

# DEVELOPING A RESEARCH PROTOCOL

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# Objectives

- Describe steps in developing a protocol
- Describe components of a protocol
- Discuss when to seek help when developing a protocol



# What is a Research Protocol?

- A document describing in detail how a research study is to be conducted in clinical practice, including the methodology, a plan for analyzing the results, and a plan to protect human subjects.

# What Steps Should I Take To Develop A Research Protocol

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# How to start developing a protocol?

- Follow the IRB guidelines: print and read carefully
- Keep a list of issues / questions
- Call your IRB rep or study mentor for clarification of instructions
- Follow instructions for assembling the protocol
  - e.g., surveys go in appendices





# How To Be Efficient When Developing A Protocol

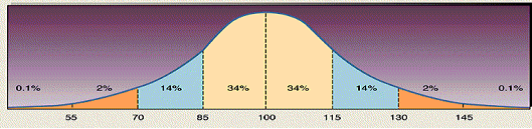
- Careful planning up front can help avoid possible disasters at the end - for example:
  - Insufficient sample size leads to:
    - ✓ Inability to draw a conclusion for a desired patient population
    - ✓ Inability to make assumptions or generalizations about findings
  - Where will you keep your study data?
    - ✓ Databases: Linking data collection to data forms, to databases.
    - ✓ Enlist help from experts, if necessary
- Work in one hour blocks of time
- Use an old protocol as a template
- Keep the protocol brief
- Write the first draft without a focus on grammar



# To Write Efficiently, Write In The Following Order

1. Cover sheet – title, investigators, contact information
2. Background of the problem (why do it?)
3. Research questions (list specifically)
4. Methods (design, setting, sample and procedures)
5. Risks, HIPAA, Informed Consent
6. Review of the literature (write it last!!)





# Protocol Development Steps

1. Know what you want to say about the study question when the study is finished
2. Write a first draft
  - Start with an outline using a completed protocol as a template
  - Do not over-write
3. Break down the protocol into components
  - Attack one component at a time





## Use A Protocol Template to:

- Replicate a study
  - To evaluate the similarities and/or differences in results from the original study
    - ✓ Recreate the study like the original study if the protocol is available
  - or
  - ✓ Use the manuscript to replicate the study





## Use A Protocol Template to:

- Construct a new study
  - Use any existing protocol as a template
    - ✓ Replicate headings
    - ✓ Borrow wordings, construction or layout
    - ✓ Research Summary Instructions available at DUHS IRB website:  
<https://eirb.mc.duke.edu/eirb/Rooms/DisplayPages/LayoutInitial?Container=com.webridge.entity.Entity%5BROID%5B2374ADAB42020F4DA3F44AD283EC1EDF%5D%5D>



# Tips For The First Draft Of A Protocol

- Keep it simple
- Use a completed protocol as a template
  - Write all components of the protocol as section headings
- Skip difficult parts
  - Farm out the task later
    - Statistical analysis section
    - Study database

# What Are Components Of A Protocol?

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# What Are Required Components for Research Protocol Submission to IRB

1. Protocol Title
2. Purpose of the Study
3. Background & Significance
4. Methods - Design & Procedures
5. Selection of Subjects
6. Subject Recruitment & Compensation
7. Consent Process – see Section 14 of the e-IRB submission form and complete the questions in that section
8. Subject's Capacity to Give Legally Effective Consent
9. Study Interventions
10. Risk/Benefit Assessment
11. Costs to the Subject
12. Data Analysis & Statistical Considerations
13. Data & Safety Monitoring
14. Privacy, Data Storage & Confidentiality



# What Should the Title Include?

1. Patient population or research question
2. The approach for the study or the comparison being made
3. Acronym if possible



# Study Title Example: SUGAR

- **SUGAR: Assessing the Suitability of Capillary Blood Glucose Analysis in Patients Receiving Vasopressors**

1. Patient population:

Patients receiving vasopressors

2. Approach or comparison being made:

“Assessing the suitability” (descriptive study)

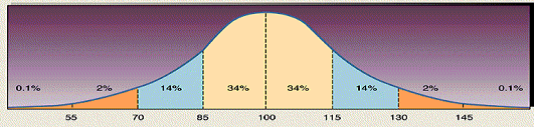
3. Acronym: SUGAR





# Study Title Example: DEET

- DEET: Descriptive Evaluation of EKG Telemetry Pathogens Study
  1. Study population:  
EKG telemetry boxes and electrodes
  2. Approach or comparison being made:  
“Descriptive evaluation”
  3. Acronym: DEET



## Study Title Example: FACTs

- **FACTs: Code Blue Registry: Identifying Factors Associated With In-Hospital Cardiopulmonary ArrestT**
  1. Study population:  
Patients with “in-hospital cardiopulmonary arrest”
  2. Approach or comparison being made:  
“Identifying Factors” (descriptive study)
  3. Acronym: FACTs



# What Is the Purpose of the Study?

- The purpose of the study is the broad problem statement
- For example, in DEET study:
  - **Purpose of the study** – The purpose of this study is to determine the relationship between surface contaminants on EKG telemetry boxes and lead wires using a new cleaning protocol as compared to standard care in Duke Heart Center cardiovascular progressive care units (7100, 7300, 3100 and 3300).



