



Children's Hospital Boston

Annual Report

of the

Clinical Research Program

FY 2003

Annual Report
of the
Clinical Research Program
FY2003

I.	Executive Summary	1
II.	Background of the Program	2
III.	Mission and Overview of Goals and Accomplishments	3
IV.	Program Organization	6
V.	Utilization of Services	16
VI.	Education and Training Courses	19
VII.	New Programs – Glaser Pediatric Research Network	22
VIII.	Collaborative Projects	24
IX.	Program Resources	33

Appendices

- A. Program Description and Request for Assistance Form
- B. Staff Publication
- C. Course Agendas

I. Executive Summary

The Clinical Research Program (CRP) at Children's Hospital, Boston is a cross-departmental program that provides methodologic support and expertise to investigators on the design, conduct, and analysis of clinical research studies and serves as an infrastructure for the data management of extramurally sponsored studies. The CRP provides such support through consultation or collaboration with investigators and educational activities targeting the clinical research community including residents, fellows, faculty, and study coordinators.

Since its inception in 1998, the Program has experienced significant growth in staff and resources and increased visibility among the clinical research community. The CRP staff has grown to 25 FTE's with staff from various disciplines, including epidemiologists, biostatisticians, application developers, research associates, data coordinators, and budget specialists. The Program occupies nearly 4000 square feet of space. Key accomplishments over the past year include:

- Successful negotiations with the Glaser Pediatric Research Network to serve as the Design, Analysis, and Coordinating Center
- Improvements in the project management process
- Development of standard operating procedures
- Development of FDA compliant databases
- Expanded and enhanced educational activities for faculty and study coordinators

II. Background of the Program

The Clinical Research Program (CRP) was established in July 1998 to support the research community of Children's Hospital in designing and implementing clinical research projects so that they may compete more successfully for funding and achieve continued excellence in conducting the highest quality clinical research. The Program was first known as the Clinical Research Core Program Office, or CRCPO, and was established as one of the interdisciplinary programs reporting to the Vice President of Research for the hospital. Financial support was provided by the hospital, with the understanding that, as time went on, further funding from various sources would be obtained and that the Program would successfully compete for grants and increase the overall clinical research funding of the hospital.

To accomplish the goals of the Program, a nationwide search for a director was launched, and the first Director, Patricia Hibberd, M.D., Ph.D., was recruited into the Department of Medicine. She, in turn, hired key staff, including David Wypij, Ph.D., Director of the Biostatistics, and began operations in close physical and administrative proximity to the Committee on Clinical Investigation. Dr. Hibberd was successful in building the Program, setting goals for operation, and putting together educational and operational programs that formed the framework for the present-day Clinical Research Program.

In the fall of 2001, Dr. Hibberd and several Program staff left Children's Hospital, and Dr. Kenneth McIntosh, former Chief of the Division of Infectious Diseases, was appointed Interim Director of the Program. Dr. Stavroula Osganian, whose recruitment had begun under Dr. Hibberd, was hired as the Associate Director shortly thereafter. The search for a permanent director of the CRP, which began as soon as Dr. Hibberd announced her departure, concluded in August 2003 without the recruitment of an external candidate. Dr. Stavroula Osganian succeeded Dr. McIntosh as Acting Director of the CRP on September 1, 2003.

III. Mission and Overview of Goals and Accomplishments

During the two-year term of Dr. McIntosh, the mission of the Program was established and the goals were identified at two annual retreats led by the management team of the Clinical Research Program (CRP).

A. 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 support, education, and collaborative assistance in the design, conduct, and analysis of clinical research.

B. Overview of Goals and Accomplishments

Many of the goals identified by the CRP leadership have been successfully accomplished. Goals in progress will be re-evaluated and prioritized for the next calendar year. This section highlights the accomplishments of the past two years, which are more fully described in the sections that follow. The goals for the 2001-2003 calendar years were as follows:

1. Goal: Complete negotiations to serve as the Design, Analysis, and Coordinating Center for the Glaser Pediatric Research Network (GPRN).

Accomplishment: One of the major events of this past year has been the signing of a contract with the Elizabeth Glaser Pediatric Research Network, which establishes within the CRP a Design and Analysis Coordinating Center for the conduct of clinical research projects carried out by members of the Network. In this role, the CRP has also been funded to develop and implement at least three specific Glaser study protocols during the past year. The GPRN contract has also significantly enhanced the external funding sources of the CRP, contributing nearly \$400,000 to the annual budget.

2. Goal: Improve the CRP project management process.

Accomplishment: A major organizational accomplishment for the Program was the refinement and widespread implementation of the Project Management process. This includes the use of the Request for Assistance Form (see appendix A) for Children's Hospital staff requesting services of the CRP, as well as the process of tracking work on requests from initiation to completion. In addition, the services provided and process of assistance offered during the development of projects were carefully codified and timed so that the expectations of researchers could be more satisfactorily defined and met. Because of the increasing demand for the services of the CRP over the year, this was an essential step in both organizing the effort and making it more efficient and accountable.

3. Goal: Make progress on administrative and research standard operating procedures.

Accomplishment: Administrative and Research Standard Operating Procedures for the group were identified and prioritized. The intent of the procedures was to standardize and ensure the quality of work within the Program as well as serve as educational tools to provide good practices to the larger research community. SOPs for all of the most critical procedures were written by the CRP staff and approved by the Director during the past year. The process will be completed during the coming year.

4. Goal: Hire into open positions.

Accomplishment: Successful growth in staff has enhanced the capabilities and multidisciplinary nature of the Program. This included one full-time senior biostatistician, Leslie Kalish, Sc.D.; a junior statistician, Clarissa Valim, M.D., Sc.D., M.Sc., S.M.; a Team Leader/Applications Developer, Jason Rightmyer, M.S.; a Senior Applications Developer, Roumen Stoyanov, B.S.; a web developer, Alan Tam; a Clinical Research Specialist, Maureen Clark, M.S.; a Data Coordinator, Michael Wake, B.A.; a Research Associate, Samuel McDaniel, M.Phil.; and a Program Administrator, Terrie Rogers, M.B.A.

5. Goal: Develop databases that meet the FDA Guidelines for computerized systems used in clinical trials for projects that must submit data to the FDA. Identify a user-friendly and cost efficient database development software that junior investigators may use more independently and develop a workshop on use of the software.

Accomplishment: With the expansion of the Program, the need emerged to develop both sophisticated data management systems for trials that required submission of data to the FDA and cost efficient, less complex but quality data management systems for smaller projects of junior investigators. The informatics group successfully developed FDA compliant databases that are maintained on the CRP server for integrity and compliance. In addition, the informatics group evaluated options for more efficient but less complex approaches and successfully implemented the use of SPSS data builder on several single-site, smaller projects.

6. Goal: Expand and enhance the educational activities of the CRP including the development of a grant-writing course.

Accomplishment: The educational activities of the CRP increased in both scope and number over the past year. For the first time, in response to popular demand, the 3-day course, Introduction to Clinical Research, was offered twice during the year instead of once. Furthermore, the course content was enhanced with additional topics on human subjects protection and informed consent procedures. In addition, a new course, Coordinating Clinical Research, aimed primarily at Study Coordinators and Research Nurses, was expanded and given twice during the year. In addition, at the request of the Department of Medicine residency program, the CRP designed and taught a two-week block for the Senior Residents in Medicine on the elements of clinical research. The CRP staff also continues to provide seminars for the Office of Faculty Development in the areas of grant writing and funding opportunities for junior faculty. The development of a grant-writing course will be addressed in the next year.

7. Goal: Implement a faculty development program.

Accomplishment: Faculty development and retention was recognized as a key factor that will determine the success of the program. Doctoral level staff in the CRP have successfully attained academic appointments at the Harvard Medical School, worked collaboratively on funded research, and co-authored manuscripts for publication. During the coming year, CRP leadership will focus on ways to facilitate continued professional growth and advancement for Program faculty.

8. Goal: Produce the first Annual Report.

Accomplishment: The first annual CRP Annual Report was successfully completed for FY03.

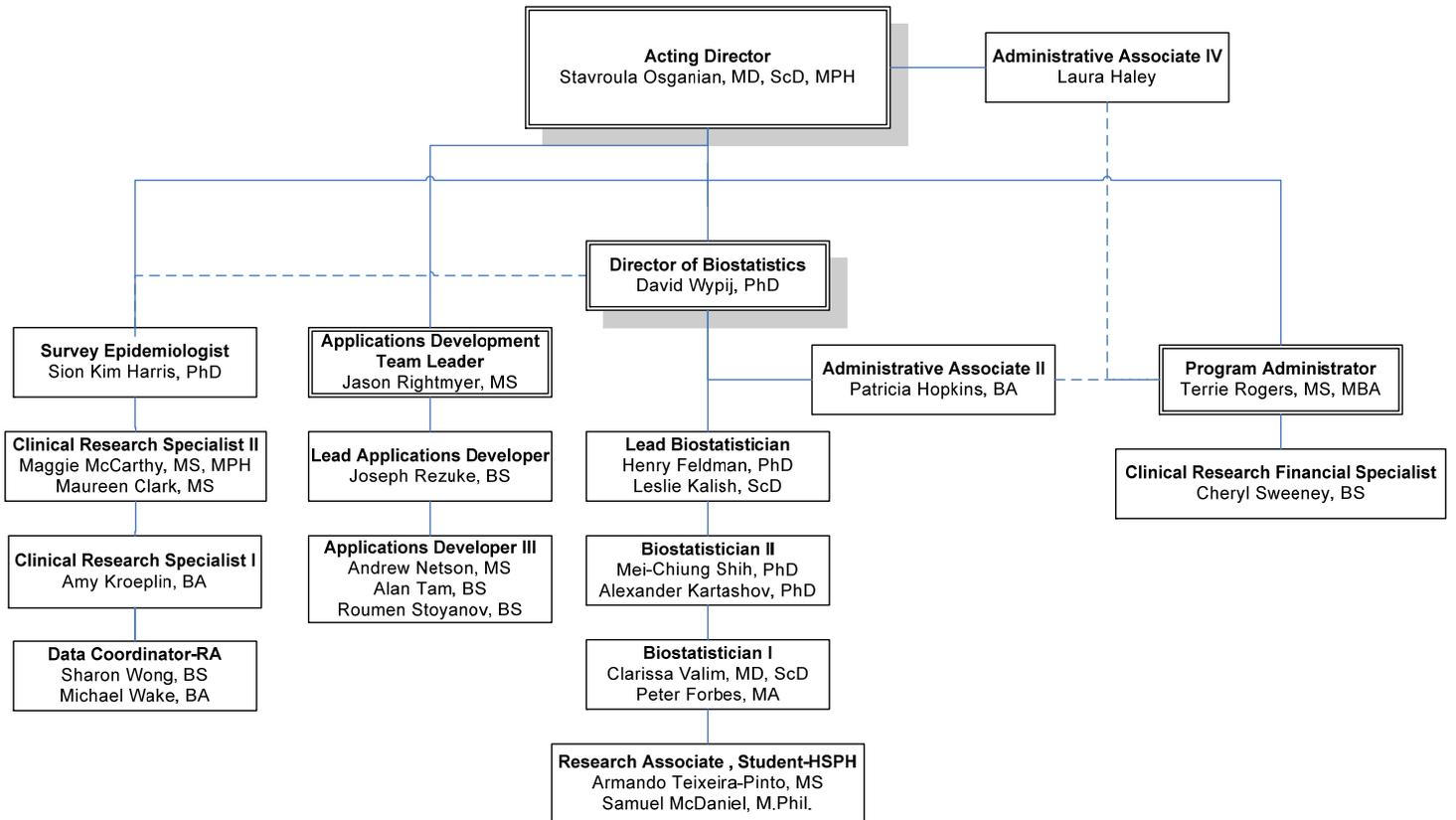
9. Goal: Organize a CRP Advisory Board.

