medicine, alternative medicine,

cystic fibrosis, and oncology. Dr. Kalish is affiliated with the Infectious Disease and Hematology/Oncology Divisions. He serves as Director of Biostatistics for the General Clinical Research Center, for which he coordinates the review of all protocols.

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**Paul Mitchell, MS, Senior Biostatistician**

Paul Mitchell came to CRP in 2007 with over 15 years experience in epidemiologic studies, survey research, and clinical trials. At New England Research Institutes he carried major responsibility for statistical programming and analysis in national multi-center trials, including the Child and Adolescent Trial for Cardiovascular Health, and co-authored over 20 publications in peer-reviewed journals. His interest and expertise focus on ordinary least squares regression, logistic regression, repeated measures over time, mixed models theory, non-parametric analysis, and power and sample size methodology. He participates in the CRP short-course program and serves as statistician for the Gastroenterology/Nutrition Division, providing collaborative assistance on study design, randomization, and data analysis to faculty and fellows.

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

Clarissa Valim has a multidisciplinary background, with graduate studies in medicine, epidemiology, and biostatistics leading to her joining CRP in 2003. Her methodological research interests are in the area of survival methods, particularly in studies with censoring due to outcome-related mortality, and in predictive models for functional outcomes in longitudinal studies. She has worked extensively with faculty and fellows in Gastroenterology/Nutrition and is currently affiliated with the Department of Surgery, collaborating on protocol development, conduct of trials, and data analysis. Dr. Valim lectures in the CRP educational program and is a biostatistician for the NIH-funded Severe Malaria in African Children clinical research network.

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**Jing Zhou, MS, Biostatistician**

Jing Zhou joined the CRP in 2006, bringing a Master's in Statistics and several years' experience in trial design, data analysis, and statistical programming at Duke Clinical Research Institute and Brown University Medical School. She has co-authored publications on obesity and thoracic surgery and currently works with the Department of Surgery to provide statistical support. She is also a statistician for the Program for Patient Safety and Quality.

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**Robin Walker, MSW, Administrative Coordinator**

Robin Walker, who joined the CRP in 2005, is in charge of financial management and administrative support 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. Ms. Walker holds a Master of Social Work with a concentration in management and planning from Boston University.

## PROJECT AND DATA MANAGEMENT CORE (PDMC)



PDMC STAFF L TO R: TRACY ANTONELLI, SUSAN McDERMOTT, HANDAN TITIZ, HAROLD THURSTON, RAJNA FILIP-DHIMA, LAURA BOGER, QIAOLI CHEN, MAGGIE McCARTHY.

### **Susan McDermott, MPH, RN, CS, *Clinical Research Team Leader***

Susan McDermott, RN, MPH, joined the CRP in August of 2006 to serve as Team Leader of the Project and Data Management Core. As such, she provides direct leadership and supervision to the PDMC team and expert advice to CHB Investigators for best practice methods in the areas of project and data management of clinical research. Ms. McDermott also serves as Course Director for the Study Coordinator Orientation and bi-monthly Study Coordinator Rounds. She serves as faculty for several Clinical Research Education Core Training programs including Introduction to Clinical Research, Do-It-Yourself Data Management as well as the Coordinator Orientation and Rounds. Ms. McDermott's 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.

### **Tracy Antonelli, MPH, *Projector Director***

Ms. Antonelli joined the CRP in February 2006. She provides expert project management and data management advice to CHB Investigators requesting assistance from the CRP. She also serves as Project Manager of a multi-site NIH-funded trial of the Obesity Research Group. Her project management responsibilities include development of case report forms, procedure manuals, and data management systems; serving as point of contact for high school personnel, subjects and guardians; conducting subject recruitment, consent and screening; and implementation of the protocol in the field. Ms. Antonelli is Course Director for the Do-It-Yourself Data Management Course, and CRP Lead/Author for selected Research Practice Guidelines.

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**Laura Boger, AB, *Research Data Coordinator***

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Ms. Boger joined the CRP in October 2006. She received an AB in Development Studies from Brown University in December 2000. After working in New York City with a non-profit health and human rights organization, Ms. Boger served as a Peace Corps health education volunteer in Guyana, South America. Upon returning from Guyana in May 2005 and before joining the CRP, Laura completed post-baccalaureate pre-medical requirements in preparation for application to medical school in 2008.

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**Rajna Filip-Dhima, BS, *Research Data Manager***

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Ms. Filip-Dhima joined the CRP in March 2004. She served originally as Research Data Coordinator, and more recently as Clinical Research Data Manager. She holds a BS in Psychology. As Data Manager she provides support and advice to research teams building simple databases, using SPSS Data Entry Builder; and she tests and validates databases developed by study staff and other CRP Data Managers. She provides training and ongoing assistance to study staff for data entry routines and SOP data management procedures. She designs case report forms, collaborates with study teams to develop more complex, relational databases, writing specifications and completing validation, and testing and training research coordinators to use them. Ms. Filip-Dhima also collaborates with study staff and biostatisticians to develop randomization products for investigators conducting randomized trials. She programs surveys using the Web Survey software, in addition to quality controlling web surveys built by co-workers.

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**Jui Haker, MD, MPH, *Epidemiologist, Project Director***

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Dr. Haker joined the CRP in January 2007 as an Epidemiologist/Biostatistician. She completed a residency in Preventive and Social Medicine. As a member of the PDMC, she provides consultation on various aspects of survey research methods, such as questionnaire development and design, and implementation of surveys including web-based surveys. She serves as project manager for overall CRP efforts on studies, study planning, and oversight for development of case report forms and data management systems. Prior to joining the CRP, she was a researcher in the Department of Radiology at the Brigham and Women's Hospital (BWH), where she was actively involved in a number of NIH funded studies as an Investigator.

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**Aruna Jayashankar, MS, *Research Data Manager***

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Ms. Jayashankar joined the CRP in August 2005. She served as both Clinical Research Specialist and later, Data Manager. She holds a Master's Degree in Biomedical Engineering. Her primary responsibilities included case report forms, data management systems and database development. She participated in development of procedures manuals, training manuals and study-specific quality assurance procedures for clinical investigators. She served as CRP Lead for studies involving CRF and database development in SPSS Data Entry Builder. Ms. Jayashankar developed the curriculum and served as Course Director for the 2-session tutorial, Developing Databases using SPSS Data Entry Builder.



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**Maggie McCarthy, MS, MPH, Project Director**

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Ms. McCarthy joined the CRP in April 2002. She has an MPH from Harvard School of Public Health and a Master of Clinical Immunology degree from Hahnemann University in Philadelphia. She serves as Project Director for several multi-center studies coordinated by the CRP, most notably the studies sponsored by the Glaser Pediatric Research Network, assisting in protocol development, development of case report forms, manuals of operations, and database specifications for the Network's data management systems. Ms. McCarthy serves as a Project Director for other multi-site studies for which the CRP functions as Data Coordinating Center (DCC). Prior to joining the CRP she served as DCC Project Director for the multi-site study, Hepatitis C Antiviral Long Term Treatment against Cirrhosis (HALT-C), a large NIH sponsored, ten center clinical trial.

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**Handan Titiz, EdM, Research Data Manager**

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Ms. Titiz joined the CRP in September 2007 as a Research Data Manager. She holds a Master's Degree in Human Development and Psychology from Harvard University Graduate School of Education. Prior to joining CRP her primary focus has been on investigating the effect of cultural and gender differences on psychological and educational phenomena. Her current responsibilities include designing and programming case report forms, writing database specifications, developing SPSS data bases and randomization schemes for single and multi-site studies, and performing quality assurance checks of the databases.

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**Sharon Wong, BS, Data Manager**

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Ms. Wong joined the CRP in September 2001. In FY07 Ms. Wong served as Data Manager for several ongoing projects. Her responsibilities included case report forms and database development, data entry and data management. Ms. Wong was most frequently assigned to research studies that required database development using SPSS Data Entry Builder or web-based survey software. In addition to database development, she provided tutorial support to investigators developing their own databases. Ms. Wong completed QC checks of databases developed in the CRP. She also created study specific ID Assignment Logs and randomization schemes; she developed case report forms and database programming specifications, and completed data entry and data cleaning procedures and general quality assurance checks.

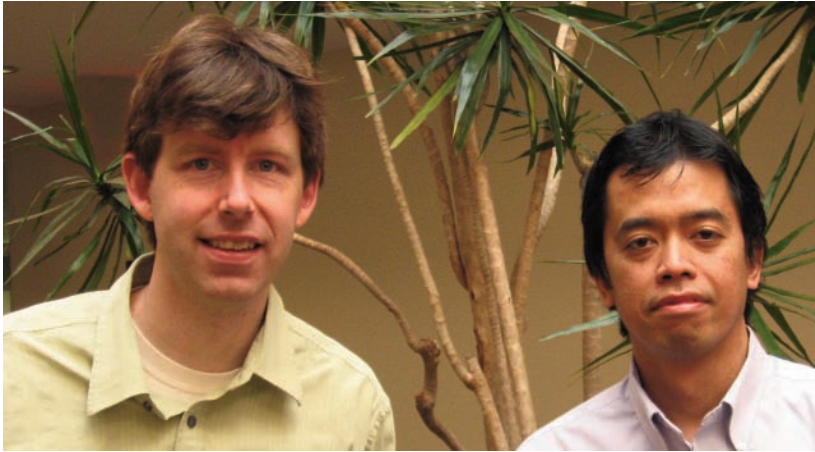
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**Harold E. Thurston, Jr., MA, MAT, Administrative Coordinator**

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Mr. Thurston joined the CRP in March 2006. He provides overall administrative and financial management support for the PDMC. Mr. Thurston's past professional experience has been primarily in the private public health research sector and the field of communications. Most recently he served as Executive Assistant to a Vice President of Communications and Media and as Patient Information Specialist. 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



CRIT CORE STAFF L TO R: JASON RIGHTMYER, MOHAMAD DANIAR.

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### **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.

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### **Mohamad Daniar, MSIS, Senior Applications Developer**

Mr. Daniar joined the CRP in November 2006. He has a Master's in Information Systems 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 SQL Server. He has worked previously for a number of high-tech software companies and is currently a Senior Applications Developer in the Clinical Research Information Technology group. He is developing a clinical trials data management system for the BASH, Omegaven and several other projects.

