

A.1. Selection of Pilot/Exploratory Studies (Aim 1)

The Biostatistical Core will collaborate with the OAIC leadership in the preliminary selection of pilot/exploratory studies and Biostatistical Core staff will consult with clinical investigators to ensure that these studies are properly designed.

A.2 Design and Analysis (Aim 2)

A primary function of the Biostatistical Core will be to collaborate with investigators on appropriate designs for studies of multifactorial geriatric health conditions, including power and sample size determinations, proper methods of sampling and/or randomization (when applicable), control of bias, robust methods for estimating treatment effects, use of proxies and of novel and efficient designs, such as factorial and crossover experiments, development of plans for interim monitoring of study progress, and considerations about cross-study analyses. A major issue in these designs will be accounting for loss of information from the experimental participants because of deaths, serious illness, etc. The appropriate use of proxies and other techniques for recording surrogate information will be introduced into the study designs to reliably capture this information.

A second primary function of the Biostatistical Core will be to collaborate with investigators on the analytic plans for OAIC studies prior to their initiation. These plans will be developed in collaboration with the investigators of each project to ensure appropriate clinical input. In general, these plans will include considerations of recruitment, baseline comparability of treatment arms, completeness of follow-up, adherence and compliance to assigned therapy, data quality, monitoring of safety and treatment efficacy, appropriateness of subgroup analyses and control for multiplicity (multiple comparisons and outcomes). Since the analysis flows from proper statistical design and appropriate hypotheses, the Biostatistical Core will ensure that the analytic plans and study designs are consistent with meeting the primary objectives of each study and of the OAIC. The Biostatistical Core will also conduct all analyses for OAIC studies according to the established project timelines. For non-OAIC studies, the Biostatistical Core will consult with investigators about study design issues for new grant applications; however, except for consultation for complex biostatistical issues and supervision of the biostatistical staff, Biostatistical Core services thereafter will be funded by external grant support.

A.3 Grant Preparation (Aim 3)

The Biostatistical Core staff will allocate some of its resources for grant preparation for non-OAIC studies that relate to multifactorial geriatric health conditions. Biostatistical Core staff will consult with investigators about issues related to study design, sample size, and analysis; however, it is expected that these studies will generate external grant support to hire additional staff.

A.4. Application/Development of New Statistical Methodology (Aims 4,5,6)

A major role of the Biostatistical Core will be the application and development of new statistical methodology to enhance OAIC research (specific aims 4 and 5). Since many of the OAIC projects will involve longitudinal analyses, informative censoring because of death or the incapacity of the study participants is likely; thus, this will be a particular area of focus for the Biostatistical Core. The Biostatistical Core will keep abreast of new methodological developments and extend techniques from applied statistics to be applicable to center projects (specific aim 6). These will often include the development of new software, which is frequently lacking in this field.

Development of new methodology will be primarily accomplished through planned development projects. Planned development projects to be conducted during the early years of the next OAIC phase will focus on four areas in which there exist gaps in the knowledge about the design and analysis of longitudinal studies of multifactorial geriatric health conditions. These areas include: 1) developing analytic approaches to determine the mechanisms of action of multifactorial interventions (Peduzzi, PI, Year 1), 2) developing analytic approaches for determining the effect of precipitating events on outcome and for handling bi-directionality (feedback loops) between risk factor or treatment and outcome (Dubin, PI, Year 1), 3) utilizing geographic information system (GIS) technology to determine the penetration of interventions in the community (Holford, PI, submitted as a Development Project in Year 2), and 4) developing designs for multifactorial interventions, which allow for the determination of which components or combination of components are most associated with outcome (Allore, PI, Supplemental Award). Other methodological development will be accomplished through grants, e.g., RO1 and RO3. Since the OAIC has a common theme of conducting studies of multifactorial geriatric health conditions, the Biostatistical Core will also introduce cross-study analyses to further broaden the exploration of this theme across the rich databases that will be generated. Thus, an aim in the design of future OAIC studies will be their utility in cross-study analyses and how to combine information across different studies under one common theme.

