

The Academic Program

Consistent with the National Institutes of Health (NIH) emphasis on the reduction and elimination of health disparities, we have just received notice of grant funded to support a Master of Science in Clinical Research curriculum (MSCR) under the umbrella of the Master of Science in Biomedical Science at UH's John A. Burns School of Medicine (JABSOM). The curriculum will provide high quality training for **doctoral and postdoctoral candidates** in order to increase the critical mass of clinical researchers, including minority investigators, at UH. In addition to offering knowledge and skills needed to pursue careers in clinical research, the MS in biomedical science will function as a supportive mechanism for newly trained investigators, actively facilitating career development and encouraging research collaborations, particularly those related to health disparities research.

By participating in the curriculum, students will acquire skills in epidemiology and biostatistics and master the scientific principles that underlie clinical research methods. They will also develop the ability to identify and resolve ethical issues involved in clinical research, ensure the safeguarding of human subjects, and understand Institutional Review Boards and other relevant requirements. Finally, students will increase their capacity to seek and obtain NIH and other extramural funding for conducting clinical research.

The curriculum has been specifically designed to produce well-educated clinical researchers capable of implementing clinical research studies. The part-time curriculum can be completed in two years and is competency based. There are three aspects of the curriculum: didactic and problem-based modules, a mentored research project, and a seminar series. The program targets junior faculty, fellows, residents, and doctoral candidates from biomedical science, Nursing, Social Work, Psychology and Public Health. Gathering trainees from diverse disciplines into a small group learning experience will broaden trainees' perspectives as well as increase opportunities for innovative, cross-disciplinary collaborations in clinical research.

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Master's Degree (Plan A or B- this refers to the UH graduate program definition)

Adult learning theory and problem-based learning will be used to ensure that graduates develop the skills to become self-directed learners. The five competency domains include research, professionalism/ethics, culturally competent leadership and communication, interdisciplinary collaboration, and self-directed learning. Traditional graduate course evaluations will be complemented by outcome evaluation criteria developed by the Curriculum Advisory Committee to determine whether students have met competency requirements.

Requirements

Table 1 Competency-Based Curriculum

Didactic Component (20) credits	Semester Credits
Introduction to Clinical Research and Informatics Applications in Research	2
Legal and Regulatory Issues, Bioethics and the Institutional Review Board	2
Applied Biostatistics in Clinical Research	3
Applied Clinical Epidemiology and Biostatistics	3
Bioanalytical Methods in Clinical Research	2
Clinical Research Protocol Development and Scientific Writing	3
Elective course opportunities	5

Note: One semester credit is equivalent to fifteen contact hours in a semester.

Trainees must earn grades of B or better in all courses for successful completion; courses that do not result in a grade of B or better will not be counted toward the degree. An overall B average must be maintained to continue in the MSCR program.

Research Component (8 credits) - equivalent to a one-year research practicum. Requirements for completion are as follows:

- Approval of a research proposal.
- Receipt of IRB approval.
- Completion of a clinical research project.
- Preparation and presentation of an abstract for an oral or poster presentation at a regional/national scientific forum/meeting/congress.
- Preparation of a manuscript for submission to a peer-reviewed scientific journal.

Seminar Component (5 credits) - Enrollment in a one-credit seminar each semester during the curriculum will be required. Requirements for completion include:

- Consistent attendance at all meetings.
- Acceptance of responsibility for all assigned seminar presentations.
- Satisfactory peer evaluations.
- Submission of self-evaluation portfolio describing learning outcomes.

PROPOSED RESEARCH ACTIVITIES AND TRAINING EXPERIENCES

Students will participate in a seminar series, attend courses, and complete a mentored research project. Seminars will explore health issues in Hawai'i, focusing particularly on

health disparities, and will enable trainees to interact with leading clinical researchers in Hawai'i. Courses will provide the methodological foundation and the practical tools that will prepare trainees to conduct clinical investigations. The mentored projects will facilitate in-depth learning that will enable trainees to become leaders in their chosen fields.