Accomplishment: A Clinical Research Task Force has been organized to assist and advise the CRP. The recommendations from this Task Force will be used to create and implement a strategic plan.

IV. Program Organization

The Program includes 25 full-time staff organized into four major functional groups: Study Operations, Applications Development, Biostatistics, and Administration.

A. Organizational Chart



B. Staff Roles and Biographies

Staff Publications can be found in Appendix B.

DIRECTORS

Kenneth McIntosh, M.D./Director

Dr. Kenneth McIntosh is an internationally known researcher in the fields of pediatric HIV infection and respiratory viral diseases. He has published extensively in many aspects of pediatric infectious diseases, particularly in the pathogenesis and prevention of respiratory infections and in clinical trials and the pathogenesis of childhood AIDS. He served from October 2001 through August 2003 as the Interim Director of the Clinical Research Program (CRP) at Children's Hospital, a position that he held while a national search for a permanent director was under way. He is also Professor of Pediatrics at Harvard Medical School and Professor of Infectious Diseases and Immunology at the Harvard School of Public Health.

Stavroula Osganian, M.D., Sc.D., M.P.H./Associate Director

Dr. Osganian is a physician-epidemiologist with over ten years of experience in the conduct of epidemiologic and clinical research. She joined the CRP as Associate Director in December 2001 and now serves as Acting Director of the Program. She is also Associate Director of the NIH-funded General Clinical Research Center at Children's Hospital and holds an appointment as Assistant Professor of Pediatrics at the Harvard Medical School.

Dr. Osganian's research interests and activities have focused on studies of youth health promotion and chronic disease prevention. She has had a leadership role in one of the largest, nationally recognized NIH-funded school-based studies of cardiovascular health promotion in the United States, the Child and Adolescent Trial for Cardiovascular Health (CATCH). The work of the CATCH collaborative group has led to significant contributions to the design, conduct, and institutionalization of school health promotion programs and the study of cardiovascular risk factors in youth.

BIOSTATISTICS

David Wypij, Ph.D./Director of Biostatistics

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

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

Henry A. Feldman, Ph.D./Lead Biostatistician

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

Dr. Feldman taught biostatistics full-time at Harvard School of Public Health from 1979-89 and, as Principal Research Scientist at New England Research Institutes from 1990-2001, served as lead analyst and Co-PI for the multi-site Child and Adolescent Trial for Cardiovascular Health (CATCH).

Peter Forbes, M.A./Biostatistician

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

Leslie A. Kalish, Sc.D./Lead Biostatistician

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

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

Alex Kartashov, Ph.D./Senior Biostatistician

Dr. Kartashov holds a doctorate in biology. He is currently working on a doctoral thesis in Biostatistics at Boston University. He has experience in the design, conduct, and analysis of observational and interventional studies, including clinical trials, cohort studies, cross-sectional analyses of large national databases, and small-scale controlled physiological studies.

Dr. Kartashov consults with investigators in the design of studies, data analysis and interpretation of study results, and preparation of manuscripts and presentations. For the last two years, he worked with investigators in the Division of Endocrinology on the analysis of a large cohort study (CARDIA). He also serves as a biostatistician with the General Clinical Research Center (GCRC), assisting with protocol review and data analysis.

Samuel McDaniel, M.Phil./Biostatistics Research Assistant

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

Mei-Chiung Shih, Ph.D./Senior Biostatistician

Dr. Shih earned her Ph.D. in Statistics from Stanford University, where she also did her post-doctoral training in the Department of Health Research. Her areas of expertise include statistical genetics, genetic epidemiology, the design and analysis of clinical trials, and pharmacokinetic modeling. She joined the CRP at Children's Hospital in September 2001, and is an Assistant Professor of Biostatistics at Harvard School of Public Health.

Armando Teixeira-Pinto, M.S./Biostatistics Research Assistant

Mr. Teixeira-Pinto is a doctoral student in Biostatistics at Harvard University. He joined the CRP in July 2002. Before joining the CRP, Mr. Teixeira-Pinto worked as an Assistant Lecturer at the Oporto Medical School in Portugal.

Clarissa Valim, M.D., Sc.D., M.Sc., S. M./Biostatistician

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

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

APPLICATIONS DEVELOPMENT

Jason Rightmyer, M.S./Applications Development Team Leader

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

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

Andrew Netson, M.S./Senior Applications Developer

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

Joseph Rezuke, B.S./Lead Applications Developer and GCRC Informatics Manager

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

Roumen Stoyanov, B.S./Senior Applications Developer

Mr. Stoyanov has a Bachelor's degree in Computer Science and is a Microsoft Certified Solutions Developer. Before joining the CRP in July 2003, he worked as a consultant at New England Research Institutes. During his tenure there, he worked on the Telecog system and developed randomization software for clinical research. Telecog was a three-tiered software system that used telephony and speech recognition technology to clinically evaluate the working memory of geriatric patients. Currently, Mr. Stoyanov is developing a clinical trials data management system for the Glaser Pediatric Research Network using open data standards and Microsoft .NET technologies.

Alan Tam, B.S./Applications Developer

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

CLINICAL STUDY OPERATIONS

Sion Kim Harris, Ph.D./Epidemiologist and Survey Design Specialist

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

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

Maggie McCarthy, M.S., M.P.H./Senior Clinical Research Specialist

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

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

Maureen Clark, M.S./Senior Clinical Research Specialist

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

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

Amy Kroeplin, B.A./Clinical Research Specialist

Ms. Kroeplin has three years of experience in implementation and management of clinical research studies including case report form design, survey design, development of study manual of operations and training of research staff in the conduct of the study. She joined the CRP in January 2001 and has been with Children's Hospital Boston since 1998. She has a bachelor's degree in Biology and Anthropology from Boston University and is working towards a Masters of Public Health in Epidemiology and Biostatistics. She is certified in Coordinating Clinical Trials and a member of the Society of Clinical Research Associates (SOCRA) and American Public Health Association (APHA).

Ms. Kroeplin is currently funded on seven NIH, Foundation, and other sponsored studies in the capacity of clinical research specialist or data manager and has worked on more than 30 funded and unfunded research projects in her tenure at Children's Hospital. Ms. Kroeplin also serves as co-director of the "Coordinating Clinical Research" course.

Michael Wake, B.A./Glaser Data Coordinator

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

Most recently, Mr. Wake had been working for three years as a research assistant on a NICHD-funded Autism program project at the University of Washington in Seattle. In addition, while at the University he also coordinated clinical services and referral resources at the University's Autism Spectrum Disorders clinic for over a year until its absorption into the larger UW Autism Center.

Sharon Wong, B.S./Research Study Coordinator

Ms. Wong joined the CRP in September 2001. Her responsibilities include testing CRP-developed databases, coordinating the data for single and multi-center clinical research studies, data entry, training and monitoring data entry clerks, data cleaning, performing quality assurance checks on entered data, and following up on any missing and conflicting data. She also assists the clinical research specialists in the editing of case report forms, and generates reports for studies and CRP courses.

Most recently, Ms. Wong has been programming databases using SPSS Data Builder. Using this program, Ms. Wong creates databases, assists in the building of databases through tutorials and supervision, installs the databases, and trains the data entry clerks

ADMINISTRATION**Terrie Rogers, M.S., M.B.A./Program Administrator**

Ms. Rogers has a M.S. in Immunology and an M.B.A., both from the University of Michigan. She has over twenty years of diversified global management experience in the healthcare, CRO, pharmaceutical, biotechnology, and genomics industries. Ms. Rogers has broad expertise and a proven record of accomplishment in healthcare service sales, marketing, project management, and strategic planning. She joined the CRP in November 2003.

Ms. Rogers' role in the CRP is to oversee the daily operations of the department on matters of billing, budgets, purchasing, and administrative procedures and personnel. In conjunction with the CRP Director, she is also involved in strategic planning for the CRP.

Laura Haley/Senior Administrative Associate

Ms. Haley has worked in the administrative field for over twenty years. She joined the CRP in July 2003. Her duties include direct administrative support to the Director, coordinating the logistics and administration of CRP-sponsored courses, general administrative support to CRP staff, and common Program responsibilities such as requisitioning items and services.

Ms. Haley is the frontline individual for investigators requesting resources from the CRP, often scheduling initial meetings, and following each new project request to ensure that it has been triaged to the appropriate Program staff. Most recently, she has been involved in the implementation of a new database to track all CRP-associated projects and their progress.

Patricia Hopkins, B.A./Administrative Associate

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

Cheryl Sweeney, B.S./Clinical Research Financial Specialist

Ms. Sweeney has a degree in Medical Sociology and came to Children's Hospital in 1986. She has held numerous positions, most recently as the Administrative Manager in the GCRC before joining the CRP in September 2000.

Her role in the CRP is to serve as the institutional resource in the budgeting, billing, and recovery of sponsored clinical research studies. She works closely with investigators, other CRP staff, and ancillary programs to ensure that budgets comply with both sponsors and Children's Hospital policies.

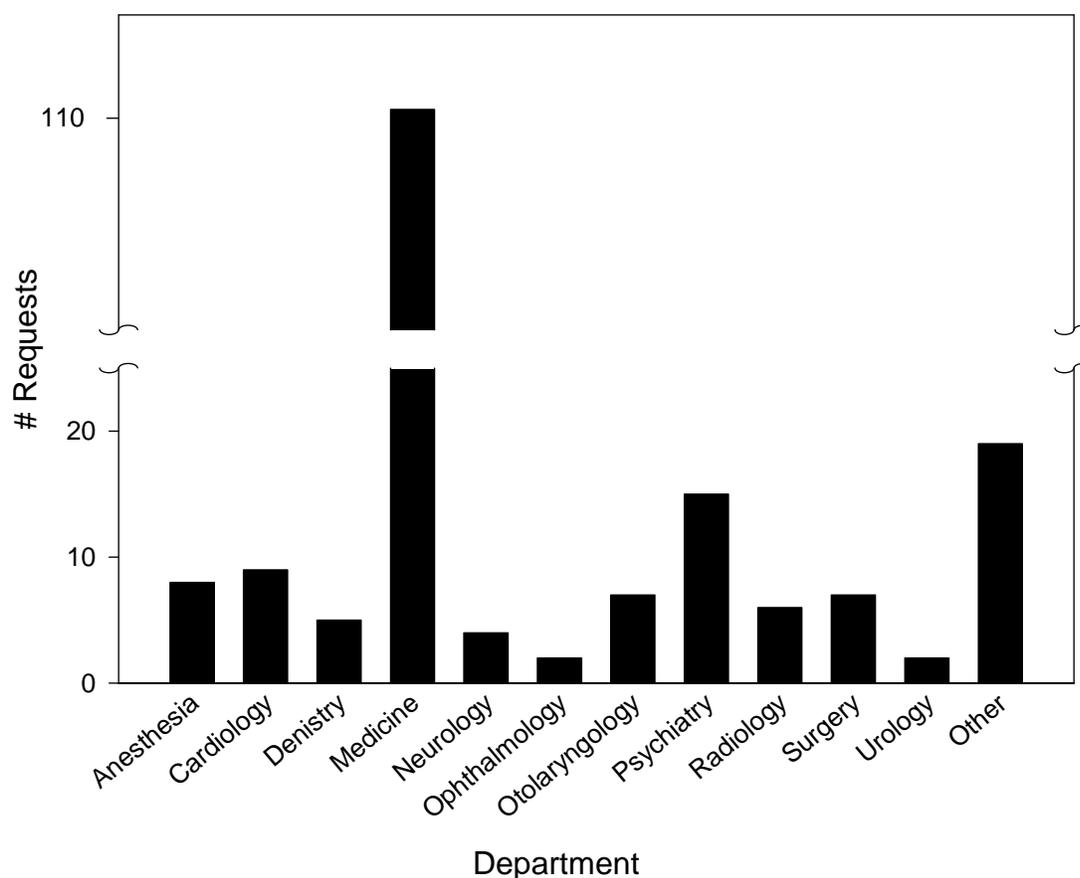
V. Utilization of Services

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 support has been provided for consultative services to unfunded studies (up to 10 hours) while more support can be provided for collaborative relationships with funding. Services include:

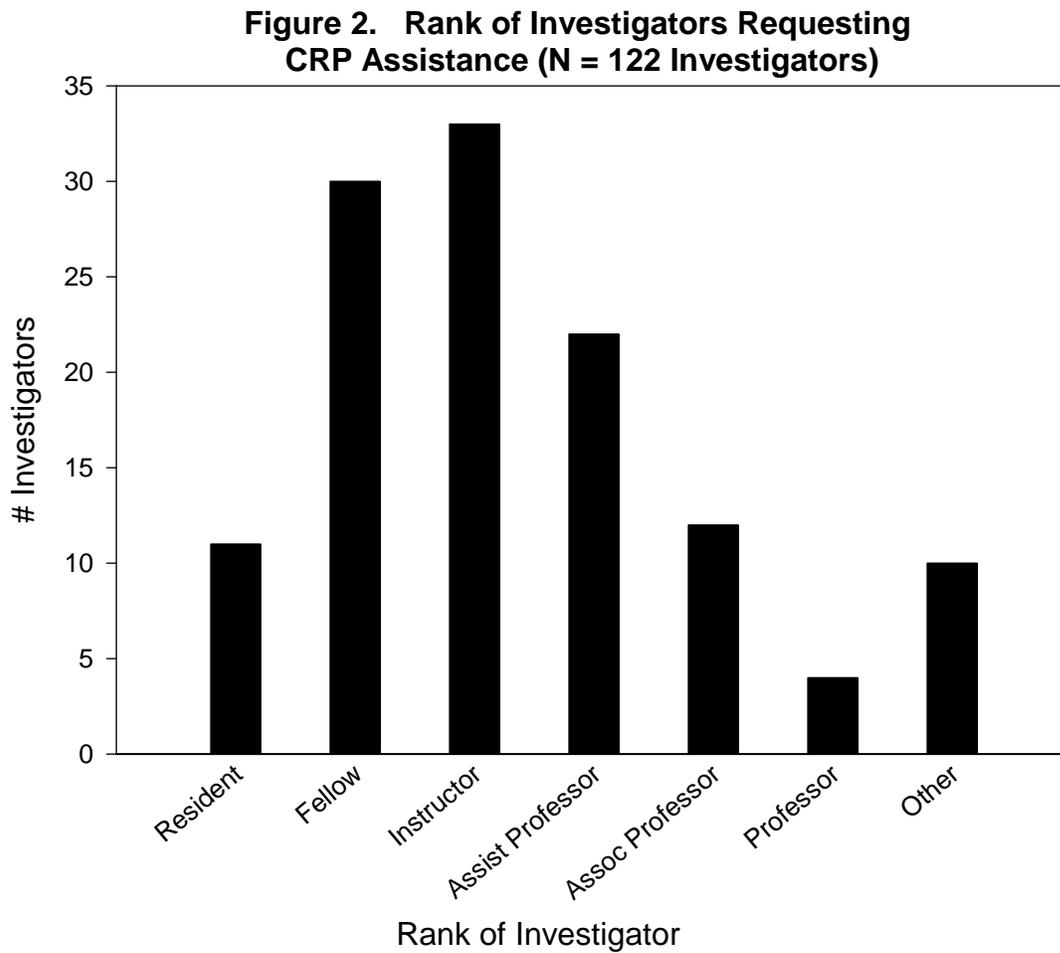
- Protocol/Grant Proposal Development
- Study Design
- Sample Size and Power Calculations
- Biostatistical Analysis Methods
- Randomization
- Case Report Form / Survey Design
- Data Management Systems Design
- Data Analysis and Interpretation
- Budget Development
- Mentoring and Education

During the past year (10/01/02 to 9/30/03), the CRP received 196 requests for assistance from 122 Children's Hospital faculty or staff. The distribution of requests according to hospital department is shown in Figure 1. The majority of requests were from investigators with appointments in Medicine (n=112) and within the Divisions of Emergency Medicine (n=19), Endocrinology (n=19), Adolescent Medicine (n=17), Hematology/Oncology (n=11), GI/Nutrition (n=11) and General Pediatrics (n=10).

Figure 1. FY03 CRP Requests for Assistance (N = 196 Requests)

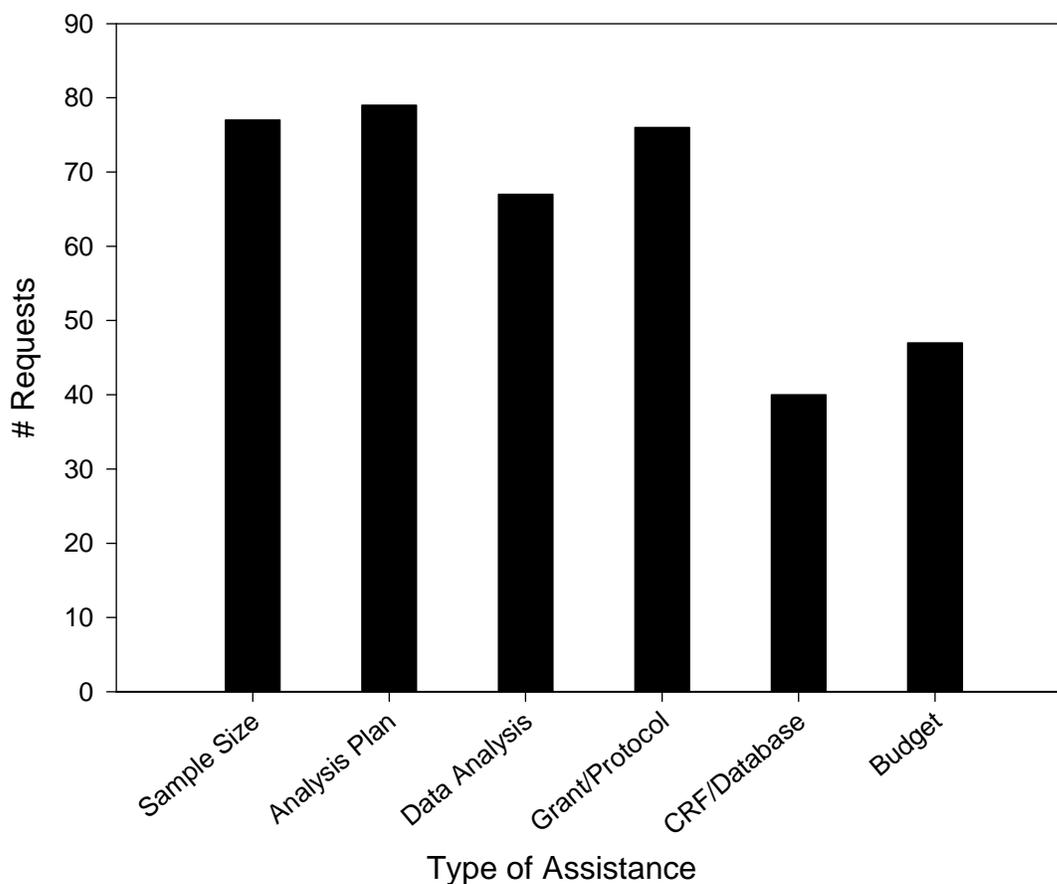


As shown in Figure 2, investigators requesting assistance were somewhat more likely to be at the rank of Fellow (n=30), Instructor (n=33), or Assistant Professor (n=22) as compared to Associate Professor (n=12) or Professor (n=4).



As shown in Figure 3, the majority of requests were for study design and statistical consultation including estimation of sample size and power (n=77), development of a statistical analysis plan (n=79), development of a grant proposal or study protocol (n=76) and/or analyses of data or data interpretation (n=67). Approximately 40 requests were related to study implementation; including case report form or survey design and/or database assistance and 47 requests were for assistance with developing a budget.

Figure 3. Services Requested (N = 196 Requests)



Only one third (n=60) of the projects using CRP resources were funded and one-third (n=60) were applying for funding. Among the funded projects, foundations (n=20) and NIH (n=17) were the primary funding sources. Among those investigators submitting grant proposals for funding, the majority (n=50) were first submissions, whereas the remainder was competing/non-competing renewals or resubmissions.

VI. 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*, *Coordinating Clinical Research*, and *Career Development Block*; which are described below. Course syllabi are located in Appendix C.

A. Introduction to Clinical Research Course

1. Description

The *Introduction to Clinical Research* course is a 3 full-day course designed to introduce participants to the following key clinical research concepts:

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

The target audience includes Junior Faculty, Fellows, Nurse Investigators, and others who will develop and write their own research protocols or grant proposal applications. The overall goal of the course is to provide participants with a knowledge base so that they may be better prepared to develop and conduct their research. Upon completion of the course, participants will gain a better understanding of or increased awareness of each of the following:

- How to select a study design that makes it possible to answer the proposed study hypotheses
- Potential biases associated with the various study designs
- How to propose a plan for data analysis and/or provide information to a biostatistician so that study quality may be maximized
- How to develop high quality data collection forms and effective approaches to data management
- How to protect human subjects and ethical issues in pediatric research
- Content of a NIH grant proposal and the application process
- Resources available for the conduct of clinical research at Children's Hospital
- Approaches to improve the quality of scientific writing and presentations

The course is sponsored by the CRP and General Clinical Research Center (GCRC) and is presently offered January and July of each year. Registration is limited to 50 participants and has reached maximum enrollment at each session.

2. Overall Evaluation

The following table summarizes participants' overall evaluation for the course since the inception of the Clinical Research Program:

Session Date	Quality of Presentation (mean score)	Relevance to Research Plans (mean score)
July 2000	3.2	3.3
July 2001	3.5	3.6
July 2002	3.4	3.5
January 2003	3.3	3.5
Session Date	Clarity of Presentations	Useful Content
July 2003	3.4	3.4
* Score Range: 1-Poor to 4-Excellent		

B. Coordinating Clinical Research

1. Description

The *Coordinating Clinical Research* course consists of three half-day sessions designed to provide participants with a knowledge base so that they may be better prepared to coordinate clinical research projects. The target audience includes Research Nurses and Study Coordinators who will be responsible for coordinating or managing a research study. Upon completion of the course, participants will gain a better understanding of each of the following:

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

The course, sponsored by the CRP, Committee on Clinical Investigation (CCI), and GCRC, is offered during the fall and spring of each year. Registration is limited to 35 participants and has reached the maximum enrollment for each session.