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### **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 FY07 Mr. Rezuke developed several advanced reporting procedures for the CRP's web-based budget tracking software application.

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**Roumen Stoyanov, BS, *Senior Applications Developer***

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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.

**CLINICAL RESEARCH EDUCATION CORE**

CLINICAL RESEARCH EDUCATION CORE STAFF L TO R:  
JENIFER R. LIGHTDALE, MAYA LEVINE.

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**Jenifer R. Lightdale, MD, MPH, *Director***

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Dr. Lightdale is an attending physician in the Division of Gastroenterology and Nutrition at Children's Hospital Boston. She completed fellowship training in outcomes research first at the Institute for Health Policy Studies at the University of California, and later in the Harvard Fellowship in Pediatric Health Services Research. Dr. Lightdale received her Master's degree from the Harvard School of Public Health. She has been on clinical staff at Children's as a gastroenterologist in the Department of Medicine since finishing her gastroenterology fellowship here in 2001. Dr. Lightdale's research has focused on improving patient safety for children receiving procedural sedation and analgesia. To date, she has been supported in her work by a Mentored Career Development Award from the Agency for Healthcare Research and Quality (K08-HS013675), a Risk Management Foundation Patient Safety Award, and the Cook Endoscopy Award from the American Society of Gastrointestinal Endoscopy.



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**Maya Levine, BA, Education Coordinator**

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Ms. Levine joined the CRP in January 2007 as the Education Coordinator. Ms. Levine provides administrative support to all faculty and students involved in courses directed and organized by the CRP. She provides the infrastructure by which to best coordinate and successfully implement a growing clinical research education curriculum at Children's.

**ADMINISTRATION**

ADMINISTRATION STAFF L TO R: LAURA HALEY, RANDI TRIANT.

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**Randi Triant, MFA, Administrative Director**

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Ms. Triant joined the CRP in January of 2006 as Administrative Director. She has over twenty-five 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.

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**Laura Haley, Program Administrative Coordinator**

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Ms. Haley joined the CRP in July 2003; she provides direct administrative support to the Program 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.

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

## **SUMMARY**

During FY07, the CRP worked on 316 clinical research projects (Table 1). The majority of these projects (n=246) did not provide funding for CRP staff. Seventy (22%) of these projects funded the CRP staff for a total of \$1,149,722.

**Table 1. FY07 CRP projects by funding status**

	Funding Status		Total
	No CRP funds received in FY07	Any CRP funds received in FY07	
No. of Projects	246	70	316
<b>Total CRP FY07 costs</b>	<b>0</b>	<b>\$1,149,722</b>	<b>\$1,149,722</b>

*\*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 70 projects during FY07 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 70 projects funding CPR in FY07**

Service areas	No. of Projects requiring funded services*	FY07 CRP Funding (% of total dollars)
PI	10	\$160,701 (14%)
Biostatistics	57	\$597,435 (52%)
Clinical Study Management	15	\$127,150 (11%)
Database Programming	11	\$178,380 (16%)
Data entry	16	\$86,056 (7%)
<b>Total</b>	<b>70</b>	<b>\$1,149,722 (100%)</b>

\*A single project often funds several service areas.

**Figure 1. CRP Direct Costs by Service Area**

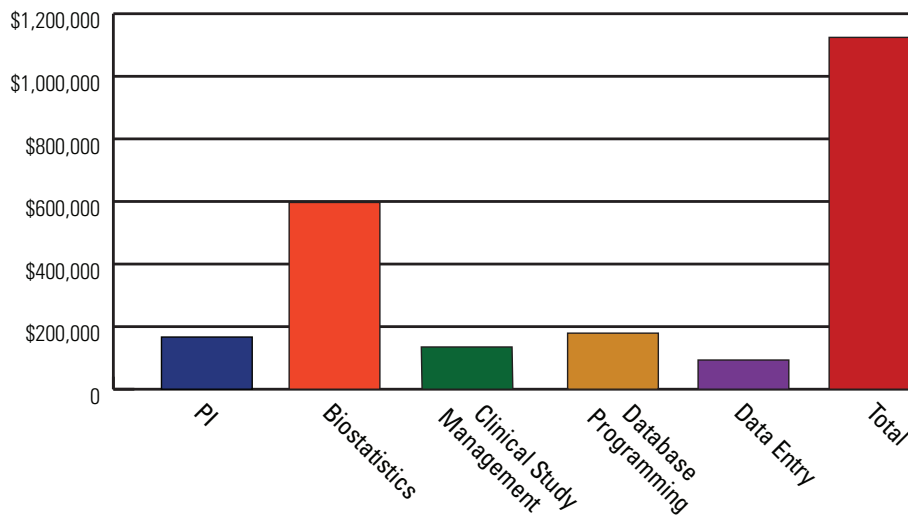
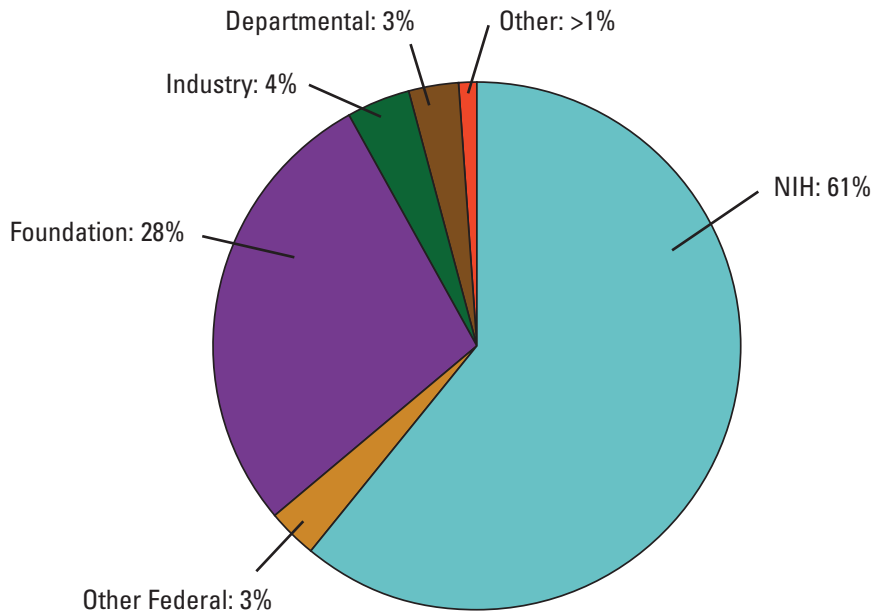


Figure 2 presents the distribution of funding sources for the 70 projects providing financial support to the CRP. NIH and Foundations were the primary sources of funding for these projects (41% and 24% of funded projects, respectively). Among the 29 NIH funded projects, 13 were funded by R01 mechanisms, 3 were R03, 3 were K23, and 10 were other funding mechanisms (K23, R37, M01, P50, etc.).

More than half (n=43) of the 70 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=3), Surgery (n=2), Otolaryngology (n=3), Neurology (n=1), Psychiatry (n=1), Anesthesia (n=3), and Urology (n=3). The Clinical Research Program faculty were PI's on five of the 70 projects. The rank of the PI for the funded projects was also variable: Professor (11%), Associate Professor (31%), Assistant Professor (28%), Fellow (2%), Instructor (20%), and Other (8%).

**Figure 2. Funding Sources for 70 Projects Funding CPR in FY07**

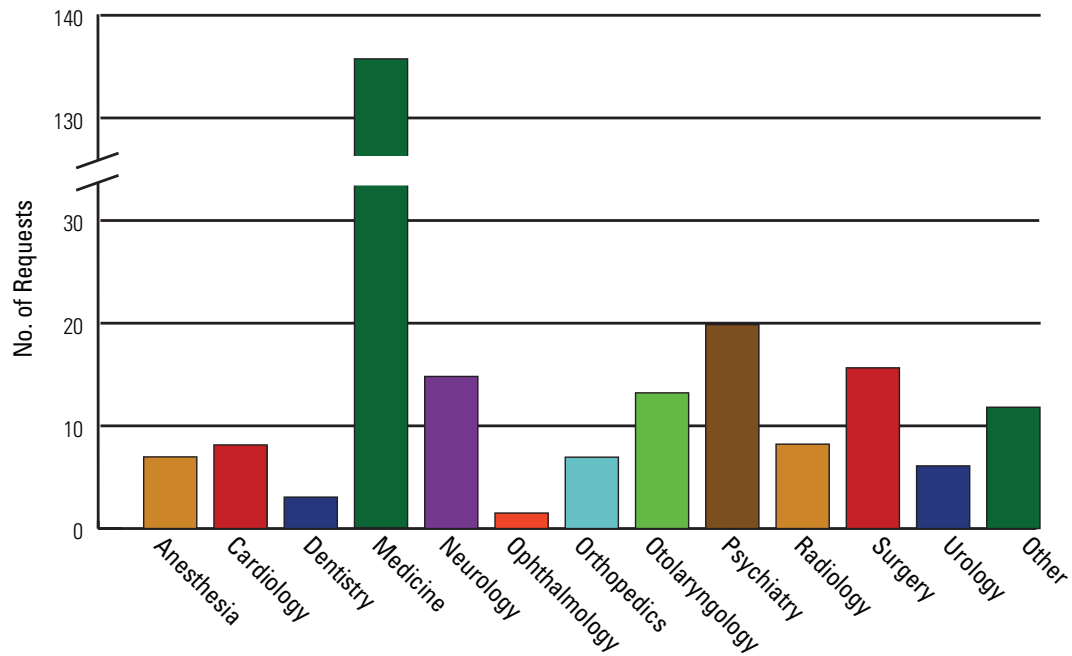


	No. of Projects	FY07 CRP Funding (% of total dollars)	
NIH	29	\$703,287	(61%)
Other Federal	6	\$37,737	(3%)
Foundation	17	\$326,729	(28%)
Industry	4	\$47,830	(4%)
Departmental	9	\$28,418	(3%)
Other	5	\$5,723	(>1%)
<b>Total</b>	<b>70</b>	<b>\$1,149,722</b>	<b>(100%)</b>

