Clinical Research Planning and Execution: What Every Researcher Should Know to Avoid Pitfalls and Maximize Success

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OVERVIEW

- Clinical research design issues
- Obtaining participants and data
- Power analysis
- Basic statistics
- Forming research teams
- Funding
- Working with statisticians and epidemiologists
CLINICAL RESEARCH VS BASIC SCIENCE RESEARCH

- Basic science research – How does this work?
  - Lab setting
  - “Participants” are typically cells, tissues, animals
  - Easier to control all conditions to look at mechanisms
  - Application not always immediately evident, but lays the foundation

- Clinical research – Is this actually useful?
  - Real world setting
  - Participants are people
  - Messier to do
  - Findings can have direct and immediate applicability to patients

- Basic science research – informs clinical research – which leads to additional basic science research
CLINICAL RESEARCH QUESTIONS

- Picking a topic
  - Interest; Overlap with current work
  - What is already known

- Designing a testable question
  - Operationalize all variables
  - Specific to population, clinical conditions, etc

- Do you need a hypothesis?
  - Can you make a prediction about the answer to the question?

- What information do you ultimately want?

Research Questions, Hypotheses, and Clinical Questions – Chapter by Judith Haber
https://medicine.utah.edu/ccts/sdbc/files/Research_Question.pdf
CLINICAL RESEARCH DESIGN

- Experimental vs Observational Designs
  - Experimental (RCT)– Cause and effects conclusions
  - Observational (i.e. correlational) – Works in more situations
  - Impacts Level of Evidence

- Choice depends on
  - Topic/Research question
  - Current state of knowledge
  - Resources

- Quality improvement efforts can be research too
  - In and of themselves
  - As a spring board for further clinical research
DESIGNING/IMPLEMENTING A CLINICAL STUDY

- Control vs real world applicability
  - Will findings apply to typical patients
  - Will findings apply to typical situations
- What’s possible and what’s not
  - RCT
  - Correlational design – Cohort study, Case control
- Prospective vs Retrospective
- Cross-sectional vs Longitudinal
- In the end – the research question and resources will dictate!
This drug has proven effective in testing of 500 women with your condition.
CLINICAL STUDY PARTICIPANTS AND SETTING

- Identifying potential participants
  - Inclusion and exclusion criteria
  - Where to find them
  - Enrolling them; retaining them


- Can you use existing data?
  - Using EHR data
  - Leveraging existing data sets

- Multi-site efforts
BIG DATA SETS

- **Using EHR data**

- **Using other big data sets**
  http://guides.lib.berkeley.edu/publichealth/healthstatistics/rawdata
  https://guides.lib.unc.edu/c.php?g=8742&p=44486
  Also – vital statistics data…
HOW MANY PARTICIPANTS ARE NEEDED?

- Statistical power – ability to conclude there is a significant effect when one does exist
- With low power – may erroneously conclude there is no effect
- Biggest driver of statistical power – sample size
- So – need to make sure you have enough participants to be able to answer your question of interest
- The smaller the effect you expect, the more participants you will need
- Also – distribution of the outcome variable impacts power
HOW MANY PARTICIPANTS ARE NEEDED?

- Example - have an intervention to improve birth weight in a population with an average birth weight of 2900gm/30% LBW rate
- How many participants do we need in the treatment and control groups to be able to determine the intervention is effective?
- What assumptions do we make, what sample size do we need?
# HOW MANY PARTICIPANTS ARE NEEDED?

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Power</th>
<th>Number of Participants Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2900g</td>
<td>3400g (normal wt)</td>
<td>80%</td>
<td>20</td>
</tr>
<tr>
<td>2900g</td>
<td>3400g (normal wt)</td>
<td>90%</td>
<td>26</td>
</tr>
<tr>
<td>2900g</td>
<td>3190g (inc by 10%)</td>
<td>80%</td>
<td>60</td>
</tr>
<tr>
<td>2900g</td>
<td>3190g (inc by 10%)</td>
<td>90%</td>
<td>80</td>
</tr>
<tr>
<td>30% low birth weight rate</td>
<td>8% (natl avg)</td>
<td>80%</td>
<td>98</td>
</tr>
<tr>
<td>30% LBW rate</td>
<td>8% (natl avg)</td>
<td>90%</td>
<td>130</td>
</tr>
<tr>
<td>30% LBW rate</td>
<td>24% (dec by 20%)</td>
<td>80%</td>
<td>1716</td>
</tr>
<tr>
<td>30% LBW rate</td>
<td>24% (dec by 20%)</td>
<td>90%</td>
<td>2296</td>
</tr>
</tbody>
</table>
BIAS IN CLINICAL RESEARCH