2. Overall Evaluation

The following table summarizes participants' overall evaluation for the course since the development of the course in 2002.

Session Date	Quality of Presentation (mean score)	Relevance to Research Plans (mean score)
November 2002	3.6	3.6
	Clarity of Presentations	Useful Content
March 2003	3.6	3.6
* Score Range: 1-Poor to 4-Excellent		

C. Career Development Block: Creating and Applying New Knowledge

The Career Development Block is an innovative, 3-month component of training for all senior residents in the Boston Combined Residency Program in Pediatrics. Faculty and residents designed the rotation jointly to enhance residents' skills in five areas: (1) knowledge and skills that are fundamental to academic and clinical pediatric careers; (2) ability to participate in creating new knowledge through pediatric research; (3) understanding and ability to apply new developments in molecular medicine to research and clinical practice; (4) ability to identify policy issues and participate effectively in advocacy for children; (5) ability to participate in improving quality of health care at individual, process, and organizational levels. The rotation includes seminars taught by investigators, methodologists, clinicians, and ethicists two mornings a week and individual house officer projects in research, education, or clinical practice mentored by faculty throughout the Harvard and Boston University academic communities.

The CRP and CCI lead the session entitled Creating and Applying New Knowledge. At the end of the 4 sessions, participants will gain a better understanding of each of the following:

- Major study designs used in clinical research, their strengths and limitations, and the interpretation of their corresponding measures of occurrence and association
- How to estimate the sample size required for a study and the underlying statistical principles (type I error, type II error, power and effect size)
- Basic methods of data analyses and interpretation of study results
- The skills necessary to critically evaluate clinical research reports and apply findings to clinical practice
- The role of a DSMB
- Human subjects requirements and ethical considerations of conducting research with children

VII. New Programs – Glaser Pediatric Research Network

In September 2002, the Clinical Research Program (CRP) entered into an agreement with the Glaser Pediatric Research Network (GPRN) to serve as Design, Analysis, and Coordinating center for GPRN's program of pediatric research and training, with Dr. David Wypij as Principal Investigator.

Scientific Director	
Charles Prober, MD	Stanford University
Site Directors	
Darrell Wilson, MD R. Lawrence Moss, MD	Lucile Salter Packard Children's Hospital, Stanford University Medical Center
Stacey Berg, MD	Texas Children's Hospital, Baylor College of Medicine
Christopher Duggan, MD	Children's Hospital Boston, Harvard Medical School
Pinchas Cohen, MD Isidro Salusky, MD	Mattel Children's Hospital, University of California, Los Angeles
Barbara Moscicki, MD Emily von Scheven, MD	Children's Medical Center, University of California, San Francisco

Based at Stanford University, GPRN is a component of the Elizabeth Glaser Pediatric AIDS Foundation, a privately funded organization created in 1988. The Foundation has an international reach and a broad agenda including prevention, advocacy, and research in AIDS. The GPRN was launched in 2000 with the mission of conducting collaborative research on other serious pediatric illnesses, drawing from the diverse patient populations and deep pool of investigators available at five major pediatric research institutions. An important adjunct mission is to draw young investigators into collaborative research careers through a sponsored Fellowship. The organization of GPRN is detailed in Table 1. Dr. Christopher Duggan, the Boston site director, was instrumental in introducing the GPRN leadership to CRP and facilitating the agreement.

The CRP functions in two ways in the operations of the Glaser research network. First, it serves a core resource, lending expertise in the design and conduct of clinical research to help the network develop and foster its programs. CRP core investigators, including Drs. Wypij, Osganian, Feldman, and Kalish, and Ms. McCarthy, participate in the evaluation of new research proposals and attend periodic meetings of the GPRN leadership at which progress of current projects is reviewed. The Glaser Scientific Director, Dr. Charles Prober, also consults CRP ad hoc as issues arise in the conduct of ongoing studies (including those predating the CRP agreement, in which CRP has no direct role), particularly where statistical or design questions are concerned. For the Fellowship program, Dr. Feldman has initiated monthly Work-in-Progress seminars via telephone, at which the new Fellows present and jointly critique each other's protocols.

Title	CRP P.I.	Start	Term (yr)
Multi-center randomized, placebo-controlled, double-blind trial of Metformin in obese adolescents	Osganian	Dec., 2002	4.25
Neonatal surgical database: necrotizing enterocolitis	Wypij	Dec., 2002	4
Open-label Phase I/II trial of rituximab for chronic, severe idiopathic thrombocytopenic purpura in children and adolescents*	Feldman	Dec., 2002	2.5
*This study has additional funding from outside GPRN, supporting five additional sites outside the network. CRP serves as coordinating center for the entire trial.			

The second function of CRP in the Glaser network is to serve as data coordinating center for GPRN studies, via separate contracts. To date, agreements are in effect for two clinical trials and one registry project, listed in Table 2. CRP staff are assigned to the full variety of clinical research tasks for these studies, including biostatistical planning, design of case report forms, database programming, randomization, data management, preparation of data and safety monitoring reports, and presentation and authorship of final results.

At least two more GPRN projects are close to execution. We expect that this agreement will be a fertile and rewarding one over the next several years and that it will help to place CRP in a prominent leadership role among U.S. pediatric hospitals sponsoring clinical research.

VIII. Collaborative Projects

The Clinical Research Program works collaboratively with numerous investigators from a wide variety of disciplines. The Program presently provides such support to the following funded studies (**all dollar figures represent Annual Direct Costs**).

A. Federal Awards

R01 DA01010 (Boyer-UMASS/CHB Subcontract: Shannon) 09/30/02-09/29/04

NIH/NIDA

\$9,224

The Relationship between the Internet and Illicit Drug Use

This is a cross-sectional study of individuals presenting to two emergency departments (one adult and one pediatric) using an interviewer-administered questionnaire. The specific aims are to determine proportion of individuals using the Internet to obtain information about the use of club and other drugs; to assess the association of knowledge, attitudes, and behavior toward drugs in which the Internet is used; and to determine the characteristics of individuals whose self-reported drug-using behavior has been altered by information obtained from the Internet.

R01 DK062363 (Castillo)

09/30/02-6/30/07

NIH/NIDDK

\$382,647

Metabolism of Endothelial Dysfunction in Renal Disease

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

R01 NR05336 (Curley)

3/01/01-02/28/05

NIH/NINR

\$387,029

Effect of Prone Positioning in Pediatric Acute Lung Injury

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

R21 HD045020 (Curley) **09/01/03-08/31/05**
NIH/NICHD **\$125,000**

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

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

R01 HS10411 (Homer) **09/30/99-11/30/03**
DHHS/AHRQ **\$52,206**

Evaluating Quality Improvement Strategies

This study takes advantage of a disease management program for childhood asthma in a Massachusetts- and Michigan-based integrated delivery system by simultaneously implementing an office-based QI strategy in different practices in the same system, and to assess via a randomized design their relative effectiveness and cost-effectiveness in improving processes and outcomes of care.

R01 EB01998 (Levine/CHB subcontract: Estroff) **07/01/03-06/30/08**
NIH/BIDMC **\$165,436**

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 DK63554 (Ludwig) **09/30/02-09/29/04**
NIH/NIDDK **\$150,000**

Sugar-Sweetened Beverages and Weight Gain

A randomized trial to determine the contribution of sweetened beverage consumption to obesity in adolescents.

R01 DK59240 (Ludwig) **4/01/02-3/31/05**
NIH/NIDDK **\$380,626**

Glycemic Index, Obesity, Insulin Resistance, and CVD Risk

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

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

Protein Metabolism in Critically Ill Surgical Neonates

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

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

Genetics and Pediatric Nonsyndromic Hearing Loss

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

S07 RR018150 (Mandell) **09/01/02-08/31/04**
NIH/NCRR **\$150,000**

Human Subjects Research Enhancements Program

The goal is to develop recommendations to strengthen the informed consent process for clinical research at Children's Hospital Boston. In addition one or more sustainable educational initiatives designed to enhance and strengthen the process of obtaining informed consent in pediatric research will be developed.

M01 RR02172 (Mandell) **12/01/98-11/30/03**
NIH/NCRR **\$1,974,472**

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.

200-2003-01601 (Mandl) **09/12/03-11/30/04**
DHHS/CDC **\$136,263**

Pediatric Hospital Based Sentinel Surveillance Network for Vaccine Preventable Diseases

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

U01 HL63411 (Newburger) **07/05/00-06/30/05**
NIH/NHLBI **\$429,255**

Clinical Trial of Hematocrit Strategy in Heart Surgery

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

- R01 HL66643 (Osganian)** **09/01/01-08/31/03**
NIH/NHLBI **\$915,645**
Relation of Diet to Serum Homocysteine Levels in Youth
 Examination of distribution of serum homocysteine levels in a large, ethnically diverse sample of healthy school-age children, as related to dietary intake of folate and vitamins.
- 5 U01 CA81457 (Boyett/CHB subcontract: Poussaint)** **01/01/03-03/31/04**
NIH/NCI **\$260,141**
Pediatric Brain Tumor Consortium (PBTC)
 The primary goal of this project is the establishment of a Neuroimaging Center for the Consortium. The center will develop and coordinate imaging protocols of PBTC trials, collect images, analyze data sets and establish a database of imaging results.
- R01 HL68922 (Platt)** **09/30/01-07/31/06**
NIH/NHLBI **\$657,960**
Genetic Modifiers of Severity in Sickle Cell Anemia
 This study proposes to identify the genes that influence baseline white blood count (WBC) in sickle cell anemia (SS) by studying a large series of nuclear and extended families with an SS proband.
- FD-R-002202 (Rufo)** **09/30/02-09/29/05**
FDA **\$149,284**
Clotrimazole Enemas for Pouchitis in Children and Adults
 This study is a Phase I/II double-blinded, placebo controlled, dose escalating trial that will test the efficacy of topical CLT therapy (delivered as a retention enema) in two cohorts of pediatric and adult patients with pouchitis.
- U19 AI45955 (Taylor/CHB subcontract: Wypij)** **09/30/99-08/31/04**
NIH/NIAID **\$34,504**
Severe Malaria in African Children: A Clinical Network
 The major goals of this project are to develop a clinical trials network for severe malaria in African children, which will provide a new structure for the rapid and efficient evaluation of novel treatments for this killing disease. The network will also provide a framework for collecting the data necessary to validate clinical observations made in individual sites and to evaluate pathogenetic hypotheses, which are necessary steps in the development of new malaria interventions.
- P01 NS38475 (Volpe)** **12/10/99-11/30/04**
NIH/NINDS **\$856,045**
Periventricular Leukomalacia in the Premature Infant
 To study the pathogenesis of periventricular leukomalacia in premature infants and to use the results to formulate innovative preventative and therapeutic interventions.