**NEW REQUESTS FOR ASSISTANCE IN FY07**

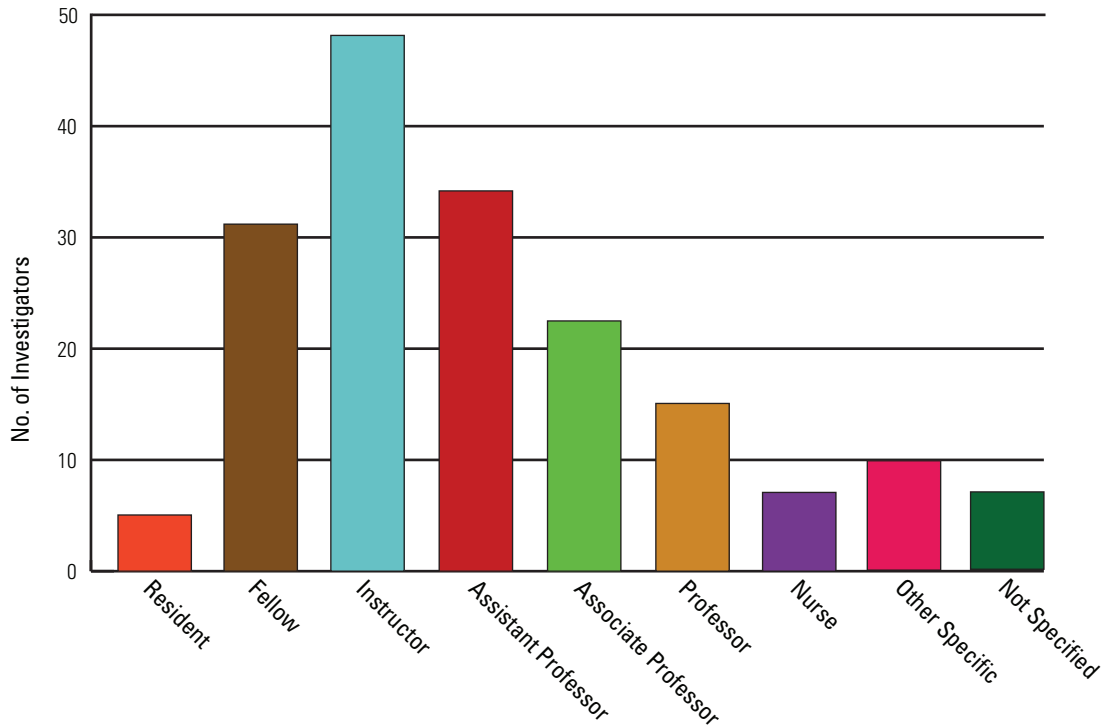
During FY07, the CRP received 253 new requests for assistance from 179 Children’s Hospital faculty or staff. The distribution of requests according to hospital department is shown in Figure 3. The majority of requests were from investigators with appointments in Medicine (n=135) and within the Divisions of Emergency Medicine (n=22), Endocrinology (n=14), Adolescent Medicine (n=12), Hematology/Oncology (n=12), GI/Nutrition (n=29), General Pediatrics (n=5), Infectious Diseases (n=7), Newborn (n=4), and Pulmonary (n=1).

**Figure 3. FY07 CRP Requests for Assistance (N=253 Requests)**



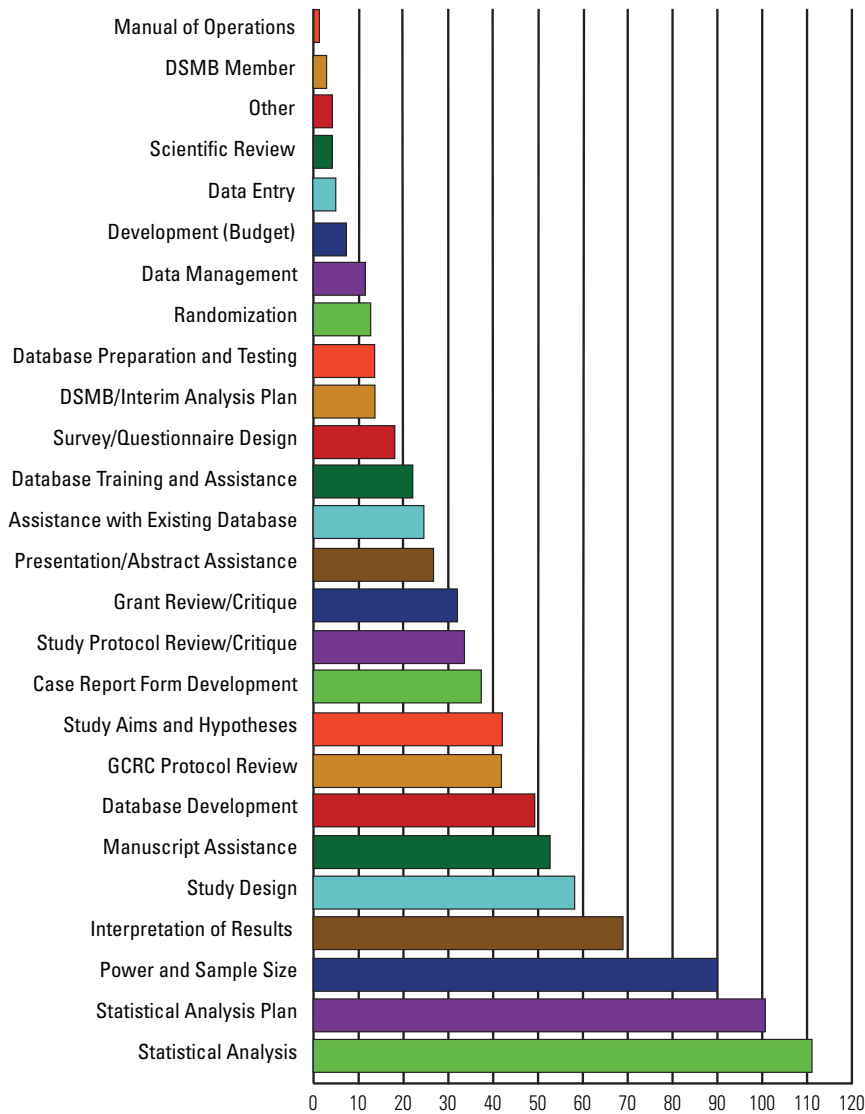
As shown in Figure 4, investigators requesting assistance were somewhat more likely to be at the rank of Instructor (n=48), Assistant Professor (n=34), Associate Professor (n=22) or Fellow (n=31), as compared to Professor (n=15) or Resident (n=5).

**Figure 4. Rank of Investigators Requesting CRP Assistance (N=179 Investigators)**



As shown in Figure 5, the majority of requests were for consultation on design and analysis including estimation of sample size and power (n=90), development of a statistical analysis plan (n=101), study design (n=57), or analyses of data (n=111). Approximately 65 requests were related to study implementation, including case report form or survey design and/or database assistance.

**Figure 5. Services Requested (N=253 Requests)**



Nearly a quarter (n=60) of the 253 new requests for CRP resources had funding to support the project and another third (n=76) were applying for funding. Among the 60 funded projects, NIH (n=12), foundations (n=17) and department funds (n=13) were the primary funding sources. Among those investigators submitting grant proposals for funding, the majority (n=54) were first submissions, whereas the remainder were mainly resubmissions (n=15).

Among the 76 new requests applying for funding, 26 were applying to NIH, 26 to foundations, 4 to other federal, 2 to department funds, 4 to Internal Award, 6 to industry, and 2 to other, and 6 to mechanisms not specified for funding. For the 26 applying to NIH, the mechanisms for funding were 9 for R01s, 1 for an R03, 6 for R21s, 6 for K23s, 2 for other mechanisms, and 2 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, (Statistical) Power and How to Get It, and Do-It-Yourself Data Management, 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. Two new lectures were added to the course in September 2007: "Authorship and Data Fraud" presented by Sadath Sayeed, JD, MD and "Industry and Philanthropy" given by Samuel Nurko, MD, MPH. 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. 2007 Participant Information

- N = 108
- 63% Fellows
- 14% Research Coordinators and Assistants
- 9% Faculty
- 8% Other
- 3% Investigator RNs
- 3% Social Workers

## 3. Overall Evaluation

The following table summarizes participants' overall evaluation of the Introduction to Clinical Research sessions that were offered in 2007.

Overall Course Evaluation*	
Level of the presentation was appropriate	3.4
Sufficient time for questions	3.6
Contact with faculty	3.5
The slides were clear	3.5
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. 2007 Participant Information

- N = 73
- 100% Research Coordinators and Study Assistants

## 3. Overall Evaluation

The following table summarizes participants' overall evaluation for the 2007 Orientation for New Study Coordinators sessions.

	Orientation Objectives Met*
Satisfaction with the Orientation overall	3.4
Orientation met expectations	3.4
Orientation provided information that can be useful in clinical research role	3.6
Would recommend Orientation to others	3.6

\*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. Topics and speakers for the 2007 Coordinator Rounds are listed below:

Date	Topic	Speaker(s)
2/7	The IRB Website	Anne Dyson and Matt Stafford
4/4	Preparing a Study Manual of Operations	Susan McDermott
6/6	Study Documentation: Common Mistakes and How to Prevent Them	Eunice Newbert
8/1	Subject Recruitment and Retention in Clinical Research	Tracy Antonelli, Rosanna Batista, and Ellen McGrath
10/3	Research Billing	Alan Abend
12/5	Genetic Research	Carrie Gill, Elicia Estrella, and Heather Peters

## 2. 2007 Participant Information

- N = 120
- 100% Research Coordinators and Study Assistants

## **D. INTRODUCTION TO BIOSTATISTICS**

### **1. Description**

Introduced in 2006, this eight-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. 2007 Participant Information**

- N = 79
- 45% Research Coordinators and Assistants
- 40% Fellows
- 7% Investigator RNs
- 7% Other
- 2% Faculty

### **3. Overall Evaluation**

- 94% of participants agreed that the lectures were useful.
- 90% 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. Paul Mitchell, MS led the lab section of the course.

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 & 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.

