# How To Design a Clinical Trial

This exercise will guide you through all the steps of your course project, in particular how to design a clinical trial. It will be helpful in preparing your project assignments.

We suggest that you review the entire file once before completing the first assignment, and then review it each week as you prepare your project assignments.

# Overview

### Experiment Design & Clinical Trial Design

# Designing an Experiment

- Goal:
  - Test a hypothesis
- Procedure:
  - Change one factor at a time (the independent variable)
  - Observe outcomes (the dependent variables)
- Example:
  - Compare effect of two different antibiotics on bacterial growth rate
  - Independent variable: type of antibiotic
  - Dependent variable: growth rate of bacteria
  - Must ensure that every variable (e.g. temperature, concentration of antibiotic, duration of experiment) remains the same *except* for choice of antibiotic

# Designing a Clinical Trial

- Goal:
  - Compare effectiveness of two different medical procedures
- Procedure:
  - Two groups of patients, each receives a different medical procedure (independent variable)
  - Observe clinical outcomes in the groups of patients (dependent variables)
    - Primary outcome: Most clinically important outcome
    - Secondary outcomes: Other clinical results of interest
- Example:
  - Compare effectiveness of two different types of antibiotics to treat bacterial pneumonia
  - Independent variable: Type of antibiotic
  - Dependent variables:
    - Primary outcome: duration of symptoms
    - Secondary outcomes: severity of symptoms
  - Must ensure that every variable (e.g. ages of patients, concentration of antibiotic, severity of initial disease) remains the same except for the choice of antibiotic

To design a clinical trial, you must be able to fill out all the information in the diagram below.

Use this template as a guide to help you design your trial.



## Sample Clinical Trial: Cardiac Stents



# **Determining Sample Size**

#### • What is sample size:

- The number of patients in the control and experimental groups
- How do we choose the sample size:
  - Ideally, the only difference between the control and experimental groups is the change in the independent variable
  - In practice, this is never true because of biological variability between subjects
  - We want our sample size to be large enough so that any differences between the experimental and control groups can be attributed to the change in the medical procedure and not just because of patient to patient differences
  - We want our sample size to be small enough so that we can afford to carry out the study
- Sample size calculation:
  - Estimate the expected outcomes
  - Decide what risk of error we can tolerate
  - Use statistical methods to calculate the sample size

# **Designing Your Clinical Trial**

Project Assignments 1-10

# Your Clinical Trial

#### • Goal:

- Propose a new technology to solve a health problem
- Present a mock design of the new technology and plans for a clinical trial to evaluate the technology

#### • Must identify:

- A disease of global health significance
- Current medical technologies to diagnose or treat the disease
- Limitations of those technologies in a resource challenged setting
- Design constraints of technologies in a resource challenged setting
- A new medical technology to diagnose or treat the disease
- An appropriate clinical trial design
  - Subjects to be tested
  - Primary & Secondary outcomes
  - Sample size
- Must submit:
  - An illustrative prototype
  - A clinical trial research protocol
  - An informed consent document
  - A presentation of your findings & proposed solution

# **Designing Your Clinical Trial**

#### **Project Steps:**

- Task 1: Define a public health problem
- Task 2: Evaluate a technologies to diagnose or treat this disease
- Task 3: Evaluate technology limitations
- Task 4: Define design constraints
- Task 5: Propose a new technology
- Task 6: Construct a prototype
- Task 7: Design a clinical trial, part 1
  - specify the standard of care and new technology to be compared
  - choose the subjects to be tested; control & experimental groups
  - determine inclusion & exclusion criteria
- Task 8: Design a clinical trial, part 2
  - determine primary & secondary outcomes to monitor in the trial
- Task 9: Design a clinical trial, part 3
  - determine the p-value and power
  - calculate the sample size
- Task 10: present your prototype and clinical trial plan

