

Selecting Clinical Trial Test Materials and Study Subjects

No short cuts!!!

Betsy B. Singh, Ph.D.

Supply Side West

Las Vegas, Nevada

11/2005

Context of Material Selection

The context should be related to the following:

What is the state of the science related to the Dx and the proposed intervention? What do we really know?

Has a foundation been laid for a rigorous clinical trial? Or, do the investigators think that with hundreds of people per group in a trial, with randomization, double blinding, and the use of a scale previously published that nothing else needs to be known?

Know the Foundation

- A researcher should 'own' the science related to a diagnosis to be investigated.
- A researcher should 'own' the science related to the action of an intervention.
- Previous animal trials may be needed, even for herbals from a tradition of 5000 years, if a precise question is the focus of a clinical trial.
- The easiest RCTs to execute are those with solid data from animal studies, PK/PD, experimental case series, and outcome studies as consecutive building blocks.

Question Formulation Matters

- A thorough understanding of the Aim of a research study and the hypotheses generated from this global aim within the context of the literature available should be a clear driving force behind the selection of appropriate materials and selection of participants.

Unfortunately

- Far too many researchers want to gloss over these connections and the tedious steps that may need to be taken via small side projects, for example, to shore up the existing knowledge before larger projects can be undertaken with scientific rigor.

Multiple Measures

- The use of multiple measures of different types are particularly important when there are weak connections between the outcome measures available and Dx or Tx.
- These include scales, survey items, face to face questions by a trained interviewer, physician assessments, and physical or biological markers. These can also be used to assist in assessing reliability of measures with little previous usage.
- Must keep in mind target audience for findings.
- 'Bilingual medical' approach may be best for a wide audience across multiple clinical disciplines.

Test Materials:

Both Global and Specific Measures

- Should choose standardized scale or physical measure specific for diagnosis
- Global measures may be used appropriately depending on the 'question' or as a reliability check on Dx specific measures selected
- Esoteric measures related to intervention may be included also
- Ex. OA studies

Summary: Measurement Selection

- Measures (instrumentation) should be chosen which will as precisely as possible be able to show change in participant or group status
- Validity and reliability of measurement tools are the core features of this selection process

Participant Selection

- The inclusion/exclusion criteria must be selected with a firm knowledge of the most accepted case definition of the Dx. *Wide differences in diagnoses utilized for studies for the same disorder create problems for subsequent systematic reviews, meta-analyses, and consensus building.*
- Depending on the trial phase, persons with co-morbidities which theoretically may create adverse events must be excluded. *One needs to know what the co-morbidity problems might be via knowledge of the literature base.*
- Sample size is important here. Under-sampled studies do not allow the theory of randomization to actually work. Thus, groups to be compared may not be equivalent at baseline. *Unless a 'nonequivalent' comparison group is appropriate for the question, nonequivalence between groups at baseline is to be avoided.*
- Persons who may not be capable of following through with the requirements of the protocol, if strenuous, should be excluded if at all possible. *Intention to treat analysis is not a 'fall back' procedure for poor sampling.*

Participant Selection, cont.

- Persons who have a condition which may interfere with execution of an outcome measure should be excluded; *e.g., walktime measure compromised due to cardiac problem, not OA*
- Persons should be screened out if they have a negative attitude toward the treatment modality; *e.g., family or friend did not improve from therapy; little or no confidence in therapeutic modality; 'my wife made me come'*
- Generally, persons should be screened out if they have utilized the intervention earlier; *e.g., will carry bias toward intervention into study*
- Persons currently involved in a lawsuit or workman's comp procedure secondary to the Dx should be excluded; *e.g., maybe be poorly motivated to improve due to pending legal action*
- Persons who may move before the protocol is completed

Summary: Participant Selection

- Participants need to be representative of persons with the target Dx, unless the research question targets a subcategory of these people.
- Precision in participant selection through targeted inclusion/exclusion screening, and randomization or matching, for example, in between group designs is essential to allow for appropriate generalization of findings.
- Researchers need to avoid adding bias into a design via poor participant selection processes.