- No study is perfect – many threats to study validity – need to consider effects
- What is validity? A study is considered valid if it uncovers the truth about relationships among variables
  - Internal validity – accuracy of study results in that sample
  - External validity – degree to which study findings generalize to a population
- Threats to validity often referred to as biases – introduction of systematic error into a study that can/does impact study results
- A LOT of identified biases (200+), different terminology and classification schemes:
  - Selection
  - Design
  - Results
BIAS IN CLINICAL RESEARCH

- Pannucci & Wilkins. Identifying and avoiding bias in research.
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917255/
- http://www.equator-network.org/
BIAS IN CLINICAL RESEARCH

"Excellent health statistics - smokers are less likely to die of age related illness"
BASIC STATISTICS FOR THE CLINICIAN

- Three published papers:

- Reviewed a randomly selected set of published papers and categorized the statistics used in each

- Identified the basic statistics that if you understand, will allow you to read and interpret 65% to 70% of the studies published in clinical fields
BASIC STATISTICS FOR THE CLINICIANS

- Descriptive statistics
- Concept of a p value
- Understanding what determines statistical test selection
- T-test; F test
- Chi-square/Fisher’s Exact Test
- Odds ratios & CIs
- Regression
- Correlations
- Basic epidemiology concepts:
  - Risk statistics
  - Incidence and Prevalence
  - Sensitivity and Specificity
"SHOULD WE SCARE THE OPPOSITION BY ANNOUNCING OUR MEAN HEIGHT OR LULL THEM BY ANNOUNCING OUR MEDIAN HEIGHT?"
FORMING RESEARCH TEAMS

- Multidisciplinary is key!
- Developing research groups around topics and interests
- Who should be on the team
  - Experts in the science
  - Experts in the methods (including analysis and interpretation)
  - Clinical experts
- Defining roles and responsibilities
- Authorship, percent effort issues
- For funding – a collaborative track record is important
Q: How many medical device professionals are needed to change a light bulb?

A: Well, you need the light bulb’s consent, first...
FINDING FUNDING

Where to find funding
- Traditional sources
- Get creative

Funders look for
- A project that logically extends from what is already known
- A testable question and feasible project
- Relevance and applicability
- Qualified team with a proven track record
- Capacity to do the project
- Potential for further work

Prepare early; Plan to be patient!
FINDING FUNDING

https://www.grants.gov/learn-grants/grant-programs.html

https://www.fic.nih.gov/Funding/NonNIH/Pages/default.aspx

https://www.grantwatch.com/cat/14/health-and-medical-grants.html

Dunlop M. Steps for successful funding applications. Injury 2010; 415:S7-S9. https://ac.els-cdn.com/S0020138310002238/1-s2.0-
S0020138310002238-main.pdf?_tid=e92abd65-874c-4d7c-b588-
9dae47f7c154&acdnat=1548731904_f57b77ee5974a3a8e639da90691
c2952
Isaac Newton struggles to write the economic impact section of his ‘gravity’ proposal.
WHAT IF YOU HAVE NO FUNDING?

- Assess what resources you do have
  - Students, trainees, volunteers
  - Institutional support
  - Existing data
- Work in teams – maximize output with more minimal effort
- Leverage current data to get funding for further work
WORKING WITH STATISTICIANS/EPIDEMIOLOGISTS

- What resources are available?
- Involve them EARLY
- Bring them up to speed on the clinical topic
- Make sure expectations are clear and realistic
- Credit and authorship
QUESTIONS AND DISCUSSION