### **2. 2007 Participant Information**

- N = 30
- 43% Fellows
- 27% Research Coordinators and Assistants
- 19% Faculty
- 5% Investigator RNs
- 5% Other

### **3. Overall Evaluation**

- 100% of participants rated the lecture as "good" or "excellent"

## **F. DO-IT-YOURSELF (DIY) DATA MANAGEMENT**

### **1. Description**

Through a series of three 2½ hour workshops, the course gives participants a hands-on opportunity to work on their study's Case Report Forms, timelines, and Manual of Operations, as well as other important components of study data management. DIY Data Management was developed by Tracy Antonelli in conjunction with the Project and Data Management Team and introduced in 2007. Topics include:

- Good Clinical Practice
- Creating Timelines
- Key Elements of Study Organization
- Developing Case Report Forms
- CRP Case Report Form Standards
- Storage of forms and study data
- Developing a Manual of Operations
- CRP MOO Standard Content

The course is designed for faculty, fellows, and others who are planning on conducting clinical studies, but who have limited experience in clinical research data management. Participants should be in the process of submitting or receiving approval for a new study.

### **2. 2007 Participant Information**

- N = 5
- 100% Fellows

### **3. Overall Evaluation**

100% of participants agreed that the content of the course lectures and workshops was/will be useful in their research.

	Overall Course Evaluation*
Level of the material was appropriate.	4.3
The range of topics was appropriate.	4.3
The content of the course lectures was/will be useful in your research.	4.3
The content of the course workshops was/will be useful in your research.	4.3
The presentations were clear.	4.3
I would recommend this course to others.	4.3

\*Score Range: 1 (Strongly Disagree) to 5 (Strongly Agree)

# Clinical Research Program Spotlights

## **A. COLLABORATIONS WITH CHB INVESTIGATORS**

### **1. Omegaven™ treatment for parenteral nutrition-associated liver disease**

Although parenteral nutrition can be essential for patients following gastrointestinal surgery, the fat emulsions contained in conventional parenteral solutions may cause liver dysfunction, leading to liver failure and death. CRP has joined with Dr. Mark Puder of the Surgery Department and Dr. Kathleen Gura, Team Leader of the Central Pharmacy, in studies examining the potential of replacing conventional fat with Omegaven™, a lipid solution made from fish oil, to treat parenteral nutrition-associated liver disease (PNALD). Under a compassionate-treatment protocol, eighteen children were treated with Omegaven™. Sixteen reversed their cholestasis (as indicated by three consecutive bilirubin levels over 2 mg/dL) within a median time of approximately 65 days, while two died from causes unrelated to PNALD. These results were striking in comparison to historical control data, in which 7 out of 23 children receiving conventional fat emulsions died and only 9 reversed their PNALD with a median time of 333 days. These findings will appear in *Pediatrics* in 2008. To obtain more rigorous evidence of the efficacy of Omegaven™ in the reversal of PNALD, the investigators are examining 32 more Omegaven™ patients and 60 contemporary historical controls with funding from the March of Dimes. A randomized clinical trial was launched in 2007, aiming to assess whether Omegaven™ can, in addition to treating cholestasis, also prevent the liver disease. Participants for CRP include Senior Biostatistician Dr. Clarissa Valim, Project and Data Management Core Leader Susan McDermott, and Project Director Maggie McCarthy. Also collaborating on the clinical trial are Dr. Christopher Duggan, Gastroenterology/Nutrition Division and Medical Director of the Clinical Nutrition Service, and Dr. Tom Jaksic, Department of Surgery.

### **2. Infections in the ICU reduced by a quality-improvement intervention**

Central line-associated bloodstream infection (CLAB) is the most common type of healthcare-associated infection occurring in multidisciplinary pediatric intensive care units. CLABs are associated with increased attributable morbidity and mortality and result in a significant financial burden to the healthcare system. In 2007 Dr. Dionne Graham collaborated on a study to determine whether a quality-improvement intervention could decrease the CLAB rate in the cardiac intensive care unit (CICU). The intervention was conducted at CHB between 2004 and 2006 and involved staff education, increased awareness, and practice change. Collaborating investigators were Drs. John Costello and Peter Laussen of the Department of Cardiology and Dr. Tom Sandora of the Division of Infectious Diseases, Hospital Epidemiologist and Medical Director of Infection Control. Dr. Graham's analysis, using an interrupted time series method, showed that the CLAB rate in the CICU decreased significantly, from 7.8 infections per 1000 catheter-days during the pre-intervention period (April – December 2004) to 2.3 infections per 1000 catheter-days during the period following full implementation of the quality-improvement initiative (April – December 2006). A report of this work, scheduled to appear in *Pediatrics* in 2008, will be the first public report of CLAB rates from a large, dedicated pediatric cardiac ICU. The group is currently collaborating on a matched case-control study to identify patient risk factors for the development of CLABs in the CICU.

### **3. A phase II trial of the oral farnesyltransferase inhibitor (FTI) lonafarnib for patients with Hutchinson-Gilford Progeria Syndrome**

Study Chair Mark Kieran, MD, PhD from Dana-Farber Cancer Institute has joined with CHB Study Co-Chairs Monica Kleinman, MD (CHB Division of Critical Care Medicine), Leslie B. Gordon, MD, PhD (CHB Division of Critical Care Medicine and Brown University Department of Pediatrics), and David Miller, MD, PhD (Genetics), in a study of children with Hutchinson-Gilford Progeria Syndrome (Progeria or HGPS), a genetic disorder which predisposes children to premature aging. Other CHB investigators contributing to the study are Robert Cleveland, MD, (Radiology), Nicole Ullrich, MD, PhD (Neurology), Catherine M. Gordon, MD, MSc (Endocrinology), Leslie B. Smoot, MD (Cardiology), Marilyn Liang, MD (Dermatology) and Andrew Sonis, MD (Dentistry). Affecting 1 in 4 million newborns, Progeria results in premature death at an average age of thirteen (range 7-20 years). While the chance of predisposition is low, Progeria has significant consequences running the gamut from the purely external of aged-looking skin, to painful joint stiffness, to the more significant morbidity factors, stroke and heart disease. Progeria is caused by a mutation in the gene called *LMNA*. The *LMNA* gene produces the Lamin A protein, the glue for holding the nucleus of a cell together. Researchers now believe that the defective Lamin A protein (called progerin) makes the nucleus unstable. That cellular instability, in turn, plays a major role in with the disease process in Progeria. In order for progerin to be created, a farnesyl group molecule must attach itself to Lamin A protein. The Phase II clinical trial began in the spring of FY07 and involves the use of a farnesyltransferase inhibitor or FTI, a drug that was used previously as a cancer treatment. It is hypothesized that the FTI lonafarnib will block the attachment of the farnesyl group molecule to Lamin A protein, thereby slowing down, or perhaps even reversing, the progression of the disease.

Staff of the Clinical Research Program (CRP) are assisting study investigators with project and data management support and research database development. Specifically, Team Leader, Susan McDermott and Data Managers Aruna Jayashankar and Rajna Filip-Dhima worked closely in FY07 with Study Coordinator William Fletcher and investigators to develop the study case report forms and related database specifications. CRP Data Managers and software Engineers from the Clinical Research Information Technology (CRIT) team are also working on the design and development of the clinical research database using the CRP's newest clinical research database technology, InForm™ by Phase Forward.

### **B. GLASER PEDIATRIC RESEARCH NETWORK**

Since September, 2002 the CRP has served as Design, Analysis, and Coordinating Center for the Glaser Pediatric Research Network (GPRN), a consortium of pediatric research centers based at Stanford University Medical Center with additional clinical sites at Children's Hospital Boston, Baylor College of Medicine, UCLA, and UCSF. The network was launched in 2000 with the mission of conducting collaborative research on serious pediatric illnesses, drawing from the diverse patient populations and deep pool of investigators available at the five institutions. An important adjunct mission is to bring young investigators into clinical research careers through a sponsored Fellowship.

As of fall 2007, CRP held active contracts with GPRN for two clinical trials, one registry project, and a Core for coordination and training. More than a dozen CRP staff took part in a full variety of clinical research tasks, including statistical planning, development of case report forms, database programming, randomization, data management, preparation of data and safety monitoring reports, data analysis, and presentation and authorship of final results.

The **registry of necrotizing enterocolitis (NEC)**, with Dr. Leslie Kalish as Principal Investigator of the coordinating center, completed enrollment of 500 infants and commenced a new phase, in which biological samples will be collected as well as clinical information. A manuscript on risk factors for progression of NEC, from medically managed condition to severe disease requiring surgery or resulting in death, was submitted for publication. A substudy of short-bowel syndrome was presented at Digestive Disease Week, the national joint meeting of American gastroenterology societies.

The **trial of metformin for treatment of obesity in adolescents**, with Dr. Stavroula Osganian as coordinating-center PI, completed data collection in 2007. The primary findings were presented at the national meeting of the American Diabetes Association, and a number of baseline and follow-up manuscripts are in progress.

The past year saw the completion of the multi-site **Phase I/II trial of rituximab** in children with chronic immune thrombocytopenic purpura, for which GPRN provided 5 of 10 sites. Dr. Feldman served as PI for the coordinating center. Primary results were published in *Blood*, and one-year follow-up findings were submitted for publication. Work continues on an ancillary study of quality of life in these patients.

The **Design, Analysis, and Coordinating Core** provides GPRN with expertise in the development and conduct of clinical research. Dr. Henry Feldman, Core PI, participated in regular GPRN management teleconferences and organized a monthly Work-in-Progress seminar for the GPRN Fellows. The Core supported statistical analysis for studies predating the CRP contract, including a trial of alendronate for steroid-associated osteoporosis presented at the 2007 national meeting of the American College of Rheumatology.

### **C. 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 Rezuze, 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-seven written reviews were completed during Fiscal Year 2007. 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 Rezuze leads the CRP informatics support, which includes helping the GCRC manage the scientific review process for newly proposed studies and study amendments, tracking laboratory specimens, administrative management support, and database development for research projects. Much of this support is implemented through a software application developed by Mr. Rezuze called CREMA (Clinical Research Executive Management Application). During the past year CREMA was extended by completion of the Budget and Staff Management Program and introduction of the Specimen Sample Tracking module, which allows for tracking of samples that are processed but not tested within the core lab. Other capabilities introduced or enhanced during the past year include the ability to import test results directly from the “Nano Drop” testing machine, the ability to look up and import sample locations, and expanding access for viewing core lab results (with permission from the study’s principal investigator). In addition to these enhancements to CREMA, continued development and maintenance of the Protocol Review Process System, which had been introduced the previous year, has further streamlined the administration of the scientific review process.



