Competing Commitments in Clinical Trials
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Why a Clinical Trial

- Effort to determine causation
- Does one treatment work better than another
- Control many variables
  - Expectations
  - Clinician biases
  - Clinical features of the subjects
  - Effects of other medications
  - Etc.
Typical Structure of Trials

- Randomization of patients
- Tight control of who is eligible
- Blinding of subjects and providers
- Comparison intervention that is the best available treatment
- Limitations on dosages
- Limitations on other medications
These features are essential

- Differences in effect between two treatments are often minimal
- The idea is to definitively determine causation and all other determinates must be controlled or eliminated.
The Problem

- Most staff in clinical trials have clinical training.
- They have a deep-seated commitment to their “patients” as most clinicians do.
- They generally, and mistakenly, think that the experimental intervention is likely to be much better for their subjects.
The Question

- How do clinical trial staff manage their competing commitments to research standards and clinical commitments?
Why does this matter?

- Clinical trials are the means by which we determine whether treatments are used
- Pharmaceutical companies, and universities, have enormous stakes in their outcomes
- You and I have an enormous stake in their outcomes
Methods 1

- Use semi-structured interviews at UMass and Harvard to learn how clinical trial staff think and talk about these issues.
- Use data to develop a survey that can ask touchy questions and still leave subjects willing to answer.
Methods 2: Sample

- Drawn from contacts on patient oriented website - Centerwatch.com
Methods 3: SurveyMonkey and Dilman Method

- Jill and Sue created a poster
- 6 rounds of different types of contacts
- Make the contacts as personal as possible
  - Real signed letters
  - Personal notes written on letters
  - Jill’s interpersonal charm on the phone
- Response rate >75%
Research centers should choose which trials to participate in based on how much the trials contribute to science.

N= 777
Researchers should only participate in trials that are likely to help the subjects that take part.
When several subjects at a site do considerably worse than would be expected in ordinary care, that site should stop recruiting for that study.
Researchers should deviate from the protocol if doing so would improve the subject’s medical care.

N= 777
The protocol should be used as a guideline rather than something to be strictly followed under all circumstances.

N = 777
Even if patients are technically eligible for a trial, they should only be recruited if being in the trial will be in their best medical interests.
It is acceptable to disregard minor entry criteria if a patient will benefit from being in a trial.
Patients who are not doing well with standard care should be recruited most actively so that being in the trial can help them.

N= 777
Clinical judgment, rather than strictly following the protocol, should be the basis for deciding to remove subjects who are not doing well.
Think of all the times during the past 2 years when you had a patient who was eligible for a clinical trial, but being in the trial seemed *not* to be in the patient’s best medical interests.
Think of all the times during the past 2 years when you have had a patient who was not technically eligible for a clinical trial, but being in the trial seemed to be in the patient’s best medical interests.
Think of all the times during the past 2 years when a medication was restricted by protocol, but giving the medication seemed to be in the subject’s best medical interests.
Think of all the times during the past 2 years when adjusting the dose of a study medication seemed to be in the subject’s best medical interests, but making the adjustment was not permitted by the protocol.
Think of the times during the past 2 years when breaking a blind without reporting it seemed to be in the subject’s best medical interests.
Think of all the times during the past 2 years when you had a subject who met termination criteria, but remaining in the trial seemed to be in the subject’s best medical interests.
Think of all the times during the past 2 years when you had a subject who did not meet termination criteria, but remaining in the trial seemed to be contrary to the subject’s best medical interests.
What do we make of his?

- Most clinical researchers follow the rules
- Most researchers try to provide good care to patients within that context.
- A significant number of clinical researchers sometimes violate the protocol in the interests of good clinical care
- There is good reason to worry about biased samples
- Because, in many cases, statistical significance depends on only a few cases, these are important problems.