R03 MH65152 (Woods) **07/01/03-06/30/05**
NIH/NIMH **\$50,000**

HIV Prevention: Providers as Agents of Change

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

B. NIH Career Development Grants

K01 DK62237 (Ebbeling) **08/15/02-06/30/05**
NIH/NIDDK **\$84,475**

Motivating Obese Adolescents to Reduce Risk for Diabetes

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

K23 HL074202 (Levy) **07/01/03-06/30/08**
NIH/NHLBI **\$116,500**

Family Based Analysis of Modifiers of CF Lung Disease

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

K08 HS13333 (Landrigan) **09/01/02-08/31/03**
DHHS/AHRQ **\$116,500**

Effects of Sleep Loss and Night Work on Patient Safety

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

K08 HS11660 (Porter) **07/01/02-06/30/05**
NIH/AHRQ **\$116,459**

Informative Technology Linking Parents and Providers

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

K23 DK02729 (Rufo) **09/30/99-06/30/04**
NIH/NIDDK **\$116,500**

Clotrimazole Therapy for Human Diarrheal Diseases

The purpose of this mentored patient-oriented research career development award is to support the career development of investigators who have made a commitment to focus their research endeavors on patient oriented research. The specific goal of this translational research project is to evaluate the efficacy of orally and topically administered imidazole antibiotic clotrimazole in the treatment of secretory and inflammatory diarrheal disease.

K23 RR016080 (Schachter, Asher) **08/01/00-07/31/05**
NIH/NCRR **\$116,200**

Nuclear Factor Kappa B in Pediatric Nephrotic Syndrome

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

C. Glaser Pediatric Research Network

(Wypij) **09/01/02-08/31/05**
Glaser Pediatric Research Network **\$145,054**

Design, Analysis, and Coordinating Center (DACC) for the Glaser Pediatric Research Network

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

(Wilson/CHB subcontract: Lenders/DACC: Osganian) **12/01/02-02/28/07**
Glaser Pediatric Research Network **\$69,682**

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) **12/01/02-5/31/05**
Glaser Pediatric Research Network **\$51,646**
Design, Analysis, and Coordinating Center (DACC): Open Label, Phase I/II
Trial of Rituximab for Chronic, Severe Idiopathic Thrombocytopenic Purpura
in Children and Adolescents

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

(Moss/CHB subcontract: Jaksic/DACC: Wypij) **12/01/02-11/30/06**
Glaser Pediatric Research Network **\$56,033**
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

(Duggan) **02/01/03-01/31/06**
Mass Vitamin Litigation Fund **\$52,241**
Body Composition in Cancer Patients Undergoing Stem Cell Transplantation

The hypothesis to be tested is that reducing parenteral nutrition intake and supplementation with Vitamin E will be associated with better tolerance of chemotherapy and reduced levels of resting energy expenditure for children undergoing stem cell transplantation. This project will continue studying recent findings that have been reported from the PI's experience with a new approach to nutrition care for patients who are highly catabolic (i.e., lose muscle mass due to the side effects of chemotherapy).

(Grand) **01/01/03-12/31/04**
Crohn's & Colitis Foundation of America **\$99,780**
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.

(Knight) **5/1/02-4/30/05**
Robert Wood Johnson Foundation **\$220,031**

Implementation of Medical Office Screening for Adolescent Substance Abuse

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

(Mooney) **11/15/02-11/14/03**
Robert Wood Johnson Foundation **\$55,220**

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.

(Nugent) **10/02/02-02/27/04**
Deborah Munroe Noonan Memorial Fund **\$60,090**

The First Assessment: Using the CLNBAS to Promote the Development of At-Risk Infants and Families in Early Intervention Settings

This study will test the effectiveness of the Clinical Neonatal Behavioral Assessment Scale (CLNBAS) (Nugent and Brazelton, 2001), as an assessment and intervention system for infants who are at-risk for developmental delay. The CLNBAS is a neurobehavioral examination, applicable for infants from birth to three months adjusted age, consisting of 18 items and designed to examine the infant's reflexes, motor behavior, crying and consolability and social interactive capacities.

(Hirsch, CHB subcontract: Osganian) **01/01/02-12/31/06**
Robert Wood Johnson Foundation **\$7,930**

Injury Free Coalition for Kids of Worcester at the University of Massachusetts Memorial Hospital

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

(Porter) **07/01/02-06/30/04**
Charles H. Hood Foundation **\$41,782**

Informative Technology Linking Parents and Providers

The project investigates outcomes of health communication and quality of care for pediatric asthma, a disease condition notable for its differential and negative impact on urban poor and minority youth. The hypotheses are 1) the provision of parents' data to providers alters parents' satisfaction in the domains of communication and partnership, and 2) the provision of parents' data to providers alters asthma-specific process measures of quality.

GERAFF (Ward) **07/01/02-06/30/04**
GE-AUR Radiology Research Academic Fellowship **\$65,000**

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

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

E. Industry

(Laufer) **05/01/03-04/30/04**
Personal Products Worldwide **\$117,909**

A Pilot Study to Determine if Changes in Selected Salivary Steroid Hormones, Urinary Gonadotropic Hormones, Vaginal pH, and Body Mass Index, Alone or in Combination, can be Used to Predict Menarche

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

IX. 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 3,300 square feet of office space located on the fourth Floor of 333 Longwood Avenue with twelve offices, thirteen cubicles, and one conference room. All staff is provided with a computer and the Program houses its own network server.

Institutional and other sources of support for the Program are shown in Table 3. Institutional support for the Clinical Research Program (CRP) has increased substantially since the inception of the Program and now totals nearly \$1.5 million. Equally exciting has been the rapid growth in funding from collaborative relationships with investigators, which now totals nearly \$1.3 million.

Table 3. CRP Funding for the period FY98 to FY04

FISCAL YEAR	INSTITUTIONAL BUDGET	GRANT SUPPORT/ OTHER FUNDING
FY98	\$299,871	
FY99	\$793,226	
FY00	\$927,204	
FY01	\$1,104,774	\$560,340
FY02	\$1,130,346	\$885,225
FY03	\$1,207,481	\$965,827
FY04	\$1,443,401	\$1,276,262*

*anticipated

Appendix A - Program Description and Request for Assistance Form

Clinical Research Program
333 Longwood Ave. – 4th Floor
Phone: 617-355-2463 / fax: 617-355-2312
crp@childrens.harvard.edu

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 support, education, and collaborative assistance in the design, conduct, and analysis of clinical research. We also closely interact with the Children's Hospital General Clinical Research Center (GCRC) and provide some support to GCRC-funded studies.

CRP Personnel:

- Directors: Senior clinical researchers with extensive experience in conducting clinical research studies.
- Biostatisticians: Skilled in protocol and grant development, study design, and data analysis.
- Survey Epidemiologists: Skilled in the design and analysis of surveys.
- Clinical Research Specialists: Skilled in the design of case report forms and questionnaires, quality assurance procedures, and the development of manuals of operations.
- Applications Specialists: Skilled in data management system design, including database and web application development.
- Budget Specialists: Experienced in budget development and the grant submission process.

Funding Sources:

The CRP receives a portion of its support from the hospital as part of the institution's commitment to clinical research. The majority of our funding comes from federal, foundation, and other awards that are obtained by either our staff or the investigators with whom we collaborate. The CRP can offer limited consultative services at no cost (up to 10 hours per project) to all clinical research investigators, but assistance that is more extensive will require a collaborative effort and funding. As we plan our role in your research, we will estimate your requirements and a realistic budget will be developed to formalize our collaboration. We also strongly encourage investigators to consider seeking GCRC support for their clinical studies wherever possible.

Core Resources:

Consultative Services:

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

Educational Seminars:

- Introduction to Clinical Research (for Junior Investigators)
- Career Development Block (for Residents)
- Coordinating Clinical Research (for Project Coordinators)

Collaboration:

- Grant Proposal Development
- Study Implementation
- Data Analysis and Manuscript Preparation

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. 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.
- Consultative and collaborative 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. 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 on a grant proposal or study protocol.

- 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.

We also ask that you plan ahead for assistance with study implementation and data analyses for manuscripts, abstracts, or presentations. Most studies require **6 to 12 months** of planning prior to recruitment of subjects. Therefore, for assistance with study implementation, we ask that you begin working with us well in advance of your anticipated start of recruitment. Similarly, data analyses require sufficient time for data cleaning, statistical programming, interaction with the investigators, and writing and review of manuscripts. Therefore, we recommend beginning to work with us **60 to 90 days** before any deadline, depending on the scope and complexity of the analyses.

CRP Contact Information:

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

CRP USE ONLYA. Form Received: ___/___/___ Entered:

B. Intro. Meeting: ___/___/___ Staff: ___

Clinical Research Program
 333 Longwood Ave. – 4th Floor
 Phone: 617-355-2463 / fax: 617-355-2312
crp@childrens.harvard.edu

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. Requestor:

Last Name _____ First Name _____ CH ID# _____

2. Title: Prof. Assoc. Prof. Asst. Prof. Instructor Fellow Resident Nurse
 Other (specify): _____

3. Department: _____ Division: _____ Office Location _____

4. E-mail _____ Phone/Ext# _____ Page # _____

5. Research Mentor (if applicable) _____

6. Principal Investigator: check if same as name of requestor

Last Name _____ First Name _____ CH ID# _____

7. Title (same as on protocol):

 _____8. **IRB Information**

a. Has the protocol been submitted to the IRB?

 Yes (Protocol # _____) No (GO TO Q. 10)

b. What is the current status of your protocol with the IRB?

 Full Approval Conditional Approval Deferred

9. What type of assistance are you requesting [see program description for explanation]? (check one)

 Collaboration

Consultation

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

a. Grant Proposal / Protocol Development

- Grant Proposal Preparation
 Protocol Preparation
 Statistical Analysis Plan
 Power and Sample Size Determination
 Data Monitoring Plans (DSMB) / Interim Analysis Plan
 Concept Proposal Development
 Budget Assistance

b. Study Implementation

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

c. Data Analysis/Interpretation

- Presentation → Due Date (MM/DD/YYYY): _____ / _____ / _____
 Manuscript → Due Date (MM/DD/YYYY): _____ / _____ / _____
 Statistical Analysis/Interpretation of Results

d. Other (Specify below)

11. **Funding Status**

- a. Is your project currently funded? Yes No
- b. Are you presently applying for funding? Yes No; Skip to Q. 13
- c. If Yes, what type of application is it? (check one)
- New Submission
 Resubmission
 Competing Renewal
 Non-Competing Renewal
- d. When is the deadline for submission? (MM/DD/YYYY): _____ / _____ / _____

12. Funding Sources

- NIH
- a. Name of Institute / Center: _____
- b. Type of funding mechanism (check one): R01 R03 R21
 K01 K08 K23 K24
- c. Is this a response to an announcement? Yes No
- i. If Yes, what is the type? RFA RFP PA
- ii. If Yes, what is the number? _____
- Other Federal Agency: _____
- Foundation / Association: 1) _____
2) _____
- Industry Sponsor: _____
- Internal Award: _____
- Department/Division/Program Funds: _____
- Other (specify): _____

13. Will data need to be submitted to the FDA? Yes No

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

a. If Yes, what is the current status?

- Approved
- Pending
- Not yet submitted

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 – Staff Publication

2003 Publications

Ariga, H., T. H. Lee, M. E. Laycock, B. A. Mohr, **L. A. Kalish**, R. Yomtovian, T. Gernsheimer, and M. P. Busch for the Viral Activation Transfusion Study (2003). "Residual WBC subsets in filtered prestorage RBCs." *Transfusion* 43(1): 98-106.

Asmuth, D. M., **L. A. Kalish**, M. E. Laycock, E. L. Murphy, B. A. Mohr, T. H. Lee, J. Gallarda, C. Giachetti, S. C. Dollard, C. M. van der Horst, R. M. Grant, and M. P. Busch for the Viral Activation Transfusion Study Group (2003). "Absence of HBV and HCV, HTLV-I and -II, and human herpes virus-8 activation after allogeneic RBC transfusion in patients with advanced HIV-1 infection." *Transfusion* 43(4): 451-8.