# 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

**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.

**5R01AI068119-02 (Crosby/CHB subcontract: Shrier)** **06/15/06-05/31/11**  
**NIH/NIAID** **\$96,456**  
*Do Condoms Protect from Non-viral Sexually Transmitted Infections?*

The major goal of this study is to determine the protective value of condoms against the acquisition of three common sexually transmitted infections: Chlamydia, gonorrhea, and trichomoniasis.

**R21 HD056009 (du Plessis)** **09/09/07-09/08/09**  
**NIH/NICHHD** **\$125,000**  
*Continuous Monitoring for Cerebral Pressure-Passivity in Premature Infants*

The overall aim of this study is to characterize the systemic and cerebral hemodynamic antecedents of germinal matrix-intraventricular hemorrhage (GM-IVH), the principal form of hemorrhagic injury in the preterm. In specific aim 1 we will examine the relationship between time-locked cerebral and systemic hemodynamic changes in infants, using frequency-domain coherence and transfer function analysis, to identify periods of pressure-passivity. In specific aim 2 we will seek to define the features of systemic BP that predispose to a pressure-passive cerebral circulation. In Specific Aim 3 we will aim to identify the baroreceptor dysfunction that leads to unstable patterns of systemic BP. Insights gained and techniques developed during the proposed research will facilitate the development of a much-needed cerebrovascular monitoring device, and ultimately to rational brain-oriented management of the critically-ill infant.

**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)**  
**NIH/NIDDK**

**01/15/06-12/31/07**  
**\$54,742**

***Weight Cycling and Mortality in Women***

This project assesses the relationship between weight cycling and mortality among 77021 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)**  
**NIH/NIMH**

**05/01/04-02/28/09**  
**\$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)**  
**NIH/NICHD**

**06/01/06-08/31/10**  
**\$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 5U01DK067767 (Jonas)**  
**NIH/NIDDK**  
***PEDS-C Trial***

**09/01/05-08/31/08**  
**\$20,690**

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 DA018848 (Knight)**  
**NIH/NIDA**

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

***Screening and Brief Advice to Reduce Teen Substance Abuse***

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

**R01 DA014553 (Knight)**  
**NIH/NIDA**

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

***A Medical Office Intervention for Adolescent Drug Use***

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

**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 DK063554-03 (Ludwig)** 03/01/06-12/31/10  
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)** 09/15/05-07/31/09  
NIH/NIDDK \$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).

**R03 DK073335 (Ludwig)** 10/01/06-6/30/08  
NIH/NIDDK \$100,000

***Glycemic Load and Infant Birth Weight in Pregnant, Glucose Intolerant Women***

A randomized trial testing whether a low-glycemic load diet during the third trimester of pregnancy will reduce the risk of high birth weight in offspring of women who are glucose-intolerant.

**M01 RR02172 (Mandell)** 04/01/04-03/31/09  
NIH/NCRR \$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.

**1R21DK077678-01 (Nurko)** 04/01/07-03/31/09  
NIH/NIDDK \$150,000

***Placebo Controlled Study of Baclofen for GERD in Children with Cerebral Palsy***

The aims of this study are: (1) to gain preliminary evidence of the efficacy of baclofen to treat symptoms of GERD, in comparison to a placebo, in children with CP; (2) to assess the efficacy of baclofen vs. placebo in reducing the number of reflux events; (3) to assess the efficacy of baclofen vs. placebo in reducing the total number of transient lower esophageal sphincter relaxations (TLESRs), and reflux secondary to TLESRs; and (4) to assess the safety and tolerability of baclofen administered over a two week period to treat children with CP and intractable GERD.

**R01 CA114556 (Pbert/CHB subcontract: Osganian)** 03/08/06-02/28/10  
NIH/NCI \$33,953

***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 HS014947 (Porter)**  
**DHHS/AHRQ**

**10/01/04-03/31/07**  
**\$233,613**

***ParentLink: Better and Safer Emergency Care for Children***

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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)**  
**NIH/NLM**

**09/01/06-08/31/09**  
**\$380,142**

***Health Literacy and Information Management in ADHD: Designing an Optimal Record***

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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.

**1R21 MH072533-01A1 (Shrier)**  
**NIH/NIMH**

**04/01/05-03/31/08**  
**\$200,094**

***Mood and HIV Risk in Depressed Adolescents***

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

**2 U01 AI45955 (Taylor/CHB subcontract: Wypij)**  
**NIH/NIAID**

**10/01/05-04/30/10**  
**\$27,869**

***Redefining Cerebral Malaria: Can Eye Findings Improve the Diagnosis***

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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.

**5 R01 GM074068-03 (Warfield)**  
**NIH/NLM**

**02/01/06-01/31/09**  
**\$221,534**

***Bioinformatics Tools for Multi-Center Diagnostic Trials***

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This proposal aims to develop a novel and general statistical validation methodological framework based on accuracy, reliability, and reproducibility metrics to evaluate the diagnostic performance of imaging findings, against a statistically best-available gold standard.

## **B. NIH CAREER DEVELOPMENT GRANTS**

**K08 HS013675 (Lightdale)**  
**DHHS/AHRQ**

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

***Improving Safety of Pediatric Sedation***

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This is a Mentored Clinical Scientist Development Award, the 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.

**5K12 HL087164-03 (Neufeld)** **10/01/06-06/30/11**  
**NIH/NHLBI** **\$368,899**  
***Clinical Hematology Research Career Development Program***

The purpose is to develop and evaluate a multidisciplinary career development program in non-malignant hematology that will equip new investigators with the knowledge and skills to address complex problems in blood diseases. The program provides training to encourage promising young physician scientists to choose non-malignant hematology as a career path, broaden the didactic experience within hematology for graduates of the program, provide structured training in clinical research methods, and evaluate the outcomes of the training program.

**K01 DP000089 (Rhodes)** **10/01/04-09/30/08**  
**DHHS/CDC** **\$194,570**  
***Health Values and Treatment of Pediatric Type 2 Diabetes***

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

### **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)** **12/01/02-04/30/08**  
**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.

**(Moss/CHB subcontract: Jaksic/DACC: Kalish)** **12/01/02-11/30/08**  
**Glaser Pediatric Research Network** **\$97,123**  
***Necrotizing Enterocolitis (NEC) Surgical Database***

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

## D. FOUNDATION/ASSOCIATION/OTHER

(Peterson/ CHB Subcontract: Austin)

07/01/05-10/31/08

**International Nutrition Foundation**

\$21,115

*Massachusetts Healthy Choices Evaluation*

---

This study provides 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.

(Bennett)

07/07/04-12/31/07

**St. Giles Foundation**

\$125,000

*Genetic Modifiers of Childhood Chronic Immune Thrombocytopenic Purpura (ITP)*

---

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

(Ericson)

07/01/06-06/30/08

**Cystic Fibrosis Foundation**

\$100,000

*A Six Month Open Label Study of Amiloride Solution for Inhalation and Tobramycin Solution for Inhalation for the Eradication of Burkholderia dolosa in Patients with Cystic Fibrosis*

---

The primary goal of this clinical trial is to determine the ability of multiple doses of amiloride solution for inhalation (ASI) and tobramycin solution for inhalation (TSI) to eradicate *Burkholderia dolosa* respiratory tract infection in patients with cystic fibrosis.

(Grand)

01/01/03-06/30/07

**Crohn's & Colitis Foundation of America**

\$99,456

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

---

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

(Harris)

1/1/06-12/31/06

**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.

(Levy)  
**Dana Foundation** 01/01/07-12/31/09  
\$100,000  
*Endotoxin-related Innate Immunity in Patients Undergoing Hematopoietic Stem Cell Transplantation*

A pilot clinical trial of rBPI21 administered to patients undergoing myeloablative allogeneic hematopoietic stem cell transplantation (HSCT). HSCT is often complicated by acute graft versus host disease (aGVHD) which is triggered by penetration of endotoxin from the intestines into the bloodstream. The protein rBPI21 is an endotoxin-neutralizing agent. This study will investigate the presence of endotoxin and how rBPI21 might alter the body's inflammatory response to it.

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.

(Puder) 04/01/07-12/31/09  
**March of Dimes Foundation** \$81,137  
*Efficacy of Omega-3 Enriched Fat Emulsion and Prevention of Parenteral Nutrition Induced Liver Injury in Infants*

The goals of this project are to: 1.) Determine whether the parenteral administration of an omega-3 fatty acid based fat emulsion reduces the proportion of cholestasis in infants. 2.) Describe biochemical tests of liver function profiles over time in the two treatment groups. 3.) Assess the safety and tolerability of an omega-3 fatty acid based fat emulsion (Omegaven™) as opposed to a conventional fat emulsion (Intralipid®).

(Richmond) 01/01/07-12/31/08  
**Charles H. Hood Foundation Child Health Research Grant** \$75,000  
*Do School Physical Activity Programs Contribute to Racial/Ethnic Disparities in Adolescent Physical Activity and Obesity?*

The goal of this project is to determine whether school programs, specifically physical education classes and/or interscholastic sports, contribute to racial/ethnic disparities in adolescent physical activity and/or obesity.

## **E. INDUSTRY**

(Nelson) 01/01/07-12/21/07  
**Delta Dental** \$139,109  
*Oral Health Needs Assessment of Children with Special Health Care Needs in Massachusetts*

HRSA national studies have found that dental care was the service most commonly reported needed, but not received for children with special health care needs. A convenience sample dental survey was used to further characterize these children's access to dental care, dental needs, and barriers to care in Massachusetts.



# Staff Accomplishments and External Contributions

## **HENRY FELDMAN, SCD**

### **National Committees**

- Data and Safety Monitoring Board: Head-off Environmental Asthma in Louisiana (HEAL) Study. Tulane University and New Orleans Department of Health, New Orleans, La.; National Institute of Environmental Health Sciences, Research Triangle Park, N.C.
- 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. 29-Aug. 10, 2007.

### **Honors**

- A. Clifford Barger Award for Excellence in Mentoring, Harvard Medical School, 2007.

