HARVARD MEDICAL SCHOOL

GLOBAL CLINICAL SCHOLARS RESEARCH TRAINING PROGRAM

PROGRAM CURRICULUM
JUNE 21, 2014 TO JUNE 6, 2015

The Harvard Medical School Global Clinical Scholars Research Training (GCSRT) Program curriculum is designed to enable scholars to develop knowledge and sharpen skills in clinical research.

FOUNDATION AND ELECTIVE COURSES

The curriculum's foundation and elective courses allow scholars to obtain a broad fund of knowledge in clinical research and then overlay specialized information in their concentration of either advanced epidemiology (Epi-GCSRT) or clinical trials (Trials-GCSRT).

Both concentrations require scholars to take the A-elective courses and their choice of B-elective courses. Depending on the concentration, scholars will take either *Principles and Practice of Clinical Trials* or *Introduction to Advanced Quantitative Methods* in the C-elective courses.

CAPSTONE PROJECT

Training in planning and writing a clinical research proposal will be accomplished through the Capstone Project. Launched during Workshop 2, scholars will develop a research question and begin writing their proposals. Feedback on the proposal will be provided by faculty.

A draft of the proposal is due March 23, 2015, the day after spring break ends. This draft will be reviewed by peers and faculty before scholars develop their final versions and submit them on May 1, 2015. The top 10% of scholars will be invited to present their studies during Workshop 3.

GCSRT PROGRAM CURRICULUM TIMELINE

FOUNDATION COURSES

F101 - Introduction to Biostatistics
This course provides a thorough introduction to the most commonly used biostatistics techniques for clinical research. Specific topics include tools for describing central tendency and variability in data; methods for performing inference on population means and proportions via sample data; statistical hypothesis testing and its application to group comparisons; and issues of power and sample size in study designs. There is an introduction to simple linear regression and survival analysis. While there are some formulae and computational elements using Stata, the emphasis is on interpretation and concepts.

F102 - Introduction to Epidemiology
This introductory course in epidemiology presents an overview but not a detailed discussion of the basic methods of epidemiology and their applications to clinical research. Lectures explore such basic principles of epidemiology as the importance of measurement, including types of outcome measures and measures of association; diverse array of study designs available in clinical research, including cross-sectional studies, cohort studies, case-control studies and experimental designs; types of potential biases, including selection bias and measurement bias; confounding and methods for its avoidance and control; and effect modification.

F103 - Applied Regression
The course is designed for students who have completed A101, i.e., students with a good working knowledge of elementary descriptive statistics; sampling distributions; one and two sample tests for means and proportions; correlation and basic linear and multiple regression model building. Initially, lectures will explore general concepts in linear regression and consider residual analysis and data transformations. Lectures will address multiple linear regression, including consideration of confounding and effect modification. Model building will be emphasized. Lastly, several lectures will explore topics in logistical regression including, 2x2 Tables and stratification, model building and assessment of goodness of fit, and smoothing and generalized additive models.

"GCSRT is a great opportunity for focusing on the concepts of epidemiology, clinical trials, and biostatistics."

Santi Trimarchi, MD, PhD
University of Milan, San Donato Milanese, Italy

F104 - Survival Analysis
This course is designed for students who have completed A101 and A103. It builds on the basic concepts of survival analysis discussed in A101, including hazard functions, survival functions, types of censoring and truncation, Kaplan-Meier estimates, log-rank tests and their generalization. The course introduces statistical models and methods useful for analyzing univariate and multivariate failure time data. After completing this course, students will be able to describe time-to-event data and compare groups with a time-to-event outcome; interpret the coefficients and control for confounding using a Cox proportional hazards model; interpret interaction terms and incorporate time varying covariates in a Cox model as well as assess the proportional hazards assumption. Lastly, students will learn how to complete a sample size calculation for a survival study.

F105 - Causal Design
Causal inference is an overarching objective of most forms of medical and epidemiological investigation. Key questions usually consist of whether an intervention works and the extent of the benefit and whether it causes harm. While a randomized controlled trial design is considered the most powerful way to infer causality, such studies may not be possible or feasible and an observational approach may be necessary to attain causal inference. This course builds on A102. At the end of the course, students will have a deeper understanding of observational approaches, especially from the perspective of overcoming the problem of confounding. Students will be able to define confounding and develop approaches toward identifying confounders. DAGs, as a structural approach to identifying confounders, will be highlighted. Other topics will include the rules of D-separation and conditioning on common effects. Propensity scores will be introduced. The differences between randomized trials and observational studies are considered and quasi-experimental designs introduced.

FOUNDATION COURSES (CONT.)

