How to Properly Design and Interpret Clinical Trials

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No Disclosures

Key Elements to a Clinical Trial

- Identify the question
- State research aims, objectives and hypothesis
- Determine endpoints
- Choose a design
- Create an analytic plan
- Justify sample size

Identify the Question

- Adequate background to support the question
- Single most important aspect of a study
- Avoid vague questions
- What defines a good research question?
  - FINER: Feasible, Interesting, Novel, Ethical, Relevant
- What are the elements of a good research question?
  - PICOT: Population, Intervention, Comparison, Outcome, Timing

FINER

<table>
<thead>
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<th>FINER: Guideline for developing a good research question</th>
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<td>Feasible</td>
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PICOT: Elements of a Research Question

- Population
  - What population are you interested in?
- Intervention
  - What is the investigational intervention?
- Comparison
  - What is the comparison group?
- Outcome
  - What will be measured, improved, or affected?
- Timing
  - What is the appropriate time for study and follow-up?

Research Aims, Objectives & Hypothesis

- Identifying the question
- State research aims and objectives
  - Typically one primary aim
  - Concrete with measurable outcomes
  - Developing a Hypothesis
    - Why is necessary to establish the hypothesis a priori?
      - Affects design of trial
      - Affects sample size
      - Impacts interpretation of results

Endpoints

- Identifying the question
- State research aims and objectives
- Determine endpoints
  - Aims ≠ Endpoints
  - Quantifiable
  - Measure of “effect” of interest (patient level)

Design

- Identifying the question
- State research aims and objectives
- Determine endpoints
- Choose a design
  - Pilot, Phase I, II, III
  - Based on the aims and endpoints
  - Other considerations: patient population, accrual possibility, other trial results

Choosing a Design

- Pilot Study: examines feasibility of an approach with goal of implementing on a larger scale
  - Evaluates feasibility of recruitment, randomization, assessment of procedures, new methods, and novel interventions
  - Does not evaluate a hypothesis or assess safety, efficacy or effectiveness
- Phase I: Evaluate safety, determine safe dosage range, identify side effects
- Phase II: Assesses effectiveness and further evaluate safety
- Phase III: Large number treated to confirm effectiveness, monitor side effects, compare to standard treatments
Analytic Plan

- Identifying the question
- State research aims and objectives
- Determine endpoints
- Choose a design
- Create an analytic plan
  - Plan for each AIM of the study
  - Goals?
    - Compare, estimate, test a hypothesis

Sample Size

- Identifying the question
- State research aims and objectives
- Determine endpoints
- Choose a design
- Create an analytic plan
- Justify sample size
  - Power or Precision
  - Based on primary aim

*Discussing all of the above with a biostatistician

Box 3. Tips for developing research questions, hypotheses and objectives for research studies

1. Perform a systematic literature review if one has not been done to increase knowledge and familiarity with the topic and to assist with research development.
2. Learn about current trends and technological advances in the topic.
3. Seek careful input from experts, mentors, colleagues and collaborators to refine your research question as this will aid in developing the research question and guide the research study.
4. Use the PICOER criteria in the development of the research question.
5. Ensure that the research question follows a PICOT format.
6. Develop a research hypothesis from the research question.
7. Develop clear and well-defined primary and secondary (if needed) objectives.
8. Ensure that the research question and objectives are answerable, feasible and clinically relevant.

PICOER = population, intervention, control, outcome, research question, exposure (for intervention studies only), comparator group, outcome of interest, time.

Summary

- Most important aspect of a study is to identify a question based on sound research
- Involve a biostatistician in the process to appropriately design and power a study
- Executing a trial takes time and team work

Thank you