### Task 1. Define a public health problem

- You may select your topic from a wide range of heath issues. You must simply demonstrate that the chosen issue significantly and adversely affects the lives of people in a country or region of your choice.
- Write a one-page (typed) summary of your disease including:
  - Epidemiology
    - Prevalence in the region/country of interest
    - Incidence in the region/country of interest
    - Risk factors
  - Pathophysiology of the disease
  - Physical signs and symptoms
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green box



# Task 2: Evaluate available technologies to diagnose/treat the selected disease

- Assess the actual effectiveness of current devices or strategies employed <u>throughout the world</u> to diagnose/treat the selected disease. Consider: What are the usage constraints? Are current solutions available only to a limited population due to cost or other factors? Could alternate materials or approaches be used to reduce the overall cost? Is there another strategy/design that has never been tried?
- Write a one-page (typed) summary of:
  - Current methods for diagnosis and their constraints
    - Summarize the scientific principles of these technologies
    - Are these technologies available in the selected region?
  - Current treatments and their constraints
    - Summarize the scientific principles of these technologies
    - Are these technologies available in the selected region?
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green boxes



# Task 3: Evaluate technology limitations to diagnose/treat the selected disease

- Assess the actual effectiveness of current devices or strategies employed in the selected country or region of the world to diagnose/treat the selected disease. Consider: Of all current technologies available, which are feasible given the current resources in your selected part of the world? What investments is the health system in the region selected making to develop or implement new solutions? Are there other efforts from the private or public sectors to develop new solutions? Are there investments in basic or applied research? Are large clinical trials underway to test new solutions? What are the limitations of these approaches?
- Write a one-page (typed) summary of:
  - Current methods for diagnosis available in the selected country or region
    - The current limitations associated with the technology
    - How does this compare to other parts of the world?
  - Current methods for treatment available in the selected country or region
    - The current limitations associated with the technology
    - How does this compare to other parts of the world?

# Task 4: Define design criteria for an ideal technology solution to the health issue

- These should be quantitative measures of both technical performance and economic constraints that a technology solution must address and satisfy. Examples of constraints to consider include:
  - necessary educational level of primary user
  - necessary education level of patient/primary caregiver
  - detection limits of new screening/diagnostic methods
  - efficacy rates of new therapies
  - infrastructure requirements (e.g. electricity, support staff, lab services)
  - cultural concerns
  - time demands (e.g. # of visits to clinic, recovery time)
  - cost
  - device size/portability
- Identify the performance capabilities and costs of existing solutions, as well as the performance that new solutions should strive for.
- Turn in a one page (typed) table summarizing the design constraints of technology solutions that address the selected health issue.
  - Each row should correspond to a specific constraint (e.g. unit cost)
  - Each column should correspond to each technology considered, i.e. one for each currently available solution assessed and one for the preferred performance of a new design

# Task 5: Propose a new technology to diagnose/treat the selected disease

- Your solution should provide an advantage compared to existing options; either as an improvement to an existing device or a totally new strategy.
- For example, if your project is to develop alternative TB therapies, you might propose an alternate drug delivery mechanism (e.g. patches, controlled-release injections, implantable devices, etc) that could be used to deliver 6 to 9 months of TB therapy.
- Improvements are not limited to device design changes, but includes changes that decrease the cost to manufacture and distribute a health technology or that increase provider and/or patient access in the field
- Turn in a one page summary of your new solution, including:
  - an overview of your design
  - the scientific principles of the design
  - the expected benefits of the design
  - the potential risks associated with the design
  - an assessment of how the design meets the constraints identified in Task 4, careful to justify trade-offs made in expected performance and cost
  - the current technology your new design is intended to replace/improve
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green boxes



### Task 6: Construct a prototype

- Your prototype does not need to actually function
- Your prototype should illustrate the scientific principles of the proposed new technology, as well as the ways in which it satisfies the design requirements.
- In constructing your prototype, we suggest that you use common household materials (plastic wrap, aluminum foil, cardboard, etc) to illustrate how the device would work.
- You are limited to a total materials cost of \$10 and you will be asked to turn in receipts to verify that you satisfied this constraint.