## **SION HARRIS, PHD**

### **Honors**

- Best Abstract Award presentation at the Association for Medical Education and Research in Substance Abuse Annual Conference: Knight JR, Harris SK, Sherritt L, Van Hook S, Lawrence N, Brooks T, Carey P, Kossack R, Kulig J, and the New England Partnership for Substance Abuse Research. Prevalence of positive substance abuse screens among adolescent primary care patients. November 2006.

## **ALKA INDURKHYA, PHD**

### **External Teaching**

- Course developer and Instructor; Biostatistical Methods using SAS; sponsored by University of Massachusetts Medical School, Summer 2007.
- Speaker and Moderator; Workshop for Junior Investigators in Mental Health Services Research, sponsored by the National Institute of Mental Health, Washington DC, Summer 2007.

### **National Committees**

- Co-Chair, National Institute of Mental Health, Mental Health Services Research Biennial Meeting, July 2007.
- Member, Program Committee, Society for Prevention Research, 2005-2007.
- Member, Services Research in Non-speciality settings, National Institute of Mental Health, Bethesda, MD, 2005-present.
- Member, Psychosocial Development and Risk Prevention Panel, Center for Scientific Review, Washington, DC, 2007-present.

## **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 Disease, 2004–present.

## **JENIFER R. LIGHTDALE, MD, MPH**

### **External Teaching**

- Case Discussion Leader, HMS II, GI Pathophysiology, Harvard Medical School; Spring 2007
- Small Group Leader; sponsored by Harvard School of Public Health, Clinical Effectiveness Program; Summer 2007

### **External Presentations**

- Session Moderator. Clinical Research Forum. NASPGHAN Annual Conference. Orlando, FL. October, 2006.
- Invited Faculty. NASPGHAN 3rd Year Fellows Conference, Scottsdale, AZ. March 22-25, 2007.

### **National Committees**

- Education and Quality Improvement Program (EQuIP) in Gastroesophageal Reflux Disease, American Academy of Pediatrics
- Chair, Endoscopy and Procedures Committee, North American Society of Pediatric Gastroenterology, Hepatology and Nutrition
- Vice-Chair, Pediatrics Committee, American Society of Gastrointestinal Endoscopy

### **Honors**

- Research Excellence in GI and Liver (REGAL) Award, Chicago, IL, 2006
- Cook Endoscopy Award, American Society of Gastrointestinal Endoscopy, Oak Brook, IL, 2007

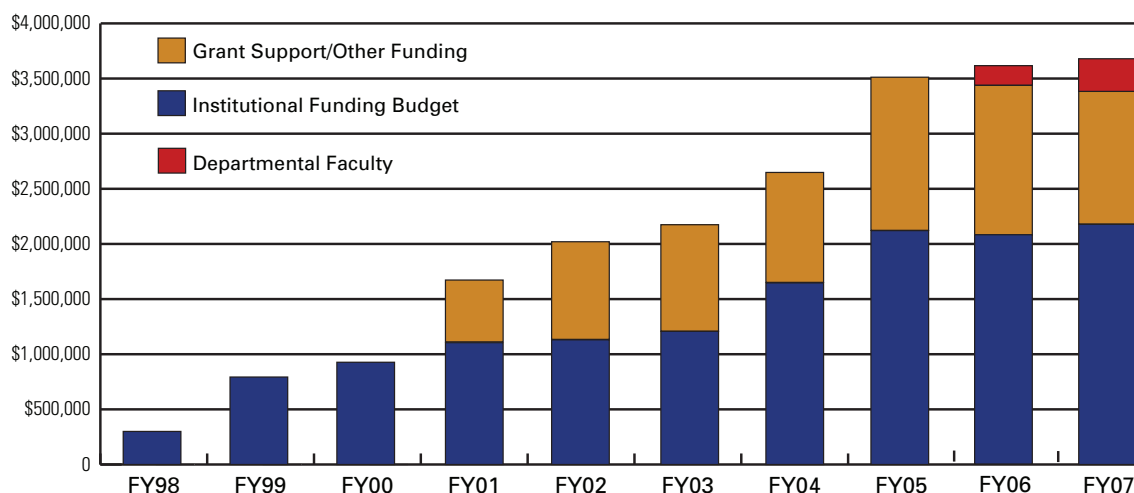
# Program Resources

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 4th Floor of 333 Longwood Avenue with fourteen offices, eighteen cubicles, and one conference room.

Institutional and other sources of support for the Program are shown in Table 1. Institutional support for the Clinical Research Program (CRP) has increased substantially since the inception of the Program and now totals \$2.1 million. Equally exciting has been the rapid growth in funding from department support for faculty (\$348,205) and collaborative relationships with clinical investigators and CRP extramural funding, which now totals over \$1.1 million.

**Table 1. CRP Funding for the period FY98 to FY07**

FISCAL YEAR	INSTITUTIONAL BUDGET	GRANT SUPPORT/ OTHER FUNDING	DEPARTMENTAL FACULTY	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	\$168,425	\$3,614,230	+3%
FY07	\$2,147,412	\$1,149,722	\$348,205	\$3,645,339	+1%



# Appendices



## APPENDIX A

# Program Description and Application

### **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 [Staff Biographies]**

#### ***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. 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 for Assistance form and submit by interoffice mail or e-mail: [crp@childrens.harvard.edu](mailto: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](mailto:crp@childrens.harvard.edu).
- Visit our website at <http://web2.childrens.harvard.edu/clinresearch/core/index.html>



# Children's Hospital Boston

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

CRP USE ONLY

A. Form Received: \_\_\_/\_\_\_/\_\_\_ Entered:

B. Intro. Meeting: \_\_\_/\_\_\_/\_\_\_ Staff: \_\_\_\_\_

## Investigator Request for Assistance

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

1. Principal Investigator:

Last Name: \_\_\_\_\_ First Name: \_\_\_\_\_ CH ID#: \_\_\_\_\_

2. Title:  Prof.  Assoc. Prof.  Asst. Prof.  Instructor  Fellow  Resident  Nurse

Other (specify): \_\_\_\_\_

3. Department: \_\_\_\_\_ Division: \_\_\_\_\_

4. Phone/Ext #: \_\_\_\_\_ Email: \_\_\_\_\_

5. Research Mentor (if applicable): \_\_\_\_\_

6. Requestor:  Check if same as name of PI

Last Name: \_\_\_\_\_ First Name: \_\_\_\_\_ CH ID#: \_\_\_\_\_

7. Title:  Prof.  Assoc. Prof.  Asst. Prof.  Instructor  Fellow  Resident  Nurse

Other (specify): \_\_\_\_\_

8. Phone/Ext #: \_\_\_\_\_ Email: \_\_\_\_\_

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

\_\_\_\_\_  
\_\_\_\_\_

10. 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)**

\_\_\_\_\_  
\_\_\_\_\_

11. What is the deadline for completion of work for this request? (MM/DD/YYYY): \_\_\_\_ / \_\_\_\_ / \_\_\_\_

12. Funding Status

- a. Is your project currently funded?  Yes  No  
b. Are you presently applying for funding?  Yes  No; Skip to Q. 14  
c. If Yes, what type of application is it?  New Submission  Resubmission

13. 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): \_\_\_\_\_

14. Will this protocol utilize the GCRC or its resources?  Yes  No

15. 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

### 2007 Staff Publications

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): 205-209.

Austin SB, Kim J, Wiecha J, Troped PJ, **Feldman HA**, Peterson KE (2007). "School-based overweight preventive intervention lowers incidence of disordered weight-control behaviors in early adolescent girls." *Arch Pediatr Adolesc Med* 161(9): 865-869.

Banerjee S, Bishop W, **Valim C**, Mahoney LB, **Lightdale JR** (2007). "Percutaneous liver biopsy practice patterns among pediatric gastroenterologists in North America." *J Pediatr Gastroenterol Nutr* 45(1): 84-89.

Bassan H, Limperopoulos C, Visconti K, Mayer DL, **Feldman HA**, Avery L, Benson CB, Stewart J, Ringer SA, Soul JS, Volpe JJ, du Plessis AJ (2007). "Neurodevelopmental outcome in survivors of periventricular hemorrhagic infarction." *Pediatrics* 120(4): 785-792.

Bechard LJ, Guinan EC, **Feldman HA**, Tang V, **Duggan C** (2007). "Prognostic factors in the resumption of oral dietary intake after allogeneic hematopoietic stem cell transplantation (HSCT) in children." *JPEN J Parenter Enteral Nutr* 31(4): 295-301.

Berry JG, Lieu TA, **Forbes PW**, Goldmann DA (2007). "Hospital volumes for common pediatric specialty operations." *Arch Pediatr Adolesc Med* 161(1): 38-43.

Blake DR, Lemay CA, **Indurkha A** (2007). "Correlates of readiness to receive Chlamydia screening among 2 populations of youths." *Arch Pediatr Adolesc Med* 161(11): 1088-1094.

Bourgeois FT, Porter SC, **Valim C**, Jackson T, Cook EF, Mandl KD (2007). "The Value of Patient Self-report for Disease Surveillance." *J Am Med Inform Assoc* 14(6): 765-771.

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.

DiVasta AD, Beck TJ, Petit MA, **Feldman HA**, LeBoff MS, Gordon CM (2007). "Bone cross-sectional geometry in adolescents and young women with anorexia nervosa: a hip structural analysis study." *Osteoporos Int* 18(6): 797-804.

DiVasta AD, Ringelheim J, Bristol SK, **Feldman HA**, Gordon CM (2007). "Skeletal measurements by quantitative ultrasound in adolescents and young women with anorexia nervosa." *J Pediatr* 150(3): 286-290, 290 e281.

**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.

Ebbeling CB, Garcia-Lago E, Leidig MM, Seger-Shippe LG, **Feldman HA**, Ludwig DS (2007). "Altering portion sizes and eating rate to attenuate gorging during a fast food meal: effects on energy intake." *Pediatrics* 119(5): 869-875.

Ebbeling CB, Leidig MM, **Feldman HA**, Lovesky MM, Ludwig DS (2007). "Effects of a low-glycemic load vs. low-fat diet in obese young adults: a randomized trial." *JAMA* 297(19): 2092-2102.

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.

