

Introduction to CTMC

NINDS Clinical Trials Methodology Course
<http://neurotrials.training>



Roger Lewis, MD, PHD
Harbor-UCLA



Laurie Gutmann, MD
University of Iowa



Robin Conwit, MD
NINDS



Chris Coffey, PhD
University of Iowa



Will Meurer, MD, MS
University of Michigan

Course Directors

- **Identify promising investigators** in the clinical neurosciences and **provide them with a rigorous foundation** in the design, funding, conduct, monitoring/oversight, ethical performance, and reporting of patient-oriented clinical research.
- **Promote ongoing professional career development** by supporting participants before, during, and after the program to allow them to follow through on their plans for clinical trials-based research.
- **Enhance the pipeline** of scientifically sound, well designed early phase clinical investigations that will provide a foundation for pivotal, confirmatory trials to reduce the burden of high impact neurological diseases.

CTMC – Specific Aims

- Early trials are the hardest
- Expertise in planning is not evenly distributed
- Early trials should lead to scientifically interesting result (that inform future scientific steps)



Address a gap

- **Blended Experience**
 - Project based – small groups
 - Small groups of 3-4 trainees led by clinician and biostatistics faculty facilitators
 - Meet by video-teleconference in spring and fall
 - Large group (public) webinars
 - Office hours
 - Residential course
 - Mock review panel

General Structure

- Patterned as evolution of Vail Course
- 2018 is our 5th cohort
- Approximately 30-40 trainees each year
- 2015-17 had “Advanced” track with clinical trial simulation
- 2017-2018 (future) had “Biostatistics” track with early career biostatistics faculty