### Task 7. Choose Subjects to be Tested

- Consider how you will test the technology in your trial:
  - What will the control group receive? What is the standard of care?
  - What will the experimental group receive? Will it be the new technology alone or the standard of care plus the new technology? Why?
- Who would be ideal subjects for a study involving your disease and your new technology?
  - In choosing the ideal subjects, consider the potential risks and benefits of your technology.
  - Remember that you want a study design with a favorable benefit/risk ratio
- What will be the inclusion/exclusion criteria for your study?
- Which patients will serve as the control group and which will serve as the treatment group?
- Turn in a design for a clinical trial. Specify the following:
  - the diagnostic/treatment standard of care and new technology to be compared
  - the experimental group and control group
  - participant inclusion and exclusion criteria
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green boxes



### Task 8. Determine Trial Outcomes

#### • Consider the outcomes of your trial.

- What will be the primary outcome monitored in your clinical trial?
- What will be the secondary outcomes monitored in your trial?
- What should be the expected values for the primary outcome in the control and experimental groups (quantitative answer)?
- What should be the expected difference in the primary outcome between the control and treatment groups (quantitative answer)?
- Turn in a design for a clinical trial. Specify the following:
  - the primary outcome of interest, and its expected values for and between your control and experimental groups
  - the secondary outcomes of interest, and their expected values for your control and experimental groups
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green boxes



### Task 9. Calculate Sample Size

- Calculate the sample size needed to compare the performance of your new technology to the standard of care. The sample size must be justified from a statistical point of view. Provide this justification.
- You may use the spreadsheet sample size calculator (provided with homework 14) to help with this exercise.
- You will need to have chosen acceptable:
  - Expected outcomes for the control and treatment groups
  - Type I error rate (p value, suggested value 0.05)
  - Type II error rate (beta, suggested value 0.2)
- Turn in a design for a clinical trial. Specify the following:
  - the preferred p-value and power, with the rational for selection
  - the calculated necessary sample size, with the equation utilized
- Attach the diagram of your trial with the appropriate box filled in.

# Your Clinical Trial: Fill in green boxes



# Task 10. Present your prototype & clinical trials plan for the new technology

- The audience for your presentation will be a scientific review panel from the World Health Organization. The panel will review the proposed designs and decide which efforts will receive funding to move into the development phase. Therefore, you must convince the panel of the severity of the problem as well as the efficacy of the proposed design.
- You should be prepared to give a 30 minute presentation.
- There will be 5 minutes for Q&A from the review panel following your presentation.



### References

University of Texas IRB approved templates <u>http://www.utexas.edu/research/rsc/humanresearch/forms/index.php</u>

Search currently supported clinical research trials <u>http://www.clinicaltrials.gov/ct</u>

An Introduction to Clinical Trials from the National Institutes of Health <a href="http://www.clinicaltrials.gov/ct/info/whatis#phases">http://www.clinicaltrials.gov/ct/info/whatis#phases</a>

### Task 9.2. Write Research Protocol

- Write a research proposal to test your technology, specifying:
  - title of the research trial
  - name of the principal investigator(s)
  - background, hypothesis, research questions, and project goals
  - research methods, design, and proposed statistical data analysis
  - human subject interactions; including source for participants, procedures for recruitment, and procedures for obtaining informed consent
  - potential risks and benefits to participants
  - sites or agencies involved in the research
- The information must be well organized and presented at the research participant's education level.
  - Example of research proposal for BME 301 Study
  - Example of research proposal for Fast EEM Study

### Task 9.3. Write Informed Consent Document

- Write a consent form for a protocol testing your technology, specifying:
  - the purpose of the study,
  - the research procedure,
  - risks and anticipated benefits to research participants,
  - alternative procedures available to diagnose/treat the health condition,
  - contact information for the principle investigator and the institutional review board,
  - the research participant's right to withdraw from the study at any time
- The information must be well organized and presented at the research participant's education level.
  - <u>Consent Form Template [Word]</u>
  - Example of informed consent to participate in BME 301 research
  - Example of informed consent for Fast EEM Study