Fleischman A, Ringelheim J, **Feldman HA**, Gordon CM (2007). "Bone mineral status in children with congenital adrenal hyperplasia." *J Pediatr Endocrinol Metab* 20(2): 227-235.

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.

Haagensen AL, **Feldman HA**, Ringelheim J, Gordon CM (2007). "Low prevalence of vitamin D deficiency among adolescents with anorexia nervosa." *Osteoporos Int*.

Hanson E, **Kalish LA**, Bunce E, Curtis C, McDaniel S, Ware J, Petry J (2007). "Use of complementary and alternative medicine among children diagnosed with autism spectrum disorder." *J Autism Dev Disord* 37(4): 628-636.

**Indurkha A**, Mitra N, Schrag D (2006). "Using propensity scores to estimate the cost-effectiveness of medical therapies." *Stat Med* 25(9): 1561-1576.

**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.

Kazan-Tannus JF, Dialani V, Kataoka ML, Chiang G, **Feldman HA**, Brown JS, Levine D (2007). "MR volumetry of brain and CSF in fetuses referred for ventriculomegaly." *AJR Am J Roentgenol* 189(1): 145-151.

LeBovidge 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.

Levy H, **Kalish LA**, Huntington I, Weller N, Gerard C, Silverman EK, Celedon JC, Pier GB, Weiss ST (2007). "Inflammatory markers of lung disease in adult patients with cystic fibrosis." *Pediatr Pulmonol* 42(3): 256-262.

**Lightdale JR**, Gershman G, Ament M, Ed: Practical Pediatric Endoscopy (Invited Book Review). *Gastroenterology*, 2007; 133: 1740.

**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.

**Lightdale JR**, Mahoney LB, Schwarz SM, Liacouras CA (2007). "Methods of sedation in pediatric endoscopy: a survey of NASPGHAN members." *J Pediatr Gastroenterol Nutr* 45(4): 500-502.

Limperopoulos C, Bassan H, **Kalish LA**, Ringer SA, Eichenwald EC, Walter G, Moore M, Vanasse M, DiSalvo DN, Soul JS, Volpe JJ, du Plessis AJ (2007). "Current definitions of hypotension do not predict abnormal cranial ultrasound findings in preterm infants." *Pediatrics* 120(5): 966-977.

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.

Mahoney LB, **Lightdale JR** (2007). "Sedation of the Pediatric and Adolescent Patient for GI Procedures." *Curr Treat Options Gastroenterol* 10(5): 412-421.

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.

Mrakotsky C, Masek B, Biederman J, Raches D, Hsin O, **Forbes P**, de Moor C, DeMaso DR, Gonzalez-Heydrich J (2007). "Prospective open-label pilot trial of mirtazapine in children and adolescents with social phobia." *J Anxiety Disord*.

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APPENDIX C  
**Course Agendas**

**INTRODUCTION TO CLINICAL RESEARCH AGENDA**

*March 19 – 21, 2007*

MONDAY, MARCH 19, 2007

***Design and Manuscripts***

- 1:00 – 1:15      ***Introduction and Overview***  
Jenifer Lightdale, MD, MPH
- 1:15 – 2:15      ***Observational Study Designs***  
Stavroula Osganian, MD, ScD
- 2:15 – 2:30      BREAK
- 2:30 – 3:30      ***Good Measures and Good Tests***  
Clarissa Valim, MD, ScD
- 3:30 – 3:35      BREAK
- 3:35 – 4:20      ***Designing Surveys and Questionnaires***  
Erinn Rhodes, MD, MPH
- 4:20 – 4:30      BREAK
- 4:30 – 5:30      ***Writing for Scientific Publication***  
S. Jean Emans, MD

TUESDAY, MARCH 20, 2007

***Grants and Analysis***

- 1:00 – 1:45      ***Grant Writing 101***  
Jenifer Lightdale, MD, MPH
- 1:45 – 2:00      ***Overview of Research Administration: Organization and Resources***  
Richard Fleck, MBA
- 2:00 – 2:15      BREAK
- 2:15 – 2:45      ***The NIH Scientific Review***  
Richard Grand, MD
- 2:45 – 3:15      ***The General Clinical Research Center***  
Kristine Jordan  
Richard Grand, MD
- 3:15 – 3:30      BREAK
- 3:30 – 4:30      ***Statistics in Clinical Research: An Overview***  
Henry Feldman, PhD

WEDNESDAY, MARCH 21, 2007

***Institutional Approval and Study Implementation***

- 1:00 – 2:15      ***Human Subjects, Institutional Review Board and HIPPA***  
Susan Kornetsky, MPH
- 2:15 – 2:45      ***Informed Consent***  
Kristin Bowling, MS
- 2:45 – 3:00      BREAK
- 3:00 – 3:30      ***Operational Issues in Conducting Clinical Research***  
Christopher Duggan, MD, MPH
- 3:30 – 4:15      ***Collecting and Managing Clinical Research Data***  
Susan McDermott, MPH, RN, CS
- 4:15 – 4:30      BREAK
- 4:30 – 5:15      ***Description and Inference***  
Henry Feldman, PhD

THURSDAY, MARCH 22, 2007

***Analysis and Presentation***

- 1:00 – 1:45      ***Clinical Trials: Design and Monitoring***  
Ellis Neufeld, MD, PhD
- 1:45 – 2:15      ***Comparing Two Groups***  
Henry Feldman, PhD
- 2:15 – 2:30      BREAK
- 2:30 – 3:15      ***Scientific Presentations***  
Michael Rich, MD, MPH
- 3:15 – 3:30      BREAK
- 3:30 – 4:30      ***Introduction to Regression***  
Henry Feldman, PhD
- 4:30 – 4:45      ***The CRP Course Wrap-Up***  
Jenifer Lightdale, MD, MPH

## INTRODUCTION TO CLINICAL RESEARCH AGENDA

September 17 – 21, 2007

MONDAY, SEPTEMBER 17, 2007

### ***Design and Analysis***

- 8:15 – 8:30      ***Introduction and Overview***  
Jenifer Lightdale, MD, MPH
- 8:30 – 9:30      ***Observational Study Designs***  
Stavroula Osganian, MD, ScD, MPH
- 9:30 – 9:45      BREAK
- 9:45 – 10:45    ***Good Measures and Good Tests***  
Clarissa Valim, MD, ScD
- 10:45 – 11:00    BREAK
- 11:00 – 11:45    ***Designing Surveys and Questionnaires***  
Erinn Rhodes, MD, MPH
- 11:45 – 12:45    ***Statistics in Clinical Research: An Overview***  
Henry Feldman, PhD

TUESDAY, SEPTEMBER 18, 2007

### ***Grants and Manuscripts***

- 8:15 – 9:00      ***Grant Writing 101***  
Jenifer Lightdale, MD, MPH
- 9:00 – 9:15      ***Overview of Research Administration: Organization and Resources***  
Richard Fleck, MBA
- 9:15 – 9:45      ***The NIH Scientific Review***  
Richard Grand, MD
- 9:45 – 10:00     BREAK
- 10:00 – 10:30    ***The General Clinical Research Center***  
Kristine Jordan
- 10:30 – 11:30    ***Writing for Scientific Publication***  
S. Jean Emans, MD
- 11:30 – 11:45    BREAK
- 11:45 – 12:15    ***Industry and Philanthropy***  
Samuel Nurko, MD, MPH

THURSDAY, SEPTEMBER 20, 2007

***Study Implementation and Investigator Responsibilities***

- 8:15 – 9:30      ***Introduction to Statistics***  
Dionne Graham, PhD
- 9:30 – 9:45      BREAK
- 9:45 – 10:15    ***Informed Consent***  
Eunice Yim Newbert, MPH
- 10:15 – 10:45   ***Collecting and Managing Clinical Research Data, Part I***  
Susan M. McDermott, MPH, RN, CS
- 10:45 – 11:00    BREAK
- 11:00 – 11:30   ***Collecting and Managing Clinical Research Data, Part II***  
Susan M. McDermott, MPH, RN, CS
- 11:30 – 12:15   ***Data Fraud and Authorship***  
Sadath Sayeed, MD, JD

FRIDAY, SEPTEMBER 21, 2007

***Institutional Approval, Design and Presentation***

- 8:15 – 9:30      ***Human Subjects, Institutional Review Board and HIPAA***  
Susan Kornetsky, MPH, CIP
- 9:30 – 9:45      BREAK
- 9:45 – 10:30    ***Scientific Presentations***  
Jonathan Finkelstein, MD, MPH
- 10:30 – 11:15   ***Clinical Trials: Design and Monitoring***  
Ellis Neufeld, MD, PhD
- 11:15 – 11:30    BREAK
- 11:30 – 12:30   ***Introduction to Regression***  
Henry Feldman, PhD
- 12:30 – 12:45   ***The CRP Course Wrap-Up***  
Jenifer Lightdale, MD, MPH



## Orientation for New Study Coordinators Schedule 2007

3/9/07, 5/18/07, 6/15/07, 7/11/07, 8/22/07, 10/19/07 & 12/14/07

8:15 - 8:30	CONTINENTAL BREAKFAST
8:30 - 8:45	<b>Welcome and Overview</b>
8:45 - 9:05	<b>Overview of Responsibilities of Study Coordinators</b> Study Coordinator's Central Role in Clinical Research
9:05 - 9:30	<b>Human Subject Protections IRB Issues: Before the Research Begins</b> <ul style="list-style-type: none"><li>• Introduction/Why are we here?</li><li>• Training Requirements</li><li>• Protocol Submissions</li></ul>
9:30 - 10:15	<b>IRB Issues: During the Research</b> <ul style="list-style-type: none"><li>• Continuing Renewals</li><li>• 3 Year Re-writes</li><li>• Amendments/Revisions</li><li>• Adverse Events</li><li>• Violations/Deviations</li></ul>
10:15 - 10:30	BREAK
10:30 - 11:30	<b>Informed Consent/Assent and Subject Recruitment</b> <ul style="list-style-type: none"><li>• Writing Informed Consent/Assent</li><li>• Research Subject Recruitment</li><li>• Communication/Shared Responsibility</li></ul>
11:30 - 12:15	<b>Obtaining Informed Consent/Assent: A Practical Approach</b>
12:15 - 12:45	CATERED LUNCH
12:45 - 1:30	<b>Resources for Conducting Clinical Research</b> <ul style="list-style-type: none"><li>• Introduction to the Clinical Trials Office</li><li>• Introduction to Clinical Office of Sponsored Programs</li><li>• Funded Research</li><li>• Patient Care Costs</li><li>• Introduction to the Clinical Research Program (CRP)</li><li>• Introduction to the General Clinical Research Center (GCRC)</li><li>• Introduction to the Education and Quality Improvement Program (EQuIP)</li><li>• Good Clinical Practices for Clinical Research Professionals</li></ul>
1:30 - 2:30	<b>Study Implementation and Data Management</b> <ul style="list-style-type: none"><li>• Study Start-up</li><li>• Manual of Operations, CRF Completion, and Quality Control</li><li>• Source Documentation</li><li>• Study Close-out and Document Retention</li></ul>
2:30 - 2:40	BREAK
2:40 - 2:55	<b>Methods of Organizing Study Documents</b> <ul style="list-style-type: none"><li>• Storage of Study Documents and Informed Consent Documents</li></ul>
2:55 - 3:30	<b>Study Documentation: Common Errors</b>
3:30 - 3:45	<b>Wrap-up, Review, Evaluations</b>