Bellinger, D. C., **D. Wypij**, A. J. du Plessis, L. A. Rappaport, R. A. Jonas, G. Wernovsky and J. W. Newburger (2003). "Neurodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial." *J Thorac Cardiovasc Surg* 126(5): 1385-96.

Chen, C., C. Botelho, **A. Cooper**, **P. Hibberd**, and S. K. Parsons (2003). "Current practice patterns in the treatment of perforated appendicitis in children." *Journal of the American College of Surgeons* 196(2): 212-21.

Curley, M. A., I. S. Razmus, K. E. Roberts, and **D. Wypij** (2003). "Predicting pressure ulcer risk in pediatric patients: the Braden Q Scale." *Nursing Research* 52(1): 22-33.

Curley, M. A., S. M. Quigley, and **M. Lin** (2003). "Pressure ulcers in pediatric intensive care: Incidence and associated factors." *Pediatr Crit Care Med* 4(3): 284-90.

Dioun, A. F., **S. K. Harris**, and **P. L. Hibberd** (2003). "Is maternal age at delivery related to childhood food allergy?" *Pediatr Allergy Immunol* 14(4): 307-11.

Duggan, C., M. E. Penny, **P. Hibberd**, A. Gil, A. Huapaya, **A. Cooper**, F. Coletta, C. Emenhiser, and R. E. Kleinman (2003). "Oligofructose-supplemented infant cereal: Two randomized, blinded, community-based trials in Peruvian infants." *American Journal of Clinical Nutrition* 77(4): 937-42.

Dusek, J. A., J. A. Astin, **P. L. Hibberd**, and M. W. Krucoff (2003). "Healing prayer outcomes studies: Consensus recommendations." *Alternative Therapies in Health & Medicine* 9(3 Suppl): A44-53.

Dzik, W. H., J. K. Anderson, E. M. O'Neill, S. F. Assmann, **L. A. Kalish**, and C. P. Stowell (2003). "Effect of universal WBC reduction [reply to letter]." *Transfusion* 43: 833-834.

Feeney, M. E., R. Draenert, K. A. Roosevelt, S. I. Pelton, **K. McIntosh**, S. K. Burchett, C. Mao, B. D. Walker, and P. J. Goulder (2003). "Reconstitution of virus-specific CD4 proliferative responses in pediatric HIV-1 infection." *J Immunol* 171(12): 6968-75.

French, J. K., **H. A. Feldman**, S. F. Assmann, T. Sanborn, S. T. Palmeri, D. Miller, J. Boland, C. E. Buller, R. Steingart, L. A. Sleeper, and J. S. Hochman (2003). "Influence of thrombolytic therapy, with or without intra-aortic balloon counterpulsation, on 12-month survival in the SHOCK trial." *Am Heart J* 146(5): 804-10.

Hansen, A., **P. Forbes**, A. Arnold, and E. O'Rourke (2003). "Once-daily Gentamicin Dosing for the Preterm and Term Newborn: Proposal for a Simple Regimen that Achieves Target Levels." *J Perinatol* 23(8): 635-9.

Harris, S. K., C. L. Samples, P. M. Keenan, D. J. Fox, M. W. Melchiono, and E. R. Woods (2003). "Outreach, mental health, and case management services: Can they help to retain HIV-positive and at-risk youth and young adults in care?" *Matern Child Health J* 7(4): 205-18.

Jonas, R. A., **D. Wypij**, S. J. Roth, D. C. Bellinger, K. J. Visconti, A. J. Du Plessis, H. Goodkin, P. C. Laussen, D. M. Farrell, J. Bartlett, E. McGrath, L. J. Rappaport, E. A. Bacha, J. M. Forbess, P. J. Del Nido, J. E. Mayer, Jr., and J. W. Newburger (2003). "The influence of hemodilution on outcome after hypothermic cardiopulmonary bypass: Results of a randomized trial in infants." *J Thorac Cardiovasc Surg* 126(6): 1765-74.

Kemper, K. J., A. Amata-Kynvi, L. Dvorkin, J. S. Whelan, A. Woolf, R. C. Samuels, and **P. Hibberd** (2003). "Herbs and other dietary supplements: Healthcare professionals' knowledge, attitudes, and practices." *Alternative Therapies in Health & Medicine* 9(3): 42-9.

Knight, J. R., L. Sherritt, **S. K. Harris**, E. C. Gates, and G. Chang (2003). "Validity of brief alcohol screening tests among adolescents: A comparison of the AUDIT, POSIT, CAGE, and CRAFFT." *Alcoholism: Clinical & Experimental Research* 27(1): 67-73.

Knight, J. R., **S. K. Harris**, L. Sherritt, K. Kelley, S. Van Hook, and H. Wechsler (2003). "Heavy drinking and alcohol policy enforcement in a statewide public college system." *J Stud Alcohol* 64(5): 696-703.

Lai, T. T. and **M. C. Shih** (2003). "Nonparametric estimation in nonlinear mixed effects models." *Biometrika* 90: 1-13.

Lee, G. M., J. F. Friedman, D. Ross-Degnan, **P. L. Hibberd**, and D. A. Goldmann (2003). "Misconceptions about colds and predictors of health service utilization." *Pediatrics* 111(2): 231-6.

Levy, O., **A. Teixeira-Pinto**, M. L. White, S. F. Carroll, L. Lehmann, **D. Wypij**, and E. Guinan (2003). "Endotoxemia and elevation of lipopolysaccharide-binding protein after hematopoietic stem cell transplantation." *Pediatr Infect Dis J* 22(11): 978-81.

Levy, O., J. S. Orange, **P. Hibberd**, S. Steinberg, P. LaRussa, A. Weinberg, S. B. Wilson, A. Shaulov, G. Fleisher, R. S. Geha, F. A. Bonilla, and M. Exley (2003). "Disseminated varicella infection due to the vaccine strain of varicella-zoster virus in a patient with a novel deficiency in natural killer T cells." *J Infect Dis* 188(7): 948-53.

Mick, E., J. Biederman, S. Santangelo, and **D. Wypij** (2003). "The influence of gender in the familial association between ADHD and major depression." *J Nerv Ment Dis* 191(11): 699-705.

Newburger, J. W., **D. Wypij**, D. C. Bellinger, A. J. du Plessis, K. C. Kuban, L. A. Rappaport, D. Almirall, D. L. Wessel, R. A. Jonas, and G. Wernovsky (2003). "Length of stay after infant heart surgery is related to cognitive outcome at age 8 years." *J Pediatr* 143(1): 67-73.

Osganian, S. K., D. M. Hoelscher, M. Zive, P. D. Mitchell, P. Snyder, and L. S. Webber (2003). "Maintenance of effects of the eat smart school food service program: Results from the CATCH-ON study." *Health Educ Behav* 30(4): 418-33.

Osganian, S. K., G. S. Parcel and E. J. Stone (2003). "Institutionalization of a school health promotion program: Background and rationale of the CATCH-ON study." *Health Educ Behav* 30(4): 410-7.

Osganian, S. K., M. J. Stampfer, E. Rimm, D. Spiegelman, F. B. Hu, J. E. Manson, and W. C. Willett (2003). "Vitamin C and risk of coronary heart disease in women." *J Am Coll Cardiol* 42(2): 246-52.

Osganian, S. K., M. J. Stampfer, E. Rimm, D. Spiegelman, J. E. Manson, and W. C. Willett (2003). "Dietary carotenoids and risk of coronary artery disease in women." *American Journal of Clinical Nutrition* 77(6): 1390-9.

Randolph, A. G., K. L. Meert, M. E. O'Neil, J. H. Hanson, P. M. Lockett, J. H. Arnold, R. G. Gedeit, P. N. Cox, J. S. Roberts, S. T. Venkataraman, **P. W. Forbes**, and I. M. Cheifetz for the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network (2003). "The feasibility of conducting clinical trials in infants and children with acute respiratory failure." *American Journal of Respiratory & Critical Care Medicine* 167(10): 1334-40.

Rawson, E. S., P. S. Freedson, **S. K. Osganian**, C. E. Matthews, G. Reed, and I. S. Ockene (2003). "Body mass index, but not physical activity, is associated with C-reactive protein." *Med Sci Sports Exerc* 35(7): 1160-6.

Rivkin, M. J., S. Vajapeyam, C. Hutton, M. L. Weiler, E. K. Hall, D. A. Wolraich, S. S. Yoo, R. V. Mulkern, **P. W. Forbes**, P. H. Wolff, and D. P. Waber (2003). "A functional magnetic resonance imaging study of paced finger tapping in children." *Pediatric Neurology* 28(2): 89-95.

Shrier, L. A., F. P. Bowman, **M. Lin**, and P. A. Crowley-Nowick (2003). "Mucosal immunity of the adolescent female genital tract." *J Adolesc Health* 32(3): 183-6.

Shrier, L. A., **S. K. Harris**, M. Kurland, and J. R. Knight (2003). "Substance use problems and associated psychiatric symptoms among adolescents in primary care." *Pediatrics* 111(6 Pt 1): e699-705.

Ullrich, N., **C. A. Botelho**, **P. Hibberd**, and H. H. Bernstein (2003). "Research during pediatric residency: predictors and resident-determined influences." *Acad Med* 78(12): 1253-8.

Waber, D. P., D. J. Marcus, **P. W. Forbes**, D. C. Bellinger, M. D. Weiler, L. G. Sorensen, and T. Curran (2003). "Motor sequence learning and reading ability: Is poor reading associated with sequencing deficits?" *J Exp Child Psychol* 84(4): 338-54.

Weiler, M. D., **P. Forbes**, M. Kirkwood, and D. Waber (2003). "The developmental course of processing speed in children with and without learning disabilities." *J Exp Child Psychol* 85(2): 178-94.

Weiner, D. L., A. J. Butte, **P. L. Hibberd**, and G. R. Fleisher (2003). "Computerized recruiting for clinical trials in real time." *Annals of Emergency Medicine* 41(2): 242-6.

Weiner, D. L., **P. L. Hibberd**, P. Betit, A. B. Cooper, C. A. Botelho, and C. Brugnara (2003). "Preliminary assessment of inhaled nitric oxide for acute vaso-occlusive crisis in pediatric patients with sickle cell disease." *JAMA* 289(9): 1136-42.

Woods, E. R., C. L. Samples, M. W. Melchiono, and **S. K. Harris** (2003). "Boston HAPPENS Program: HIV-positive, homeless, and at-risk youth can access care through youth-oriented HIV services." *Semin Pediatr Infect Dis* 14(1): 43-53.

Wypij, D., J. W. Newburger, L. A. Rappaport, A. J. du Plessis, R. A. Jonas, G. Wernovsky, **M. Lin**, and D. C. Bellinger (2003). "The effect of duration of deep hypothermic circulatory arrest in infant heart surgery on late neurodevelopment: The Boston Circulatory Arrest Trial." *J Thorac Cardiovasc Surg* 126(5): 1397-403.

2002 Publications

Alexander, S. W., K. C. Wade, **P. L. Hibberd**, and S. K. Parsons (2002). "Evaluation of risk prediction criteria for episodes of febrile neutropenia in children with cancer." *Journal of Pediatric Hematology/Oncology* 24(1): 38-42.