Seminar series

The seminar series will provide a broad overview of research, health and health disparities topics in Hawai'i. The series will invite participation of leaders from both research and community settings. Seminar topics will include ethnic disparities in health research, Native Hawaiian health, childhood research initiatives, fitness and obesity research, social and cultural factors related to health outcomes, and ethical aspects of research. Lists of seminar topics and instructors that have offered to participate are available for review, and we expect this list to expand as the MSCR gains momentum. The seminar series will cover both studies of clinical outcomes and health services. As small group discussions, seminars offer a forum for exchange of ideas and nurturing of students' relationships with instructors, many of whom may also serve as mentors for trainees' individual projects.

As an extension of the seminar series, the UCSF consultants, Stephen Hulley, Charles McCulloch, Bernard Lo, Deborah Grady, and Jeff Martin, will conduct an annual two-day teaching seminar, focusing on current issues in clinical epidemiology, biostatistics, and bioethics.

Course offerings

All of the required courses, as described below, have been specifically designed for the proposed MSCR. Courses were developed to give a greater clinical focus than is possible with currently available courses. The new courses complement electives. UH and UCSF offer a wide range of courses the trainees might elect.

Introduction to Clinical Research, 2 semester credit, REQUIRED Faculty: Dr. Harrigan, Associate Dean, Interdisciplinary Research

The Introduction to Clinical Research will be essential in bringing all new trainees to the same level. The main objective of the course is to educate trainees in the essential aspects of clinical research and the basic processes of building patient-oriented research studies. This course explores the basic concepts of clinical research, starting with the history of fundamental studies and the researchers that have contributed to the field. In addition, this course will include the fundamentals of study conception (hypothesis), design (approach), and conduct (implementation) of clinical research with an emphasis on different clinical settings and analyses. In this course, trainees will:

- acquire the skills for designing and interpreting clinical research;
- produce a complete concise draft of a research protocol;
- help others in the class to develop these skills and protocols;
- provide feedback that will improve the workshop and its materials; and
- in time, contribute to the field by teaching these skills to others.

Management, ethics, funding, publications, and regulatory aspects will also be discussed. A brief description of different bioanalytical methods, bioinformatics and genetics will be presented. The fundamentals of biostatistical analysis as applied to clinical research will also be addressed to bring all trainees up to baseline. Topics will include: measures of central tendency and dispersion; basic probability concepts; probability distributions; sampling; estimation; hypothesis testing; student's t-test; analysis of variance; regression and correlation; the Chi-square test; and non-parametric and distribution-free statistics. Textbooks: *Designing Clinical Research*, 2nd Ed., (Hulley et al, Lippincott, Williams and Wilkins, 2001; *Biostatistical Analysis*, 2nd Edition (Zar JH, Prentice-Hall Resources: Clinical Researchers).

Legal and Regulatory Issues and Bioethics and Institutional Review Board, 2 semester credits, REQUIRED Faculty: TBA

This course is intended to provide a broad base of information about the legal and regulatory issues of the clinical research enterprise. Legal aspects of research with human participants will include the development of federal and state rules and regulations promulgation and implementation. Special topics concerning international harmonization and good clinical practice efforts will be discussed. Legal issues, such as the participation of children, women, prisoners, and impaired participants in clinical research, will be presented. Special attention will be given to stem cell and genetic therapy research. Information will also be provided about bioethical issues concerning the participation of human subjects in the clinical research enterprise. Ethical issues in clinical research such as voluntary participation, minimal risk, justice, and beneficence, will be presented. Text will include Dr. Bernard Lo's *Resolving Ethical Dilemmas*, 2nd ed., Lippincott, Williams & Wilkins, 2000.