F106 - Longitudinal and Correlated Data
A longitudinal study refers to an investigation where outcomes and possibly treatments or exposures are collected at multiple follow-up times. A longitudinal study generally yields multiple or "repeated" measurements on each subject, which may correlate over time. With correlated outcomes, it is useful to understand the strength and pattern of correlations. Characterizing correlation can be approached using mixed-effects models or generalized estimating equations (GEE). This course covers methods to analyze longitudinal data, including the use of linear regression models. Topics will include polynomial trends for time (e.g., linear or quadratic) and linear mixed-effects models. At the end of the course, students will be able to interpret the results from a multilevel model and understand how to incorporate multiple random effects into the model. Students will be able to understand the types of missing data that occur in longitudinal and cross-sectional analysis as well as understand the assumptions associated with each analysis approach. This course requires completion of A101, A103, and A104.

F107 - Special Topics in Biostatistics
This course seeks to synthesize the importance of key topics that have already been covered (e.g., power analysis and sample size) and discuss other important statistical topics such as agreement studies and factorial design. The lectures will play an integrative role with lectures in F101, F103, and F104. For example, the power analysis lecture identifies and distinguishes the design factors affecting the precision and power of a planned investigation and addresses the trade-offs among design parameters within constraints of time and resources. At the end of the course, students will be able to prepare a thorough and pertinent statistical justification for sample size, precision, power, and detectable effects in a planned investigation as well as interpret and evaluate the power-analysis aspects of a research proposal or published report.

"The online courses provide flexibility in my schedule, and the workshops are a valuable tool for networking and for team building."

Krishna Soujanya Gunturu, MD
Tufts Medical Center, Boston, Mass., USA

2013-14 GCSRT Program Scholars

A-ELECTIVE COURSES

A101 - Career and Leadership Development
This course examines different aspects of working and leading a team. Lectures will discuss the need to manage a talented group of people effectively, pilot successful collaborations within and outside a group, navigate the complexities of the institution, and manage the inevitable conflicts that arise in a high-stakes environment.

A102 - Ethics and Regulation
This course reviews some common challenges in the conduct and review of biomedical human subjects research. Lectures examine the history and evolution of ethical codes and regulations; the role and responsibility of physicians as investigators; the preparation of research protocol applications and informed consent documents; and the challenges of conducting research involving children and adolescents.

A103 - Biostatistical Computing
The ability to import data into a statistical package from a database or Excel spreadsheet is considered essential in clinical research. Introductory lectures will consist of teaching the basic functions of the Stata program, including learning key commands, creating a do-file, getting data into the shape needed for analysis, and checking for errors. More advanced lectures will focus on using Stata for regression and survival analysis. Lastly, there will be lectures on developing polished manuscript-ready tables and figures.

B-ELECTIVE COURSES

B101 - Survey Design
This course covers the crafting of survey questions, the design of surveys, and different sampling procedures that are used in practice. Longstanding basic principles of survey design are covered. Statistical aspects of analyzing complex survey data will be featured, including the effects of different design features on bias and variance. Different methods of variance estimation for stratified and clustered samples will be compared. The handling of survey weights will be discussed. The capabilities of Stata for such analyses will be emphasized.

B102 - Drug Development, Drug Regulation, and Drug Safety
Drug development, drug regulation, and drug safety are complex and highly interrelated activities that involve bringing a pharmaceutical, diagnostic, or device discovery to approval and market. Seminar topics include: *How are Drugs Discovered and Developed*, *Case Study of the Pre-clinical Stages of Drug Development*, *Moving a Compound Through the Drug Development Process*, *Good Manufacturing Practices—a Global Perspective*, and *Overview of Diagnostic Device Development*. Overviews of drug regulation focusing on the activities of the U.S. Food and Drug Administration and European Medicines Agency are also covered. Lastly, lectures on drug safety include the following topics: *Methods in Drug Safety Monitoring* and *Drug Safety in the Pre- and Post-approval Phases*. The course is largely webinar-based and consists of discussions by experts from academia, industry, and government with years of hands-on experience with large and small pharmaceutical, biotechnology, and related organizations.

C-ELECTIVE COURSES

C101 - Principles and Practice of Clinical Trials
This course focuses on how to conduct clinical trials effectively. The course content includes lectures on study design and implementation including different designs, endpoints, study protocol, study population, recruitment, baseline assessment, randomization, stratification, and blinding. Other key issues that are covered include data analysis and sample size and power, treatment regimens and follow-up procedures, and monitoring and interim analysis plans. Lastly, other areas covered include data management and ethical issues, including protection of human subjects.

C102 - Introduction to Advanced Quantitative Methods
This course will provide students with the application of advanced quantitative methods as they pertain to T4 translational research. Topics include an overview of comparative and cost-effectiveness research, meta-analysis, quasi-experimental designs including instrumental variables and marginal structural modeling, propensity scores, and time-series analysis.