Becker, C. M., F. A. Farnebo, I. Iordanescu, D. J. Behonick, **M. C. Shih**, P. Dunning, R. Christofferson, R. C. Mulligan, G. A. Taylor, C. J. Kuo, and B. R. Zetter (2002). "Gene therapy of prostate cancer with the soluble vascular endothelial growth factor receptor Flk1. [comment]." *Cancer Biology & Therapy* 1(5): 548-53.

Brooks, T. L., **S. K. Harris**, J. S. Thrall, and E. R. Woods (2002). "Association of adolescent risk behaviors with mental health symptoms in high school students." *Journal of Adolescent Health* 31(3): 240-6.

Dusek, J. A., J. B. Sherwood, R. Friedman, P. Myers, C. F. Bethea, S. Levitsky, P. C. Hill, M. K. Jain, S. L. Kopecky, P. S. Mueller, P. Lam, H. Benson, and **P. L. Hibberd** (2002). "Study of the Therapeutic Effects of Intercessory Prayer (STEP): Study design and research methods." *American Heart Journal* 143(4): 577-84.

Dwyer, J. T., **H. A. Feldman**, M. Yang, L. S. Webber, A. Must, C. L. Perry, P. R. Nader, and G. S. Parcel on behalf of the Catch Cooperative Research Group (2002). "Maintenance of lightweight correlates with decreased cardiovascular risk factors in early adolescence." *Journal of Adolescent Health* 31(2): 117-24.

Feldman, H. A. (2002). "Mathematical modeling of cell lineage data. Appendix to Fishman MP, Melton, DA. Pancreatic lineage analysis using a retroviral vector in embryonic mice demonstrates a common progenitor for endocrine and exocrine cells." *International Journal of Developmental Biology* 46: 201-207.

Feldman, H. A., C. Longcope, C. A. Derby, C. B. Johannes, A. B. Araujo, A. D. Coviello, W. J. Bremner, and J. B. McKinlay (2002). "Age trends in the level of serum testosterone and other hormones in middle-aged men: Longitudinal results from the Massachusetts male aging study." *Journal of Clinical Endocrinology & Metabolism* 87(2): 589-98.

Goldberg, R. J., **S. Osganian**, J. Zapka, P. Mitchell, V. Bittner, M. Daya, and R. Luepker (2002). "Prehospital delay in individuals with acute coronary disease: Concordance of medical records and follow-up phone interviews." *Cardiology* 97(3): 159-65.

Gordon, C. M., E. Grace, S. J. Emans, **H. A. Feldman**, E. Goodman, K. A. Becker, C. J. Rosen, C. M. Gundberg, and M. S. LeBoff (2002). "Effects of oral dehydroepiandrosterone on bone density in young women with anorexia nervosa: A randomized trial." *Journal of Clinical Endocrinology & Metabolism* 87(11): 4935-41.

Hingson R, **S. K. Harris**, K. Kelley, J. R. Knight, T. Callahan, H. Harner, J. Schinazi, K. Herr-Zaya, D. K. Walker, D. Piken, I. L. Wong, and B. Harrington (2002) "Underage drinking in Massachusetts: The facts and the future." MA Youth Alcohol Prevention Task Force.

Jean-Mary, M. B., **J. Dicanzio**, J. Shaw, and H. H. Bernstein (2002). "Limited accuracy and reliability of infrared axillary and aural thermometers in a pediatric outpatient population." *J Pediatr* 141(5): 671-6.

Johnson, C. C., D. Li, C. L. Perry, J. P. Elder, **H. A. Feldman**, S. H. Kelder, and E. J. Stone (2002). "Fifth through eighth grade longitudinal predictors of tobacco use among a racially diverse cohort: CATCH." *Journal of School Health* 72(2): 58-64.

Kelder, S. H., **S. K. Osganian**, **H. A. Feldman**, L. S. Webber, G. S. Parcel, R. V. Leupker, M. C. Wu, and P. R. Nader (2002). "Tracking of physical and physiological risk variables among ethnic subgroups from third to eighth grade: the Child and Adolescent Trial for Cardiovascular Health cohort study." *Preventive Medicine* 34(3): 324-33.

Kemper, K. J., A. Amata-Kynvi, D. Sanghavi, J. S. Whelan, L. Dvorkin, A. Woolf, R. C. Samuels, and **P. Hibberd** (2002). "Randomized trial of an internet curriculum on herbs and other dietary supplements for health care professionals." *Academic Medicine* 77(9): 882-9.

Knight, J. R., L. Sherritt, L. A. Shrier, **S. K. Harris**, and G. Chang (2002). "Validity of the CRAFFT substance abuse screening test among adolescent clinic patients." *Archives of Pediatrics & Adolescent Medicine* 156(6): 607-14.

Lin, Y. S., T. J. Smith, **D. Wypij**, K. T. Kelsey, and F. M. Sacks (2002). "Association of the blood/air partition coefficient of 1,3-butadiene with blood lipids and albumin." *Environmental Health Perspectives* 110(2): 165-8.

MacDonald, A. J., P. S. Turaga, C. Harmon-Brown, T. J. Tierney, K. E. Bennett, **M. C. McCarthy**, S. C. Simonek, P. A. Enyong, D. W. Moukatte, and S. Lustigman (2002). "Differential cytokine and antibody responses to adult and larval stages of *Onchocerca volvulus* consistent with the development of concomitant immunity." *Infection & Immunity* 70(6): 2796-804.

Nicklas, T. A., J. Dwyer, **H. A. Feldman**, R. V. Luepker, S. H. Kelder, and P. R. Nader (2002). "Serum cholesterol levels in children are associated with dietary fat and fatty acid intake." *Journal of the American Dietetic Association* 102(4): 511-7.

Osganian, S. K., J. G. Zapka, **H. A. Feldman**, R. J. Goldberg, J. R. Hedges, M. S. Eisenberg, J. M. Raczynski, P. G. McGovern, L. S. Cooper, D. K. Pandey, A. C. Linares, and R. V. Luepker for the REACT Study Group. (2002). "Use of emergency medical services for suspected acute cardiac ischemia among demographic and clinical patient subgroups: The REACT trial. Rapid Early Action for Coronary Treatment." *Prehospital Emergency Care* 6(2): 175-85.

Palmert, M. R., C. M. Gordon, **A. I. Kartashov**, R. S. Legro, S. J. Emans, and A. Dunaif (2002). "Screening for abnormal glucose tolerance in adolescents with polycystic ovary syndrome." *Journal of Clinical Endocrinology & Metabolism* 87(3): 1017-23.

Pereira, M. A., D. R. Jacobs, Jr., L. Van Horn, M. L. Slattery, **A. I. Kartashov**, and D. S. Ludwig (2002). "Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study. [comment]." *JAMA* 287(16): 2081-9.

Randolph, A. G., **D. Wypij**, S. T. Venkataraman, J. H. Hanson, R. G. Gedeit, K. L. Meert, P. M. Lockett, **P. Forbes**, M. Lilley, J. Thompson, I. M. Cheifetz, **P. Hibberd**, R. Wetzel, P. N. Cox, and J. H. Arnold for the Pediatric Acute Lung Injury and Sepsis Investigators (2002). "Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. [comment]." *JAMA* 288(20): 2561-8.

Shih, M. C. and A. S. Whittemore (2002). "Tests for genetic association using family data." *Genetic Epidemiology* 22(2): 128-45.

Shrier, L. A., **S. K. Harris**, and W. R. Beardslee (2002). "Temporal associations between depressive symptoms and self-reported sexually transmitted disease among adolescents." *Archives of Pediatrics & Adolescent Medicine* 156(6): 599-606.

Thomas, S. M., O. Ndir, T. Dieng, S. Mboup, **D. Wypij**, J. H. Maguire, and D. F. Wirth (2002). "In vitro chloroquine susceptibility and PCR analysis of pfcr1 and pfmdr1 polymorphisms in Plasmodium falciparum isolates from Senegal." *American Journal of Tropical Medicine & Hygiene* 66(5): 474-80.

Woods, E. R., C. L. Samples, M. W. Melchiono, P. M. Keenan, D. J. Fox, and **S. K. Harris** for the Boston HAPPENS Program Collaborators (2002). "Initiation of services in the Boston HAPPENS Program: Human immunodeficiency virus-positive, homeless, and at-risk youth can access services." *AIDS Patient Care & STDs* 16(10): 497-510.

2001 Publications

Andorsky, D. J., D. P. Lund, C. W. Lillehei, T. Jaksic, **J. Dicanzio**, D. S. Richardson, S. B. Collier, C. Lo, and C. Duggan (2001). "Nutritional and other postoperative management of neonates with short bowel syndrome correlates with clinical outcomes." *J Pediatr* 139(1): 27-33.

Bellinger, D. C., **D. Wypij**, A. J. du Plessis, L. A. Rappaport, J. Riviello, R. A. Jonas, and J. W. Newburger (2001). "Developmental and neurologic effects of alpha-stat versus pH-stat strategies for deep hypothermic cardiopulmonary bypass in infants. [comment] [erratum appears in *J Thorac Cardiovasc Surg* 2001 May; 121(5):893]." *Journal of Thoracic & Cardiovascular Surgery* 121(2): 374-83.

Bloom, S. S., **D. Wypij**, and M. Das Gupta (2001). "Dimensions of women's autonomy and the influence on maternal health care utilization in a north Indian city." *Demography* 38(1): 67-78.

Boyer, E. W., M. Shannon, and **P. L. Hibberd** (2001). "Web sites with misinformation about illicit drugs." *New England Journal of Medicine* 345(6): 469-71.

Cilio, M. R., **A. I. Kartashov**, and F. Vigevano (2001). "The long-term use of felbamate in children with severe refractory epilepsy." *Epilepsy Research* 47(1-2): 1-7.

Doctor, A., B. Price, N. Bhargava, **J. Dicanzio**, and J. H. Arnold (2001). "High-frequency oscillatory ventilation of the perfluorocarbon-filled lung: Dose-response relationships in an animal model of acute lung injury." *Crit Care Med* 29(4): 847-54.

Dunbar-Masterson, C., **D. Wypij**, D. C. Bellinger, L. A. Rappaport, A. L. Baker, R. A. Jonas, and J. W. Newburger (2001). "General health status of children with D-transposition of the great arteries after the arterial switch operation." *Circulation* 104(12 Suppl 1): I138-42.

Kirkwood, M. W., M. D. Weiler, J. H. Bernstein, **P. W. Forbes**, and D. P. Waber (2001). "Sources of poor performance on the Rey-Osterrieth Complex Figure Test among children with learning difficulties: A dynamic assessment approach." *Clinical Neuropsychologist* 15(3): 345-56.

Kocher, M. S., **J. Dicanzio**, D. Zurakowski, and L. J. Micheli (2001). "Diagnostic performance of clinical examination and selective magnetic resonance imaging in the evaluation of intraarticular knee disorders in children and adolescents." *Am J Sports Med* 29(3): 292-6.

Lin, Y. S., T. J. Smith, K. T. Kelsey, and **D. Wypij** (2001). "Human physiologic factors in respiratory uptake of 1,3-butadiene." *Environmental Health Perspectives* 109(9): 921-6.

Meier, P. M., C. B. Berde, **J. Dicanzio**, D. Zurakowski, and N. F. Sethna (2001). "Quantitative assessment of cutaneous thermal and vibration sensation and thermal pain detection thresholds in healthy children and adolescents." *Muscle Nerve* 24(10): 1339-45.