Applied Clinical Epidemiology and Biostatistics, 3 semester credits, REQUIRED Faculty: Dr. Katz and Dr. Davis

Clinical Epidemiology and Biostatistics will introduce epidemiologic and biostatistical methods as applied to clinical research. The epidemiology lectures will cover study design, bias and causal associations, screening tests, and randomized clinical trials. Trainees will be taught epidemiologic measures such as relative risks and odds ratios and how to interpret these measures and their 95% confidence intervals in the context of clinical studies. Trainees will learn how to interpret screening tests in terms of reliability, validity, sensitivity, specificity, and positive and negative predictive values. The epidemiology lectures will teach the difference between "observational" and "experimental" studies, and will place substantial emphasis on the design of randomized clinical trials. The biostatistics section will include both lectures and computer applications. Trainees will learn how to analyze studies of differing designs, including randomized trials, cross-over trials, sequential clinical trials, single-subject designs, cohort studies, nested case-control studies, case-cohort designs, and case-crossover designs. For traditional cohort and case-control studies, the trainees will learn methods of stratified analysis. Reading assignments will include the 11 part "Epidemiology Series" published in *Lancet*, 2002; selected chapters from Fletcher RH, Fletcher SW, Wagner EH. *Clinical epidemiology: The Essentials*, 3rd ed., Baltimore: Williams & Wilkins, 1996; and *Methods in Observational Research*, 2nd ed., Oxford University Press, 1996, as well as handouts related to analyzing studies of various designs.

Applied Biostatistics in Clinical Research, 3 semester credits, REQUIRED

Faculty: Dr. Davis

This course will combine a didactic introduction to multivariable regression with the “hands-on” analysis of a clinical dataset. Lectures will introduce regression methods for normally distributed, binary, and count data, as well as for time-to-event data. Lectures will also cover both model building and model evaluation. To complement the lectures, each trainee will perform the secondary analysis of a clinical dataset. The datasets will be created from administrative (claims) data. Trainees will be given the opportunity to select (or suggest) a topic that interests them. Trainees can elect to analyze clinical outcomes or health service research data. Trainees will be asked to further review the literature, then to design analyses that answer a clinical hypothesis. Analyses will include descriptive statistics and multivariable regression models. The trainees will be taught basic data management skills as needed to perform their analyses. The trainees will be required to include at least one analysis using each of the regression methods they are taught. Exams will emphasize questions based on the analysis of their own and other trainee projects. The final exam will be a seminar presenting their research findings. Course readings will include selected chapters from *Statistical Analysis of Epidemiologic Data*, Selvin S., Oxford University Press, 1998, and *Multivariable Analysis: A Practical Guide for Clinicians* by Mitchell H. Katz, Cambridge University Press, 1999, as well as handouts that detail regression methods.

Bioanalytic Methods in Clinical Research (2) REQUIRED

Faculty: Dr. Csiszar

This course will provide training in concepts and techniques in molecular biology and molecular genetics. Topics will include an introduction to the molecular genetics of human diseases, methods to identify and map candidate genes, approaches to the analysis of mutations and the use of markers to study polymorphisms, evaluations of gene and protein expression using Northern, RT-PCR, real time PRC assays and Western blots. Bioanalytic Methods will also cover methods for collection, preparation and analysis of representative tissue and body fluid specimens, including the extraction of DNA, RNA and proteins. Potential applications of patient skin fibroblast cell cultures will be evaluated. Special emphasis will be given to qualitative and quantitative assays and the critical interpretation of data. Required reading will include relevant literature.

Clinical Research Protocol Development and Scientific Writing (3)

REQUIRED Faculty: TBA

The goal of this course is to further enhance the career development of outstanding clinical researchers by providing didactic training in writing skills and proposal development. Other topics to be covered in this course include: governance structure of funding agencies; identifying appropriate funding opportunities; how funding decisions are made; peer review and secondary review; the NIH application processing; how to read a Request for Application; compliance issues covering fiscal, human subjects, and animal subjects; and awarding procedures. Trainees will be judged on the merits of their mentored research proposals, which they will write as NIH Small Grant applications. Required reading will include relevant literature.

Mentored research projects

Trainees are required to complete an 8-unit (minimum) mentored research project of relevance to minority health and health disparities. To provide flexibility, trainees can extend this requirement to an extra semester with an additional 4 units of mentored research to complete their projects and manuscript preparations. Priority research areas for the mentored projects are obesity, cardiovascular disease, oral health, asthma, diabetes, HIV/AIDS, cancer, and preterm birth. Health disparities have been documented in these areas, and they are important health priorities for Hawai'i. In addition, we have identified committed mentors in each area of research. Selection and secured commitment of mentors will be guided by the PI, Co-PI, and Program Director and will require approval of an established Research Committee (specific for each trainee) and the CAC. Mentors will be accomplished clinical researchers with the time, expertise and willingness to nurture trainees' development.

