

# Introduction to CTMC

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



Roger Lewis, MD, PHD  
Harbor-UCLA



Laurie Gutmann, MD  
Indiana University



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**

- You should be the scientific leader of the project
- You should be ready to conduct a trial like this
- You should have the tools (including a local mentor to support you\*) to design, improve, and implement the study you propose

\*Mentor needs to be more than a supervisor

## Expectations

- **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
- U01
  - 2019 6<sup>th</sup> overall cohort, 1<sup>st</sup> under NeuroNEXT DCC
  - Approximately 20 trainees per year
  - 2019 Biomarker track
  - Will be integrated in 2021
    - (There was no Course in 2020 due to COVID-19)
- R25
  - 2018 was our 5<sup>th</sup> cohort
  - Approximately 30-40 trainees each year

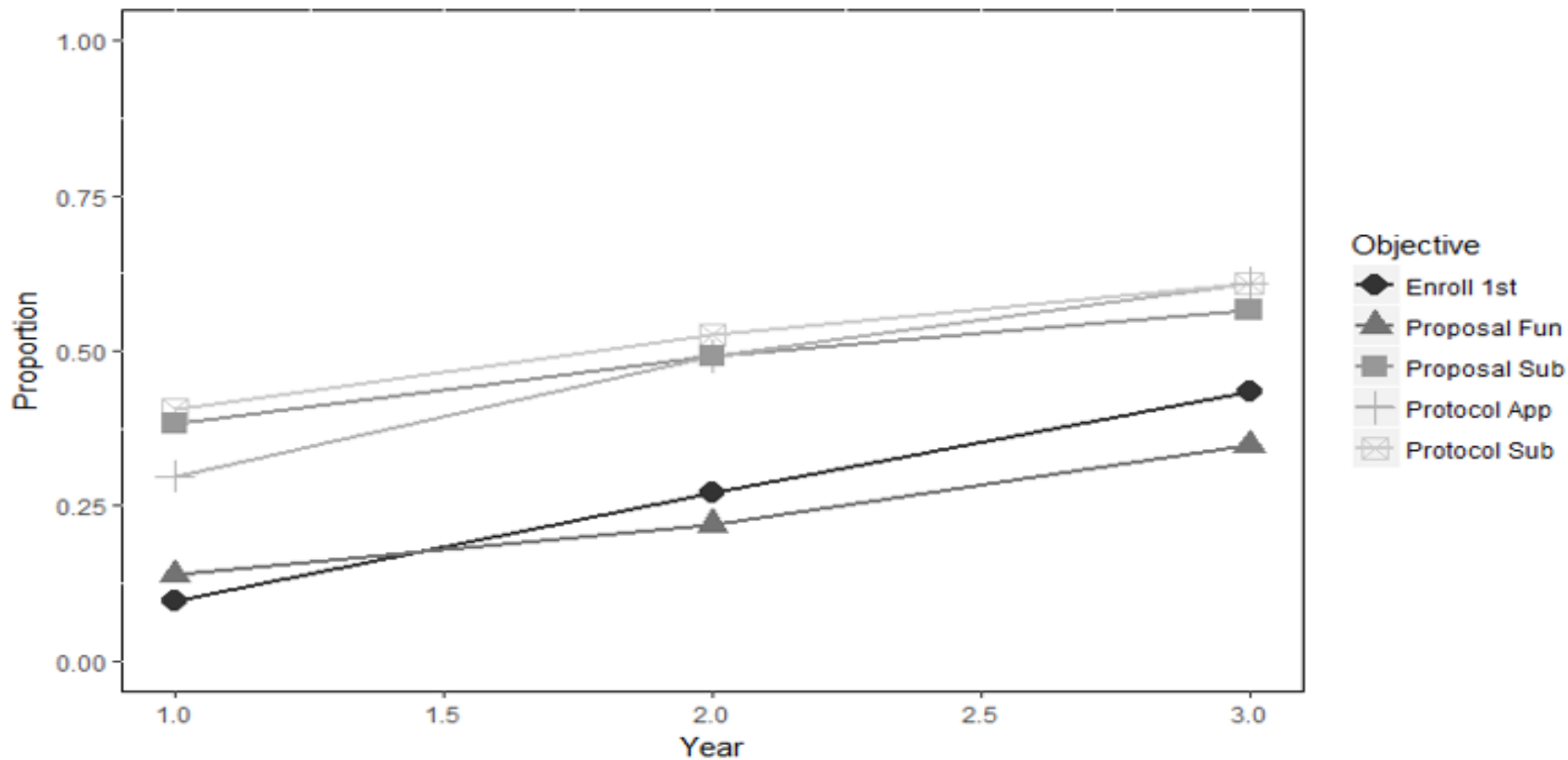
## History

- Small groups every 2 weeks before in-person course
- Assignments
- Webinars
- Draft protocol before in-person course
- **MUST ATTEND INTENSIVE EXPERIENCE (July 19-22, 2021)**
- Meetings in fall to develop grant applications
- Expect the course will **SHAPE** and **CHANGE** your idea (having local mentor engagement and flexibility is **KEY**)

## **Level of Commitment**



### Proportion of Eligible Individuals to Reach Outcome Measure by Year



**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
<b>Total</b>	<b>60</b>	<b>30</b>	<b>16</b>	<b>18</b>

## Funding Cohorts 2014-2016

- **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: Team Members**
  - List the members of your team (mentor, coordinator, biostatistician, data management, engineer, etc.) include their role in your proposed project, expertise, and email.
    - These members will be invited to your small group meetings (their attendance is not required).
  - Provide a brief paragraph summarizing how you will organize and interact with the team.
- **Part 4a: Your Biosketch**
  - Please follow the instructions for the 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 4b: 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.)
- **Part 6: Other materials**
  - If you plan to seek use of an investigational compound – you **MUST** provide in writing evidence of the availability of the compound to you for this potential clinical trial.

# Application

- Team applications are being considered for 2021
- Resubmissions get an extra page to address prior critiques

**Team Applications / Resubmission**



- Key pitfalls in applications
  - Not proposing a clinical trial
  - Proposing a phase III study
  - Proposing an underpowered phase III trial
  - Lack of a clear question or study (too much clinical or biological background)
  - Lacking preclinical data / rigor
  - Sole emphasis on safety\*
  - How this study fits – unclear what comes after
  - Study started or being conducted already
  - Changing institutions in the middle of 2021

\*Not quantitatively evaluating feasibility, proof of concept, or effect

## Discussion

- Applications Due – Feb 28, 2021
- Baseline survey will go out after you apply
- Decisions Made – March 15, 2021
- Small group “Match” – March 15-22, 2021
  - 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)
- Intensive Experience July 19-22 (Ann Arbor or virtual TBD) 2021

## Tentative Timeline

**PROPOSAL DEVELOPMENT**

Match into a small group

March

Webinars  
Small Group Meetings  
Travel / Logistics

April – July

Didactics / Workshops / Small  
Groups **MANDATORY**

July 19–22, 2021  
Ann Arbor or virtual TBD

**PROTOCOL DEVELOPMENT**

Small Groups / Mock Study  
Sections

August - November

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



**Questions**