History

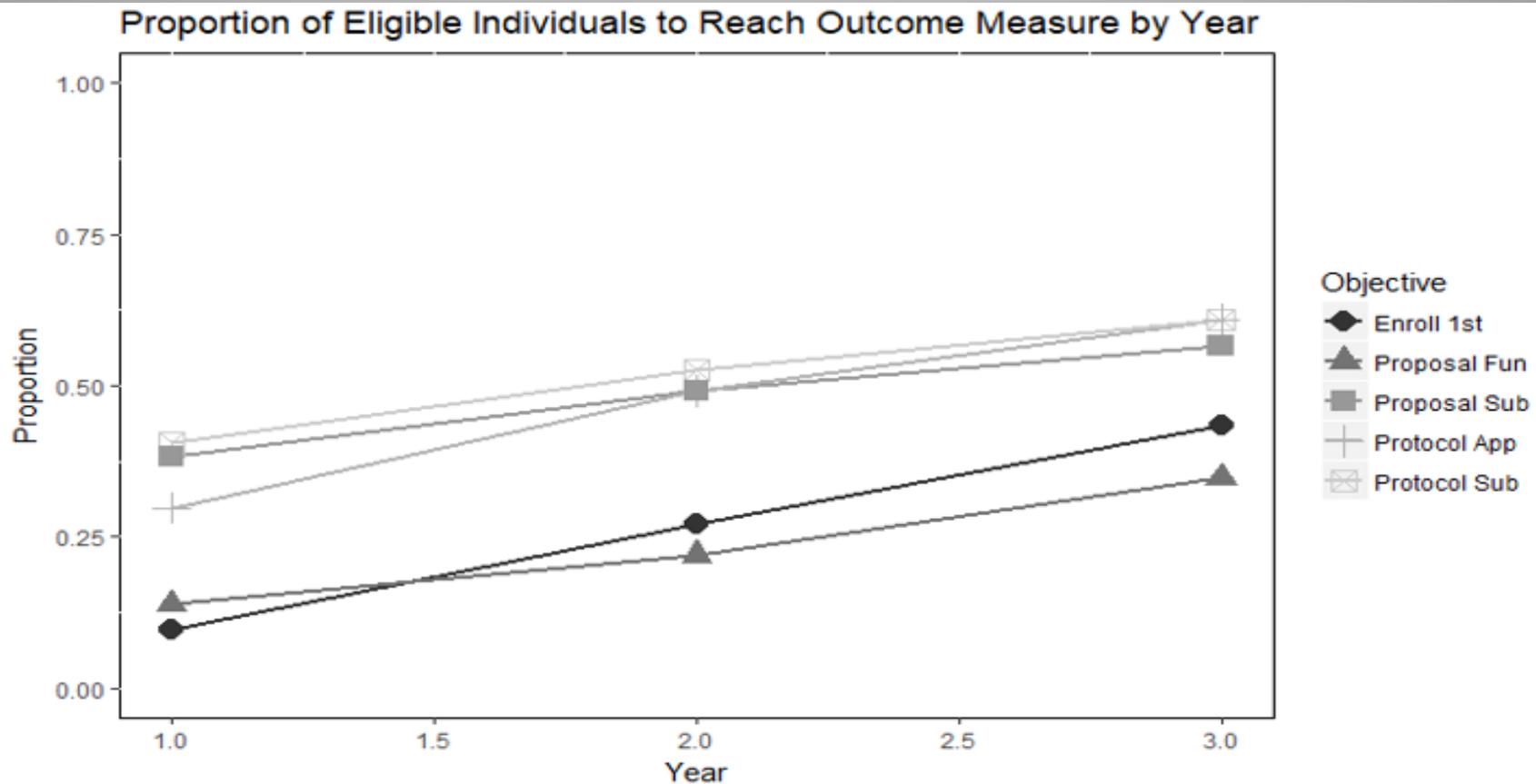


Figure 1 | Calculations for plot: Numerator is the number of people who have met an objective at or before the current time point. The denominator is the number of people of who are eligible at the current time point.

Example: 59 people are eligible to have responded to the year 2 survey. For the objective “Proposal Fund”, 13 individuals reported they received funding by the end of year 2. Therefore the proportion of people who have met this objective at year two is $13/59 = 0.22$, as seen in the above graph.

Counts	Funded	Direct	Indirect	Unrelated
NIH_K	3	3	0	3
CTSA	4	3	2	2
Foundation	11	4	5	1
Industry	6	2	1	0
R03	0	0	0	0
R01	4	1	1	2
R21	1	0	1	0
Other NIH	4	5	1	1
Other	8	6	1	3
Institutional	8	3	1	3
Departmental	5	1	1	3
Site PI NIH	1	0	0	0
Site PI Industry	5	2	2	0
Total	60	30	16	18

Funding Cohorts 2014-2016

- **Pathway A: Foundations Clinician/Investigator**

- For applicants from a clinical discipline who are designing a clinical trial. We define a clinical trial as a research project that delivers some intervention (drug, device, diagnostic, behavioral) to patients in a prospective way. While most applications are expected from individual investigators, coordinated applications from multidisciplinary teams of investigators with complementary expertise working on a single project will also be considered. If selected, all team investigators are required to participate fully in all course activities. Each team member should submit a separate application, but parts 1 and 2 should be exactly the same.

- **Pathway B: Foundations Biostatisticians**

- For applicants from biostatistics interested in developing skills in the design of clinical trials in neurological disease and injury. Those applying to this pathway do NOT need to have a partner from pathway A.

- **Pathway E: Biomarker Clinician/Investigator (applications to this track from more senior investigators are encouraged)**

- “Biomarker” refers to a measurable quantity, previously identified and specific to the individual patient at a specific time.
- Clarify the intended use of the biomarker and include supporting references. We will consider applications proposing a single biomarker that is identified a priori. Studies intended to search for new biomarkers will NOT be considered.