Another area of emphasis will be the introduction of statistical methods from other fields into geriatric research. Some of these include: use of GIS, path analysis, structural equation models, renewal processes, stochastic models, functional data methods and generalized additive models. In order to accomplish these goals, the Biostatistical Core has developed a collaborative arrangement with the Division of Biostatistics at the Yale University School of Epidemiology and Public Health of which Dr. Peduzzi, the Biostatistical Core Director, is a faculty member.

A.5. Education and Training (Aims 7,8)

A strategic objective of the Biostatistical Core is education and training. Programs will be established to train statisticians and epidemiologists in geriatric research methods through one-on-one didactic sessions, seminars and journal clubs. Unlike other clinical areas, such as cancer, HIV and cardiology, little training is presently available in this area. A strategic goal of the Biostatistical Core is thus to establish such a training program. Another major focus of the Biostatistical Core will be the education of young investigators in clinical research methods to enhance their training and ultimately the quality of their research projects. The Biostatistical Core, in collaboration with the Research Career Development Core, will create a collaborative environment with junior clinical investigators to discuss their projects while educating them about proper clinical research methods. To accomplish this goal a member of the Biostatistical Core staff will be assigned to each young investigator for mentoring. Seminars also will be held focusing on clinical research methods and will be used to provide an opportunity to discuss investigators' projects.

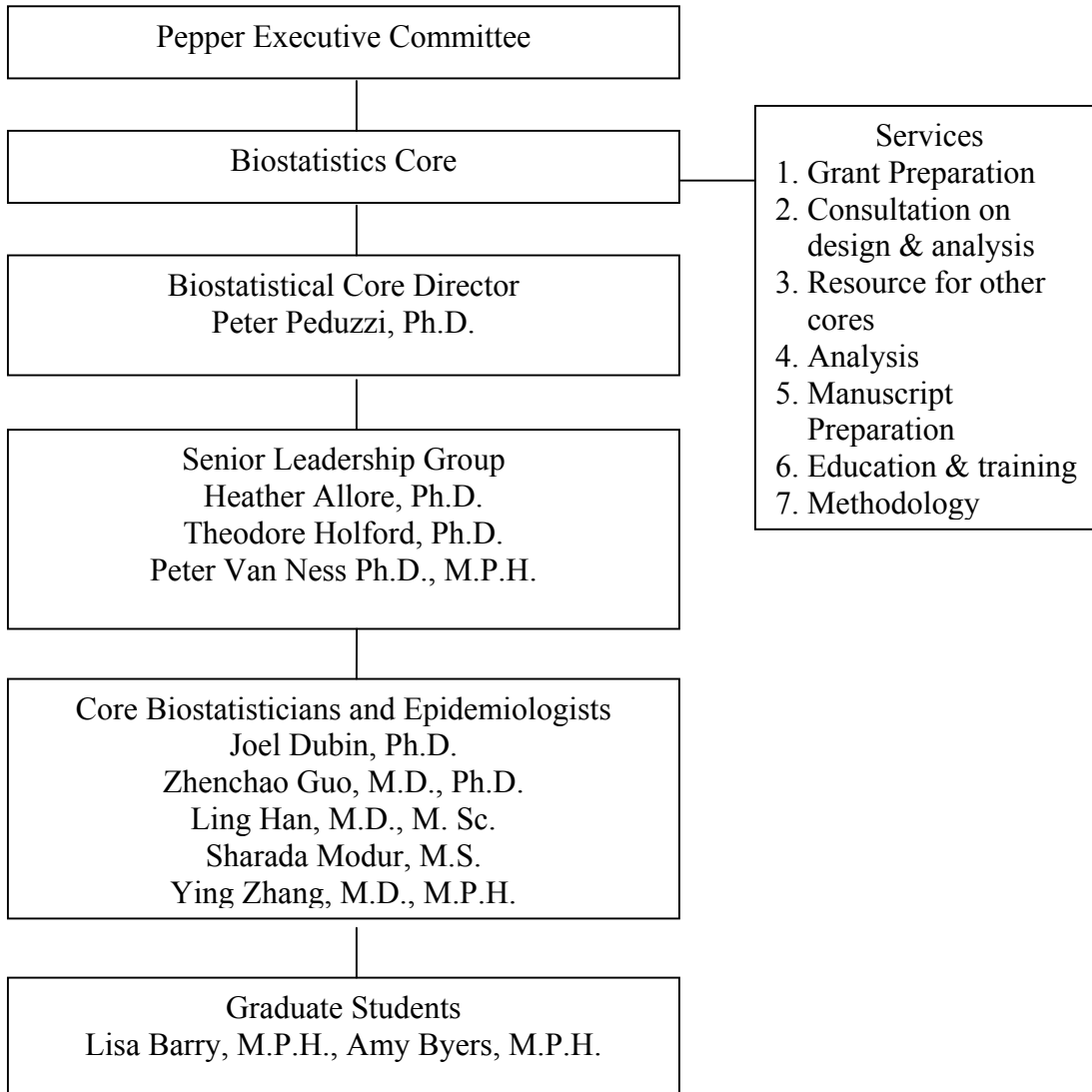
A.6. Collaboration with Other OAIC Cores (Aim 9)

