NIDDK has funded several clinical research networks including the NASH Clinical Research Network, Adult-to-Adult Living Donor Liver Transplantation Cohort Study, Adult Acute Liver Failure Study Group, Pediatric Acute Liver Failure, Drug-Induced Liver Injury Network, Childhood Liver Disease Research and Education Network, Hepatitis B Research Network, Hepatitis C Antiviral Long-term Treatment against Cirrhosis, and Peds C. Within this group, the size of individual disease populations spans a range from very large (NASH, hepatitis B and C) to “rare”, the latter being defined as less than 200,000 cases in the United States. Rare or orphan diseases are ideally suited to the Network approach since the number of annual cases seen by any one institution is vanishingly small. When institutions combine forces using a common reporting mechanism, then the overall spectrum of disease becomes visible to all and resources can be found to support the effort.

The session will focus on clinical research network support for rare diseases and will have the following learning objectives:

1. To describe the scope of rare disease consortia: (a) Observational studies of outcomes, (b) pathobiology including genetics, (c) therapeutic trials, with industry partnering as appropriate (d) teaching and training.
2. To describe the components of a grant application that will be competitive for funding: (a) Investigators who are expert in the disease and manage a cohort of patients sufficient to ensure that enrollment during the first year will meet the needs of at least the primary project(s). (b) Resources for specialized tests within the applicant group. (c) Partnership with a lay patient-support foundation that is capable of co-funding the project.
3. To discuss the challenges and opportunities specific to rare disease consortia. An inherent challenge is designing meaningful clinical studies with small groups of patients. An opportunity is working with patients who often are highly committed, and using the consortium to raise the visibility of the disease and create new resources for patients.
Breakout Session II:
Handout Not Received
Session Description:

Data quality is essential to clinical research as data errors otherwise threaten to compromise the validity of study results. The data cleaning process offers an opportunity to transform an erroneous raw dataset into a usable analysis dataset of improved quality. This session will provide an overview of the fundamental components in creating a usable analysis dataset. Common errors encountered in raw data will be discussed, as well as, strategies to detect and correct these errors.

Learning Objectives:

- Understand key elements for constructing a usable analysis dataset.
- Identify invalid character responses and implausible numeric values within a dataset.
- Apply techniques to correct erroneous records without altering the raw data.

References:

Research questions relating to epidemiology, natural history, prognosis and causal/risk factors of disease, can be examined using an array of observational study designs.

Cohort studies are valuable for describing the natural history of disease as well as the impact of interventions, and can also identify pathogenic risk factors. Cohort studies may be prospective or retrospective.

Rare conditions or conditions where there is a long period between exposure and disease are better suited to a case-control study design, although their retrospective nature can lend them to bias.

Cross-sectional designed studies are useful for examining disease prevalence and associations, which may be “hypothesis driven” or “hypothesis free” (e.g. genome-wide association studies).

The PICO framework (Population, Intervention [or exposure in the case of observational studies], Comparison, Outcome) can be useful for crystalizing a research question into a research study with a view towards applying an appropriate study design. However, the pragmatic reality of limited data, resources, and time may necessarily lead to an alternative study design.

Attention to optimizing your data collection and minimizing the potential for bias and confounding factors, as well as developing a logical analytical framework prior to implementation of your study are vital to avoid weaknesses in study design.

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement has been developed as a guide for the reporting of studies and provides useful information to avoid pitfalls during the study design phase.

This Clinical Research Workshop Breakout Session will outline these methods for developing an appropriate observational study design and highlight ways to maximize the study quality with examples from the literature.

References and Resources

http://www.cebm.net/study-designs/
http://www.bmj.com/about-bmj/resources-authors/bmj-pico

Clinical Research Workshop

Observational Studies: Leveraging Clinical Data to Drive Innovative Research
Friday, November 13, 2015
12:00 pm – 3:00 pm

Breakout Session V: Healthcare Delivery Research

Michael Volk, MD

This breakout session will discuss Health Services Research, also called “The Science of Healthcare Delivery.” The Institute of Medicine has shown that patients receive proven treatments only half the time, and estimates that more patients die from medical errors than traffic accidents. Therefore, improving healthcare delivery could benefit patients as much or more than improved treatments. We will focus on observational studies, and discuss the traditional methods for analyzing deficits in healthcare delivery. We will also briefly discuss the new Public Health and Healthcare Delivery SIG.

A. Introductions
B. Why is healthcare delivery research important?
C. Traditional methods for observational studies in healthcare delivery
   1. Geographic variation
      a. Example: Dartmouth Atlas
   2. Disparities
   3. Quality of care
      a. Structure, Process, Outcome
   4. Patient safety
   5. Decision making, behavior and externalities
      a. Utilizing methods of econometrics
   6. Impact of public policies
   7. Workforce
D. Constructing mechanistic, hypothesis-driven models
   1. Using conceptual models
   2. Refining specific hypotheses
   3. Distinguishing between confounders, mediators and moderators
E. Funding opportunities
F. New Public Health and Healthcare Delivery SIG
G. Additional resources

AHRQ Healthcare Delivery Resources:
Comparative Effectiveness Research (CER) is the conduct and synthesis of systematic research comparing different interventions and strategies to prevent, diagnose, treat, and monitor health conditions. The purpose of CER is to inform patients, providers, and decision-makers about which interventions are most effective for which patients under which circumstances. We as doctors are most concerned about the relative benefits and harms of one treatment as compared with another for a particular patient, but traditional randomized trials are seldom designed to answer these types of practical questions. CER assess comparative benefits and harms of different competing strategies (and not just comparison against placebo) for diverse patient populations. Therefore, health policymakers, health insurers, and providers are increasingly interested in the information that could be obtained from studies of the comparative effectiveness of various treatments for specific conditions. This workshop will cover the basics of CER.

Outline:

Goal of CER
- To compare interventions head to head and monitor harms as well as benefits.
- Some examples include: comparing disease specific treatments, comparing cross-condition treatments, comparing models of care.

Patient population in CER
- CER is meant to include diverse populations representative of those cared for in clinical practice.

Study designs:
- Both experimental as well as observational designs can be used for CER.
- Although preferable, conducting randomized, controlled trials can be difficult in some cases.
- Observational research can better accommodate the large, heterogeneous populations needed to examine treatment effects and outcomes under real-world conditions over long periods.
- However, confounding and bias limit observational studies’ capacity to distinguish treatment effects from the effects of patient-related, disease-related, and provider-related factors.
- Employ analytical methods that account for biases such as confounding by indication.

Explicit evaluation of the heterogeneity of treatment effects
- Although studies typically report average effects, most participants experience...
more or less benefit and harm than average.

- Treatments must be compared within homogeneous risk strata, defined according to characteristics that affect both benefit and harm from those treatments.
- Homogenous strata can be defined based on key demographic characteristics or more importantly by employing risk-stratification models and reporting harms and benefits according to risk strata.

Outcomes of CER

- In general CER focuses on broader health outcomes than clinical research generally considers (e.g. hospitalization, need for surgery, complications of therapy)
- Emphasis on health outcomes that are relevant across diseases (e.g., function, symptom burden, activity, survival, active life expectancy).
- Account for health transitions over time.
- Evaluate longer-term changes in benefits and harms of treatments as patients’ age and acquire additional conditions.