Preparation for mentored projects will begin as soon as trainees enter the MSCR. The PI, Co-PI and Program Director will meet with the trainees, identify the trainees' research interests, determine whether trainees have identified a mentor, and make suggestions as to appropriate potential mentors. The PI, Co-PI and Program Director will encourage trainees to communicate with several potential mentors as early as possible to discuss research projects and facilitate determination of research focus. By the end of the second semester, all trainees will be matched with mentors.

In the fall semester of Year 01, trainees will write their research proposal during the Clinical Research Protocol Development and Scientific Writing course. The proposal will include a critical review of relevant background literature, study hypotheses and objectives, a discussion of sample size (and sampling methods, if applicable), a discussion of diagnostic criteria and other measurement issues, a timeline, and an analysis plan, including control methods for confounding variables and test methods for potential interactions.

Also by this semester the trainees will have established contact with their Research Mentoring Team. This will consist of 2 members: the trainee's mentor (committee chair), and an epidemiologist or biostatistician. The team will guide the trainees in finalizing their study designs, and will assist with project implementation. A vital component of the MSCR, however, is self-directed study, and trainees will be expected to complete their research studies independently, following the guidance and oversight of their Research Committees. We expect that by successfully completing the mentored project, including active participation in regular meetings with their Research Committees, trainees will be exposed to invaluable experience through which they will develop the tools to become skilled clinical researchers.

Sample Individual Candidate Curriculum

The Table below illustrates the proposed curriculum model for full time students. In that a number of candidates are expected to be part time (medical students, interns or residents) an example of a part time curriculum has been developed and is available for review.

TABLE 1: Program Curriculum Model

	Year 01	Year 02
S p r i n g	Introduction to Clinical Research and Informatic Applications in Research (2) Legal and Regulatory Issues and Bioethics and Institutional Review Boards (2) Applied Clinical Epidemiology and Biostatistics (3) Seminar Series (1) <p style="text-align: center;">8 credits</p>	Clinical Research Component (4) Seminars in Clinical Research (1) <p style="text-align: center;">5 credits</p>
S u m m e r	Bioanalytic Methods in Clinical Research I(2) Applied Biostatistics in Clinical Research (3) Elective course opportunity (2) Seminar Series (1) <p style="text-align: center;">8 credits</p>	Clinical Research Component (4) Seminars in Clinical Research (1) <p style="text-align: center;">5 credits</p>
F a l l	Clinical Research Protocol Development and Scientific Writing (3) Elective course opportunity (3) Seminar Series (1) <p style="text-align: center;">7 credits</p>	Possible elective choices: Qualitative Research Methods (3) Survey Research Methods (2) Medical Informatics (2) Gender Considerations in Research (2) Multivariate Methods (3) Principles of Human Genetics (3) Health Economics and Policy (3)

Total 33 credits

It will be possible for students who have completed previous course work to present requests for waivers in accordance with Graduate Division policy so that previous course work can be used to meet course requirements. Decision making regarding such petitions will be the responsibility of the Curriculum Advisory Committee and decisions made on an individual basis.

Application for Admission and Funding

Our goal is to enroll eight trainees the first year (**six funded by the grant** and a maximum of 10-12 full-time trainees in subsequent years. It is expected that the remainder of students will have other sources of funding i.e., career development funds, faculty tuition waivers, other grants). In addition, we anticipate that there will be many

trainees who choose to enroll in selected courses in the curriculum without any requirement for funding.

For the first year, we will attempt to enroll a combination of junior MD faculty members from JABSOM (or any of the programs listed above), a PhD faculty member, and a medical student based on the priorities set for selection as well as a consideration of individual qualifications. The final selection of the first cohort will be made when the Admission Committee meets to review the formal applications to the Graduate Division.

It is important that all applicants state explicitly the specific expectations/request for funding and the percent effort that will be dedicated to the Master's program.