An overarching aim of the Biostatistical Core will be to become fully integrated into the OAIC and to interact effectively with other Research Cores and the Executive Committee. Thus, the primary aims and functions of the Biostatistical Core have been designed to meet the goals, aims and objectives of the OAIC. The Biostatistical Core will be involved in all aspects of the design, conduct and analysis of OAIC projects and in the training and education of the next generation of geriatric researchers.

B. Administration

B.1. Organization/Structure/Composition

The administration of the Biostatistical Core will be a collaborative effort among the members of the Biostatistical Core under the direction of the Biostatistical Core Director who will be responsible for its overall operations and functions. The organizational structure of the Biostatistical Core is presented in the following figure.



B.1.1. Senior Leadership Group

A main component of the organizational structure includes the establishment of a Senior Leadership Group composed of Dr. Peter Peduzzi (Director), Dr. Heather Allore (Associate Director), Dr. Peter Van Ness (Assistant Director) and Dr. Theodore Holford (Professor in the Biostatistics Division of the Department of Epidemiology and Public Health in the Yale University School of Medicine). The Senior Leadership Group will be responsible for the scientific direction and overall operations of the Biostatistical Core, including the development of a strategic planning initiative, implementation of standard operating procedures, adherence to project timelines, assignment of staff to projects in collaboration with the OAIC Executive Committee, planning of development projects, and institution of training and education programs. The Senior Leadership Group will meet monthly to discuss issues related to the Biostatistical Core and plan strategies. Dr. Peduzzi will be responsible for the overall operations of the center, tracking of Biostatistical Core resources, and for education and training; Drs. Allore and Van Ness will oversee the daily operations of the Biostatistical Core, the tracking of projects through the Biostatistical Core and the personnel management of the Biostatistical Core staff; and Dr. Holford will oversee all methodological development and mentoring of Research Career Awardees whose focus is in biostatistics. Dr. Joel Dubin, an Assistant Professor in the Biostatistics Division, will assist Dr. Holford in some of his supervisory tasks and methodology development. In addition, the Senior Leadership Group will assume the primary collaborative role with investigators in the preparation of all new major grant applications, e.g., ROI's, and the generation of development projects.

B.1.2. Biostatistical Core Expertise

The Biostatistical Core staff has a broad range of expertise that will enable them to effectively contribute to the mission of the OAIC. The statistical expertise of the individual Biostatistical Core members is summarized in the following table.