Pathways

- **Part 1A: Statement of Scientific Area and Key Information**

- Area of study where you will develop a clinical research trial proposal.
 - The most highly weighted criterion is a research project that delivers some intervention (drug, device, diagnostic, behavioral) to patients in a prospective way.
- Potential scientific questions and areas of important scientific uncertainty in the field.
 - This intervention should have a good basis in biology (or theory, for behavioral interventions). The best designs for this course will seek to confirm important pre-clinical estimations of dose, mechanism, or target acquisition. The goal is to learn whether and how a follow-up trial should be conducted.
- The trial design you think might be appropriate.
 - Consider the NINDS Transparency in Reporting Guidelines when drafting this section and discuss the scientific premise underlying your idea.
- The critical summary of the existing preclinical or prior clinical work that supports the evaluation of this therapy.
 - Specifically address the rigor and reproducibility of the methods of preclinical experiments that justify implementing your proposal in a clinical trial.

Application

- **Part 1B: Summary of Research Question**

- For the primary goal, do not state “establish safety.” It is well known that most safety outcomes occur relatively infrequently and small sample size studies will not reduce uncertainty about these. If establishing safety is a goal, “establish that the symptomatic intracerebral hemorrhage rate is not likely to be greater than 20%” would be responsive.
 - Indicate the target condition
 - Indicate the specific phenotype, if applicable
 - State in one sentence what the main goal of the current clinical trial or study will be
 - Describe the biological rationale (and relevant preclinical evidence)
 - State the primary clinical endpoint
 - Estimate the general scale of the sample size you believe is needed (range is preferred)
 - If this study is successful, what would the next study look like
 - State how findings from this line of work would change practice
 - Biomarker track: Describe the biomarker and how it would interact with the treatment or inform a clinical trial design

Application

- **Part 2: Potential Funding Sources**

- The second most highly weighted criterion is the review committee's estimated likelihood that the clinical trial that you are designing will actually enroll patients. Projects that use existing resources (e.g. study coordinators from local infrastructure, PI protected time for research, etc.) will receive the highest priority for participation in this course.
 - Describe at least three specific, potential areas of funding to conduct the clinical trial protocol
 - Discuss why your potential project might be desirable to the funder.
 - You should review funding histories or NIH project reporter to assess whether clinical trials in this area are ongoing or within funding priorities of these potential sources.

Application

- **Part 3: Your Biosketches**

- Please follow the instructions for the 2015 NIH biosketch format and append into your application.
- Please ensure that you have edited your personal statement to address your motivation for taking this course.

- **Part 4: Mentor Biosketches**

- The third most highly weighted criterion for selection is a dedicated mentor at your home institution that can help facilitate the project's success.
- The mentor personal statement should describe the mentorship plan and who will help them implement the project.

Application

- **Part 5: Chair's Letter (Department Chair or Division Chief)**
 - Describe the applicant's research training, experience, and potential for a successful clinical research career
 - Outline the applicant's current competing responsibilities and availability of protected research time for the two years after the clinical trials course
 - For clinician applicants: Describe the resources are currently available (contingent on IRB approval) for the applicant to conduct a clinical trial (study coordinators, project management, data management, lab processing, etc.)
 - For biostatistician applicants to advanced track: Describe the release time the applicant will have available to conduct simulations and attend planning sessions in the Spring and Fall before and after the residential course.
- **Part 6: Other materials**
 - If you plan to seek use of an investigational compound – provide in writing evidence of the availability of the compound to you for this potential clinical trial.

Application

- Applications Due – Feb 28, 2019
- Baseline survey will go out after you apply
- Decisions Made – March 15, 2019
- Small group “Match” – March 15-22
 - Trainees will rank groups based on time they meet and potentially faculty expertise area
- Small groups start meeting in April or May (remote via video teleconference)
- “Reunion” at AAN in Philadelphia
- IN-person Iowa City 2019 (odd years) , Ann Arbor (even years)

Tentative Timeline

PROPOSAL DEVELOPMENT

Instruments / Pre-Review

March

Webinars
Small Group Meetings
Travel / Logistics

April – July

PROTOCOL DEVELOPMENT

Didactics / Workshops / Small
Groups **MANDATORY**

July 22–25, 2019
Iowa City

Small Groups / Mock Study
Sections

August - October

- Reminder – use chat function to ask
- Also check out the website <http://neurotrials.training>



Questions