## 2007 COORDINATOR ROUNDS

*Wednesdays, 10:00am -11:00am*

<b>Date</b>	<b>Topic</b>	<b>Speaker(s)</b>
2/7	The IRB Website	Anne Dyson and Matt Stafford
4/4	Preparing a Study Manual of Operations	Susan McDermott
6/6	Study Documentation: Common Mistakes and How to Prevent Them	Eunice Newbert
8/1	Subject Recruitment and Retention in Clinical Research	Tracy Antonelli, Rosanna Batista, and Ellen McGrath
10/3	Research Billing	Alan Abend
12/5	Genetic Research	Carrie Gill, Elicia Estrella, and Heather Peters

## Introduction to Biostatistics with SPSS Lecture Agenda

*January/February 2007*

- January 9      **LECTURE 1: *Summary Statistics and Graphical Methods***
- Data Types
  - Graphical Display: Bar Charts, Histograms, Boxplots
  - Summary Statistics: Measures of Central Tendency, Measures of Spread
- January 16      **LECTURE 2: *Estimating the Mean***
- Normal Distribution
  - Principles of Estimation
  - Estimating the Mean
  - Confidence Intervals for the Mean
- January 23      **LECTURE 3: *Hypothesis Testing and Comparing Two Means***
- Inference Overview
  - Introduction to Hypothesis Testing
  - Comparing Two Means: Paired t-test, Two sample t-test
  - Interpreting p-values
- January 30      **LECTURE 4: *Comparing k-Means, Non-Parametric Tests, Correlation***
- Comparing Three or More Means: ANOVA
  - Nonparametric Tests: Wilcoxon rank sum; Kruskal Wallis
  - Correlation
- February 6      **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
- February 13      **LECTURE 6: *Odds Ratios and Diagnostic Tests***
- Odds Ratios
  - Sensitivity and Specificity of Diagnostic Tests
- February 20      **LECTURE 7: *Putting It All Together***
- Picking the right test
  - Interpreting the literature

## SPSS Computer Lab Schedule

*January/February 2007*

January 12	<b>LAB 1: <i>Introduction to the SPSS Interface</i></b> <ul style="list-style-type: none"><li>• Opening an existing SPSS database</li><li>• Graphical data analysis</li><li>• Descriptive statistics</li><li>• Subsetting data sets</li></ul>
January 19	<b>LAB 2: <i>Data set basics</i></b> <ul style="list-style-type: none"><li>• Confidence intervals for the mean</li><li>• Introduction to SPSS syntax</li><li>• Descriptive analysis by group</li><li>• Subsetting data sets</li><li>• Creating a new data set from “scratch”</li></ul>
January 26	<b>LAB 3: <i>Tests and by-group analysis</i></b> <ul style="list-style-type: none"><li>• Two sample t-test</li><li>• Paired t-test</li><li>• More SPSS syntax</li></ul>
February 2	<b>LAB 4: <i>More dataset basics and tests</i></b> <ul style="list-style-type: none"><li>• ANOVA</li><li>• Wilcoxon and KW tests</li><li>• Variable creation and recoding</li><li>• Correlation</li><li>• Variable creation and recoding with menus and with syntax</li></ul>
February 9	<b>LAB 5: <i>Tests for proportions</i></b> <ul style="list-style-type: none"><li>• One sample test for proportions</li><li>• Crosstabs</li><li>• Chi squared test</li><li>• Fisher's exact test</li><li>• Reading data from other data formats</li></ul>
February 16	<b>LAB 6: <i>Odds ratios and diagnostic tests</i></b> <ul style="list-style-type: none"><li>• Odds ratios</li><li>• Sensitivity and specificity</li><li>• Understanding and using date variables</li><li>• Exporting SPSS output to Word or PowerPoint</li></ul>
February 23	<b>LAB 7: <i>Additional SPSS features you need</i></b> <ul style="list-style-type: none"><li>• Tutorials</li><li>• Case studies</li><li>• Syntax Reference</li><li>• Lab wrap-up and discussion</li></ul>

## Introduction to Biostatistics with SPSS Lecture Agenda

September – November 2007

- September 25      **LECTURE 1: *Graphical Methods and Summary Statistics***
- Data Types
  - Graphical Display: Bar Charts, Histograms, Boxplots
  - Summary Statistics: Measures of Central Tendency, Measures of Spread
- October 2          **LECTURE 2: *Estimating the Mean and Confidence Intervals***
- Normal Distribution
  - Principles of Estimation
  - Estimating the Mean
  - Confidence Intervals for the Mean
- October 9          **LECTURE 3: *Hypothesis Testing and Comparing Two Means***
- Inference Overview
  - Introduction to Hypothesis Testing
  - Comparing Two Means: Paired t-test, Two sample t-test
  - Interpreting p-values
- October 16        **LECTURE 4: *Comparing Three or More Means***
- Analysis of Variance (ANOVA)
- October 23        **LECTURE 5: *Non-Parametric Tests, Correlation***
- Nonparametric Tests: Wilcoxon rank sum; Kruskal Wallis
  - Correlation
- October 29        **LECTURE 6: *Estimating and Testing Proportions***
- Estimating a Proportion
  - Confidence Intervals for Proportions
  - Comparing Two or More Proportions: Chi-squared test, Fisher's exact test
- November 6        **LECTURE 7: *Comparing Two Proportions: Measures of Effect***
- Risk difference
  - Risk ratio
  - Odds ratio
- November 13      **LECTURE 8: *Putting It All Together***
- Picking the right test
  - Interpreting the literature

## SPSS Computer Lab Schedule

*September – November 2007*

September 27	<b>LAB 1: <i>Introduction to the SPSS Interface</i></b> <ul style="list-style-type: none"><li>• Opening an existing SPSS database</li><li>• Graphical data analysis</li><li>• Descriptive statistics</li><li>• Creating a new data set from “scratch”</li></ul>
October 4	<b>LAB 2: <i>Data set basics</i></b> <ul style="list-style-type: none"><li>• Descriptive analysis by group</li><li>• Subsetting data sets</li><li>• Confidence intervals for the mean</li><li>• Introduction to SPSS syntax</li></ul>
October 11	<b>LAB 3: <i>Tests and by-group analysis</i></b> <ul style="list-style-type: none"><li>• Two sample t-test</li><li>• Paired t-test</li><li>• More SPSS syntax</li><li>• Variable creation and recoding with menus and with syntax</li></ul>
October 18	<b>LAB 4: <i>Comparing 3 means</i></b> <ul style="list-style-type: none"><li>• ANOVA</li><li>• Variance components</li></ul>
October 25	<b>LAB 5: <i>More tests</i></b> <ul style="list-style-type: none"><li>• Wilcoxon and KW tests</li><li>• Correlation</li><li>• More graphs</li></ul>
November 1	<b>LAB 6: <i>Tests for proportions</i></b> <ul style="list-style-type: none"><li>• One sample test for proportions</li><li>• Crosstabs</li><li>• Chi squared test</li><li>• Fisher’s exact test</li><li>• Reading data from other data formats</li></ul>
November 8	<b>LAB 7: <i>Comparing proportions</i></b> <ul style="list-style-type: none"><li>• Odds ratios</li><li>• Understanding and using date variables</li><li>• Exporting SPSS output to Word or PowerPoint</li></ul>
November 15	<b>LAB 8: <i>Additional SPSS features you need</i></b> <ul style="list-style-type: none"><li>• Tutorials</li><li>• Case studies</li><li>• Syntax Reference</li><li>• Questions and discussion</li></ul>

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

HENRY FELDMAN, PHD

PAUL MITCHELL, MS

***Lectures, November 30, 2007 and December 6, 2007  
3:00pm – 5:00pm***

***Lab, December 1, 2007  
9:30am – 12pm***

### 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 and 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

## Do-It-Yourself Data Management Course Agenda

May 2007

### SESSION 1

- 10:00 – 10:20 **Welcome and Introductions**
- 10:20 – 10:25 **Course Overview**
- 10:25 – 11:15 LECTURE 1: **Developing a Manual of Operations**
- 11:15 – 11:45 LECTURE 2: **EQUIP (Education and Quality Improvement Program)**
- 11:45 – 12:00 **Workshop: Variable List Descriptions and Assignment**
- 12:00 – 12:30 **Lunch**

### SESSION 2

- 9:00 – 9:30 **Workshop: Variable List Review**
- 9:30 – 10:15 LECTURE 3: **Developing Case Report Forms**
- LECTURE 4: **CRP Case Report Form Standards**
- 10:15 – 10:30 LECTURE 5: **Timelines**
- 10:30 – 10:45 **Review of Timeline Handout**
- 10:45 - TBD **Breakout for one-on-one discussions as needed**

### SESSION 3

- 9:00 – 9:20 LECTURE 6: **Good Clinical Practice (GCP)**
- 9:20 – 9:40 **Workshop: Timeline Review**
- 9:40 – 10:40 **Workshop: CRF Review**
- 10:40 – 11:30 **Closing: Intakes and Evaluations**