Biostatistical Core Member	Statistical Expertise
Peter Peduzzi, Ph.D.	Randomized clinical trials, novel study designs (factorial, crossover, etc.), survival analysis, variable selection procedures, prognostic models, longitudinal models with informative censoring
Theodore Holford, Ph.D.	Epidemiological and observational studies, GIS, longitudinal analysis, survival analysis, log-linear models
Heather Allore, Ph.D., M.S.	Experimental design, parametric and non-parametric statistical methods, time-series analysis, longitudinal analysis, infectious disease modeling, simulation modeling, economic modeling, quantitative genetics
Van Ness, Peter, Ph.D., M.P.H.	Ordinal regression modeling, loglinear modeling, methodology of scale construction, categorical and longitudinal data analysis; social epidemiology, especially the impact of religious and socioeconomic factors on health
Ling Han, M.D., M.Sc	Longitudinal analyses, design and analysis of epidemiological studies of drug-health outcome relationships, evaluation of diagnostic instruments, psychiatric epidemiology and mental health of aging
Zhenchao Guo, M.D., Ph.D.	Epidemiology of aging, longitudinal analysis, categorical analysis, survival analysis, design of epidemiological studies, generalized linear models.
Joel Dubin, Ph.D.	Longitudinal analysis, functional data analysis, survival analysis, graphical methods
Ying Zhang, M.D., M.P.H.	Epidemiological studies, clinical trial design, linear, logistic and log-linear modeling, longitudinal and survival analysis
Sharada Modur, M.S.	Bayesian analysis, empirical Bayes methods
Amy Byers, MPH, Doctoral Candidate, Yale University, Epidemiology and Public Health	Extensive knowledge and application of SAS. Proficient in Longitudinal Analyses and Non-Gaussian distributions.
Lisa Cataldi Barry, MPH, Doctoral Candidate, Yale University, Epidemiology and Public Health	Extensive experience in data management and analysis using SAS. Proficient in multivariate modeling

B.1.3. Standard Operating Procedures

One of the first objectives of the Biostatistical Core will be to establish standard operating procedures (SOP's) to address: efficient resource allocation, access to Biostatistical Core resources, documentation of procedures, interfacing with other Pepper Center Cores, communications, professional development, education and training programs, and strategic planning initiatives. Although many of the SOP's already exist in practice, an initial strategic objective will be to codify and expand upon these procedures for the Biostatistical Core. Links to some relevant documents are provided below.

B.3. Prioritization of Access to Biostatistical Core

The priority of access to Biostatistical Core resources will be:

- (1) OAIC Pilot/exploratory studies
- (2) OAIC career development awardees
- (3) Biostatistical Core developmental projects
- (4) Other Yale OAIC cores
- (5) Non-OAIC projects (involving consultations with junior and senior faculty for the preparation of new grant application for addressing complex analytic and design issues, and for supervising biostatistical staff).

Priority will be given to Pepper Center activities that are funded directly by the OAIC. The initial plan is to allocate FTE according to the priorities listed above. The utilization of Biostatistical Core resources will be carefully tracked and the initial plan for allocating FTE will be evaluated and modified as necessary. The top priority will be given to pilot/exploratory studies and to development projects. In addition, each career awardee will be assigned a member of the Biostatistical Core for consultation for up to four hours a week and help in identifying biostatistical support. To maximize resources, the Senior Leadership Group will initially collaborate with investigators in all aspects of the statistical design for new major grant applications. This will include consultation about the type of design, sample size and power determinations, and plans for analysis. It is anticipated that over the five-year grant period junior Biostatistical Core staff, with proper mentoring, will assume more of a leadership role in this area. Outside grants will be expected to generate beyond Biostatistical Core resources to hire additional personnel; Biostatistical Core resources will not be used to support non-Pepper Center grants except, as noted above, to provide consultation on complex analytic issues and to supervise biostatistical staff assigned to non-OAIC projects. In addition, time has been allocated for Biostatistical Core staff to prepare grant submissions for professional development to support research endeavors that are consistent with the mission of the OAIC. This funding will be used to provide protected time for these research activities and to hire additional staff to cover Biostatistical Core activities. It is important to note, that while prioritizing access to Biostatistical Core resources is necessary and methods for establishing these priorities have been developed, the goal is to ensure that all worthy planned and ongoing projects addressing multifactorial geriatric health conditions have the necessary biostatistical support. The plan is to build on the Biostatistical Core by adding staff as needed to meet the needs of all non-OAIC projects. As in the past, the presence of the Biostatistical Core will allow us to more efficiently build the biostatistical staff and, more importantly, will allow us to recruit outstanding biostatisticians who are attracted to the stimulating intellectual environment created by the Biostatistical Core.