# What Is the Background Information that Supports the Significance of the Problem?

- The broad problem statement
  - Important for setting the stage and alerting the reader to the importance or significance of the proposed research
  - Establish the argument or need for doing the study
    - The information known about the problem is used for emphasizing the unknown



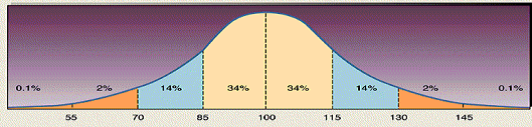
## Example of Background Information and the Significance of the Problem

- In DEET study:
  - Significant in-patient hospital pathogenic organisms have impressive lengths of survival on surfaces without adequate cleaning...
  - Various patient risk factors for acquiring nosocomial infections have been identified, including severity of illness, prolonged hospitalization and antecedent antibiotic therapy... cross-contamination between patients is an increasingly strong risk factor of hospital-acquired infection.



# What Is Study Design?

- Describe how to conduct the study:
  - **What** you intend to do
  - Population and setting:
    - **Who, When and Where**
- Example: in DEET study
  - This study will be a prospective, cross-sectional, controlled intervention study to evaluate colonization of surface contaminants on telemetry boxes and lead wires in the Heart Center.
  - Medical and surgical adult cardiac patients' rooms
    - Medical units,  $7100/7300 = 32$  randomly selected
    - Surgical units,  $3100/3300 = 32$  randomly selected



# What Are Study Procedures?

- Explain How You Would Collect The Data:
- Describe logistical questions
  - **What:** data to be collected
  - **When and how:** to collect data
  - **Who:**
    - Research personnel to perform intervention and data collection
    - Sample population = study participants
- Describe the exact sequence of events, time relationships and individuals involved during the data collection





# What Are Study Procedures?

- Example: in DEET study
  - A sterile swab (single annulet) is opened by the nurse investigator using clean gloves
  - The swab will be moistened with sterile water before swabbing the telemetry box and a wire
  - Using one swab one swipe of the telemetry box , at the lead connection site, and the green EKG lead wire is made and swab is returned directly to the sterile vial without making contact with any other site



# How To Write Design Section

- Use supporting literature
  - Find a description of how the study was set up to answer the question in the “Discussion” section
    - Recommendations from authors related to design
  - Design may also be discussed under “Limitations” in the manuscript
- If design is not found in reviewed manuscripts.
  - Evaluate your own clinical setting and patient population
  - Determine **what you think** will be the best way to go about gathering data to answer your question
  - Call one or two authors of similar studies and discuss design
    - Ask why a particular design was selected and if the author recommends changes



# When Writing Design Section

- Examine the variables and their relationships
  - **Variables:** “A variable is a characteristic measured or observed by information gathering that either varies among the persons, events, or objects which make up data or is a constant.”
    - Independent variables : represent the value being manipulated or changed
    - Dependent variables: observed result of the independent variable being manipulated
  - **Example:** in DEET study
    - Independent variables : telemetry boxes and lead wires
    - Dependent variables: colonization of surface contaminants



# When Writing Design Section

- Examine the variables and their relationships
  - **Relationships** between the variables are compared, described, identified, predicted, or in some way evaluated to make a statement at the end of the study to make a statement
  - **Example:** in SUGAR study
    - The data will be analyzed using a one-way repeated-measures ANOVA. This design allows for analysis of multiple correlations of finger stick and arterial blood glucose for each subject.



# What Is “Selection of Subjects”?

- Description of how subjects will be selected for the study
  - Appropriate number of subjects is based on
    - Type of research design
    - Statistics and significance level
    - Variables being measured
    - Anticipated effect of the study intervention on the dependent variables
  - Selection of Subjects
    - List inclusion/exclusion criteria
    - How subjects will be identified?
- Example: in SUGAR study
  - The principal nurse investigator or research nurse will identify potential subjects. Fifty adult (age 18 years and above) post-operative cardiothoracic subjects on insulin and vasopressor infusions will be enrolled in the study.



# What to Say in “Subject Recruitment & Compensation” Section

- Describe recruitment procedures
  - Who will introduce the study to potential subjects?
  - Ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a))
- Define subject compensation, if there is to be any
  - Provide specific prorated amounts to include expenses such as travel and/or lost wages
  - Provide specific prorated amounts to be provided for incentive to participate



# What to Say in “Subject Recruitment & Compensation” Section

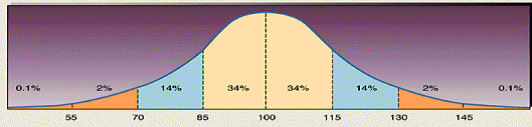
- Example: in SUGAR study
  - The study personnel will recruit all patients meeting inclusion criteria listed above from a convenience sample of post-operative cardiothoracic subjects on insulin and vasopressor infusions on the cardiothoracic intensive care unit of Duke University Hospital (Unit 3200). The study subject will receive no form of compensation and no expense will be incurred as a result of participation our study.