Molrine, D. C. and **P. L. Hibberd** (2001). "Vaccines for transplant recipients." *Infectious Disease Clinics of North America* 15(1): 273-305.

Rahbar, R., C. D. Robson, R. A. Petersen, **J. Dicanzio**, K. W. Rosbe, T. J. McGill, and G. B. Healy (2001). "Management of orbital subperiosteal abscess in children." *Arch Otolaryngol Head Neck Surg* 127(3): 281-6.

Rahbar, R., C. D. Robson, J. B. Mulliken, L. Schwartz, **J. Dicanzio**, M. A. Kenna, T. J. McGill, and G. B. Healy (2001). "Craniofacial, temporal bone, and audiologic abnormalities in the spectrum of hemifacial microsomia." *Arch Otolaryngol Head Neck Surg* 127(3): 265-71.

Shrier, L. A., **S. K. Harris**, M. Sternberg, and W. R. Beardslee (2001). "Associations of depression, self-esteem, and substance use with sexual risk among adolescents." *Preventive Medicine* 33(3): 179-89.

Singer-Harris, N., **P. Forbes**, M. D. Weiler, D. Bellinger, and D. P. Waber (2001). "Children with adequate academic achievement scores referred for evaluation of school difficulties: information processing deficiencies." *Developmental Neuropsychology* 20(3): 593-603.

Snydman, D. R., M. E. Falagas, R. Avery, C. Perlino, R. Ruthazer, R. Freeman, R. Rohrer, R. Fairchild, E. O'Rourke, **P. Hibberd**, and B. G. Werner (2001). "Use of combination cytomegalovirus immune globulin plus ganciclovir for prophylaxis in CMV-seronegative liver transplant recipients of a CMV-seropositive donor organ: a multicenter, open-label study." *Transplantation Proceedings* 33(4): 2571-5.

Waber, D. P., M. D. Weiler, P. H. Wolff, D. Bellinger, D. J. Marcus, R. Ariel, **P. Forbes**, and **D. Wypij** (2001). "Processing of rapid auditory stimuli in school-age children referred for evaluation of learning disorders." *Child Development* 72(1): 37-49.

Wang, C., M. G. Sholas, C. B. Berde, **J. Dicanzio**, D. Zurakowski, and R. T. Wilder (2001). "Evidence that spinal segmental nitric oxide mediates tachyphylaxis to peripheral local anesthetic nerve block." *Acta Anaesthesiol Scand* 45(8): 945-53.

Winickoff, J. P., **P. L. Hibberd**, B. Case, P. Sinha, and N. A. Rigotti (2001). "Child hospitalization: an opportunity for parental smoking intervention." *American Journal of Preventive Medicine* 21(3): 218-20.

2000 Publications

Bassuk, S. S., **D. Wypij**, and L. F. Berkman (2000). "Cognitive impairment and mortality in the community-dwelling elderly." *American Journal of Epidemiology* 151(7): 676-88.

Connolly, L. P., D. Zurakowski, C. A. Peters, **J. Dicanzio**, P. Ephraim, H. J. Paltiel, J. C. Share, and S. T. Treves (2000). "Variability of diuresis renography interpretation due to method of post-diuretic renal pelvic clearance half-time determination." *J Urol* 164(2): 467-71.

Diamond, D. A., H. J. Paltiel, **J. Dicanzio**, D. Zurakowski, S. B. Bauer, A. Atala, P. L. Ephraim, R. Grant, and A. B. Retik (2000). "Comparative assessment of pediatric testicular volume: Orchidometer versus ultrasound." *J Urol* 164(3 Pt 2): 1111-4.

Harris, S. K. (2000) Massachusetts Department of Public Health. "The Challenge Fund Teen Pregnancy Prevention Statewide Annual Report: 1996-1997". Boston MA: Office of Statistics and Evaluation.

Lin, E., L. P. Connolly, D. Zurakowski, **J. Dicanzio**, L. Drubach, K. Mitchell, T. Tetrault, S. P. Laffin, and S. T. Treves (2000). "Reproducibility of renal length measurements with 99mTc-DMSA SPECT." *J Nucl Med* 41(10): 1632-5.

Lin, E., L. P. Connolly, L. Drubach, D. Zurakowski, **J. Dicanzio**, K. Mitchell, and S. T. Treves (2000). "Effect of early emptying on quantitation and interpretation of liquid gastric emptying studies of infants and young children." *J Nucl Med* 41(4): 596-9.

Mick, E., S. L. Santangelo, **D. Wypij**, and J. Biederman (2000). "Impact of maternal depression on ratings of comorbid depression in adolescents with attention-deficit/hyperactivity disorder." *Journal of the American Academy of Child & Adolescent Psychiatry* 39(3): 314-9.

Soul, J. S., G. A. Taylor, **D. Wypij**, A. J. Duplessis, and J. J. Volpe (2000). "Noninvasive detection of changes in cerebral blood flow by near-infrared spectroscopy in a piglet model of hydrocephalus." *Pediatric Research* 48(4): 445-9.

Waber, D. P., M. D. Weiler, D. C. Bellinger, D. J. Marcus, **P. W. Forbes**, **D. Wypij**, and P. H. Wolff (2000). "Diminished motor timing control in children referred for diagnosis of learning problems." *Developmental Neuropsychology* 17(2): 181-97.

Waber, D. P., P. H. Wolff, **P. W. Forbes**, and M. D. Weiler (2000). "Rapid automatized naming in children referred for evaluation of heterogeneous learning problems: How specific are naming speed deficits to reading disability?" *Child Neuropsychology* 6(4): 251-61.

Appendix C – Course Agendas

A. Coordinating Clinical Research

Coordinating Clinical Research Schedule October 28, 2003 / November 4, 2003 / November 6, 2003

**Farley 1 Classroom
8:30am-12:00pm**

October 28, 2003: Human Subjects Protection

8:30 – 9:00 Continental Breakfast

9:00 – 9:10 Welcome and Course Overview Stavroula Osganian

9:10–11:00 Human Subject Protection Responsibilities
for Research Nurses/ Study Coordinators Susan Kornetsky
and IRB staff

Before the Research Begins

- Training Requirements Josh Fiedler
- Protocol Submissions/ 3 year rewrites Christina DiTomasso
- Research Subject Recruitment Jillian Richard

During the Research

- Continuing Renewals Josh Fiedler
- Amendments/ Revisions Jillian Richard
- Adverse Events Jillian Richard

After the Research

- How Should We Thank Research
Subjects? Susan Kornetsky
- Working as a Research Team Susan Kornetsky

11:00 – 11:15 Quality Improvement and Human Subject
Protection Eunice Yim-Newbert

11:15 – 12:00 Obtaining Consent/Assent: Practical
Techniques Carol Sweeney

November 4, 2003: Clinical Research Study Implementation: Part I

8:30-9:00	Continental Breakfast	
9:00-9:10	Introduction to the CRP	Stavroula Osganian
9:10-9:45	Introduction to the GCRC	Meg McCabe Kris Jordan Christine Clark
9:45-10:30	Overview of Clinical Research	Stavroula Osganian David Wypij
10:30-10:50	Operationalizing the Study Protocol: Manual of Operations and Training	Amy Kroeplin
10:50-11:10	Case Report Form Design and Completion	Amy Kroeplin
11:10-11:30	Managing the Data: Database Design, Data Entry, Reports, and Error Resolution	Amy Kroeplin
11:30-12:00	Questions and Discussion	

November 6, 2003: Clinical Research Study Implementation: Part II

8:30 - 9:00	Continental Breakfast	
9:00 – 10:00	Clinical Research Financial Management	Kris Jordan Paula Longden
10:00 - 10:45	Quality Control of Data Collection <ul style="list-style-type: none"> • Internal Study Performance Monitoring and External Study Audits • Source Documentation (What, Why and How) Study Close-out and Records Retention	Cathy Kneut Rosemary Galvin
10:45 – 11:00	Training and Certification Resources	Maureen Clark
11:00 - 11:30	Questions and Discussion	

November 6, 2003: Clinical Trials: FDA regulations and ICH Good Clinical Practice

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

12:00 – 3:00

Regulatory historical framework
Code of Federal Regulations
PA, MA, CCRA
(ICH) Good Clinical Practices

Terry Himmelmann

B. Introduction to Clinical Research**INTRODUCTION TO CLINICAL RESEARCH SCHEDULE**
Tuesday, July 15

8:00-8:30	<i>BREAKFAST</i>
8:30-9:15	<i>Introduction and Course Overview</i> Voula Osganian, MD, ScD David Wypij, PhD
9:15-10:10	<i>Introduction to Study Design</i> Voula Osganian, MD, ScD
10:10-11:00	<i>Bias and Confounding</i> Alison Field, ScD
11:00-11:15	<i>BREAK</i>
11:15-12:15	<i>Designing Surveys and Questionnaires</i> Sion Kim-Harris, PhD
12:15-12:30	<i>Clinical Research at Children's Hospital</i> James Mandell, MD
12:30-1:15	<i>LUNCH with Researchers from Children's Hospital</i>
1:15-2:45	<i>Introduction to Data Analysis</i> David Wypij, PhD
2:45-3:00	<i>BREAK</i>
3:00-4:00	<i>Writing for Scientific Presentation</i> Jean Emans, MD

INTRODUCTION TO CLINICAL RESEARCH SCHEDULE
Wednesday, July 16

8:00-8:30	<i>BREAKFAST</i>
8:30-9:45	<i>Data Analysis I: Comparisons and Associations</i> Henry Feldman, PhD
9:45-10:00	<i>BREAK</i>
10:00 -11:00	<i>Logistics of Data Collection and Data Management</i> Amy Kroeplin, BA Jason Rightmyer, MS
11:00-11:30	<i>Scientific Presentations</i> Jonathan Finkelstein, MD
11:30-12:00	<i>The General Clinical Research Center (GCRC)</i> Richard Grand, MD Kristine Jordan
12:00 -12:45	<i>LUNCH with GCRC staff</i>
12:45-1:45	<i>Case - Control and Cohort Studies</i> Donald Goldmann, MD
1:45 - 2:45	<i>Data Analysis II: Correlation and Regression</i> Henry Feldman, PhD
2:45 - 3:00	<i>BREAK</i>
3:00 - 4:00	<i>Clinical Trials</i> Jane Newburger, MD

INTRODUCTION TO CLINICAL RESEARCH SCHEDULE
Thursday, July 17

- 8:00-8:30** ***BREAKFAST***
- 8:30-9:45** ***Statistical Issues in Study Design***
David Wypij, PhD
- 9:45-10:30** ***Ethical Issues in Pediatric Research***
Walter Robinson, MD
- 10:30-10:45** **BREAK**
- 10:45-12:00** ***Human Subjects and the Institutional Review Board***
Susan Kornetsky, MPH
- 12:00-1:00** ***LUNCH with CRP staff***
- 1:00-2:00** **Obtaining Informed Consent**
Kristi Thomas, MS, RN
- 2:00-2:30** ***Writing a Grant and Applying for Funding***
Voula Osganian, MD ScD
- 2:30-3:00** ***Developing a Budget and Budget Management***
Cheryl Sweeney
- Your Grant Application's Pathway through Children's Hospital
and the Office for Sponsored Programs***
Liam O'Connor
- 3:00-3:15** **BREAK**
- 3:15-3:45** ***The NIH Peer Review***
Voula Osganian, MD, ScD
- 3:45-4:00** ***Wrap-up***
Voula Osganian, MD, ScD
David Wypij, PhD