# What Is a Consenting Process?

- Description of how the study consent will be obtained from subjects
- Example: in SUGAR study
  - The patient's care provider will ask permission for participation in the study. Informed consent will then be obtained by the nurse investigator in accordance with the Waiver, which states that the nurse investigator will explain the study to the subject or legally authorized representative (LAR) if the patient is temporarily unable to give legally effective consent, and will also read through the informed consent with the patient once he/she is capable, prior to obtaining signature.



# What Is “Subject Capacity To Give Legally Effective Consent” ?

- Description of who will consent to participate in the study
- Example: in CHIME study
  - Subjects must have the capacity to give legally effective consent to be included in this study.



# What Are Study Interventions ?

- Description of research activities that will be done to/for subjects for participating in the study
- Example: in SUGAR study
  - All research activities to be carried out for this protocol are part of standard clinical practice for patients on insulin infusions and no additional activities, exclusively for research purposes, will be carried out other than obtaining temporally matched peripheral and arterial samples. No investigational drugs or devices are proposed.



# What Is Risk/Benefit Assessment?

- Description of risks and benefits that might incur to subjects due to the study intervention.
- Example: in SUGAR study
  - No study related injuries are anticipated. If a patient in the study were injured, it would be covered as part of the costs for the typical recovery of a post operative patient since study protocol is consistent with routine care.
  - The potential benefits of participating in this research study will be indirect. The knowledge gained from participation in this study may benefit the participants or others who have insulin drips and also require vasopressor infusions.



# What Are Costs to the Subject??

- Description of whether the research will incur any costs from the subjects.
- Example: in SUGAR study
  - No extra monetary cost or compensation to the subject will be needed as all blood drawn/procedures listed above are standard practice on in our ICU.



# What Are Data Analysis & Statistical Considerations?

- Include preliminary plans for data analysis
- General ideas about analysis are acceptable
  - May change with the eventual completion of the study
- Specific idea of the statistical tests that will be used
  - Helpful in considering every piece of data that will be required for the analysis
- Example: in SUGAR study
  - The data will be analyzed using a one-way repeated-measures ANOVA. This design allows for analysis of multiple correlations of finger stick and arterial blood glucose for each subject.



# What Is Data & Safety Monitoring?

- Describe how the data will be kept safe
- Example: in SUGAR study
  - After recruitment and consent, all patient data will be de-identified by assigning a Study ID number for each patient. Patient identifiers will be removed from data collection and stored in a separate password protected database as described below. The research plan includes provisions for continuous monitoring of data collection procedures and data storage to ensure the protection of the subject. Specifically, all patient identifiers will be removed and the data sheets will be kept in a separate locked file that is only accessible to the principle investigator.





# What Is Data Storage & Confidentiality?

- Describe how the data will be kept confidential
- Example: in SUGAR study
  - Research data will be collected and stored on a secured Microsoft Access database located at a HC network drive. The research data will be secured via Username and Password-restricted access to the database, in accordance with HIPAA (Health Insurance Portability and Accountability Act) guidelines. Only the investigator will know the Username and Password required to access the research data. Data with subject identifiers will not be released.

# When, How And Whom To Ask For Help

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# For Example, Study Design...Methods

## **Sometimes You're the Expert!**

- Use existing study methods as a template
  - “Tweak” design and procedures to fit your unit
  - Do a “walk through” to identify procedure glitches

## **Sometimes You're Not!**

- Sample size estimation
- Research design
- Validity and reliability of instruments
- Informed consent – construction and loopholes





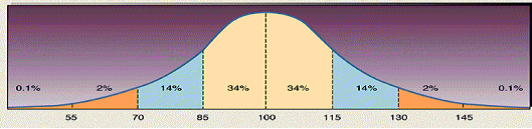
# When Writing Design Section

- Validate design choice with an expert
  - Discuss your thoughts with a statistician or an author of a similar study to validate your choice
    - Data analysis is based on the relationships between your variables
      - It is important to design data collection to reflect the correct or desired relationship between variables
      - Enlist the same expert in the beginning that will be helping you analyze the data in the end
- Be as specific as possible
  - Include enough detail that another researcher would be able to repeat the study if desired



# Enlist the Help of Expert

- DTNI: email [dtni@mc.duke.edu](mailto:dtni@mc.duke.edu)  
**919-668-2344**
- DUSON ORA:  
**919-684-5376**
- DUHS Research Nurse Scientist:  
**919-613 6406**



# Additional Resources

- [www.cehjournal.org/0953-6833/20/jceh\\_20\\_61\\_017.html](http://www.cehjournal.org/0953-6833/20/jceh_20_61_017.html)
- [highered.mcgraw-hill.com/sites/0073049506/student\\_view0/glossary.html](http://highered.mcgraw-hill.com/sites/0073049506/student_view0/glossary.html)