Conducting Your Research: Basic Principles of Clinical Research Project Design and Procedures
STEPS OF IDEAS

1. Absolutely New!
2. Literature Search
   - Well known?
     - Learning experience!
     - Looked at, but need more data
     - Protocol? Methods?
       - Hard work!
   - Presentation/Publication
EXPECTATIONS OVER TIME

- Nobel Prize
- Revolutionize Field
- NEJM Paper
- Local Abstract
- Regional Conference
- Share Powerpoint With Family
GOOD RESEARCH QUESTIONS

• Master the literature
• Be alert to new ideas (conferences)
• Be creative
• Choose a mentor
Example: Among patients with symptomatic pulmonary hypertension [population], can sildenafil (20, 40, or 80mg) [comparison] orally 3 times daily [intervention] for 12 weeks [time] compared to placebo [comparison] improved functional status? [outcome]
FINER

• Feasibility
  – Sample size, technical expertise, time, resources/funding, scope/focus
• Interesting
  – Personal experience, asking “why?”
• Novel
  – Literature (“need for more research”), controversy, challenge evidence
• Ethical
  – Benefits > risk
• Relevance
  – Increase knowledge, influence policy or clinical practice
STUDY DESIGNS
HIERARCHY OF EVIDENCE

- Systematic Reviews
- Randomized Controlled Trials
- Cohort Studies
- Case-Control Studies
- Case Series, Case Reports
- Editorials, Expert Opinion
WHAT IS THE STUDY DESIGN?

• Researchers observed 18 patients with sarcoidosis who underwent renal transplantation.

• Subjects were identified retrospectively in 8 renal transplant departments.

• Medical charts, demographics, and transplant outcomes were reviewed.

• These data established that renal transplants may be carried out safely in transplant candidates with sarcoidosis.
Your poll will show here

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CASE SERIES

• Observational/descriptive
• Usually more than 10 patients, hypothesis-generating rather than evidence

WHAT IS THE STUDY DESIGN?

• Researchers looked into racial disparities in motorcycle-related mortality.

• They analyzed data from the National Trauma Data Bank (2002-2006).

• They found Black motorcyclists more likely to use a helmet compared with Whites, but also more likely to die after a motor collision.
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CROSS-SECTIONAL

- Inexpensive, multiple risk factors analyzed simultaneously

WHAT IS THE STUDY DESIGN?

- Study of association between use of common psychotropic medications and traffic accidents.
- Researchers reviewed data from pharmacy prescriptions, police traffic accidents, and diving license data.
- They compared drivers with accident requiring medical assistance and those with license and no accident during 2000-2007.
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CASE-CONTROL

- Consider in retrospective chart review (inexpensive, convenient)
- Useful for rare conditions
- Watch for selection bias

WHAT IS THE STUDY DESIGN?

• A study enrolled 3000 individuals at 7 sites with broad spectrum of renal disease severity.

• Subjects undergo extensive clinical evaluation and follow up visits including diet, activity, health behaviors, depression, cognitive function, health care utilization, CVD evaluations, and quality of life.

• The study is designed to look at risk factors of kidney disease and cardiovascular disease progression.
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COHORT (PROSPECTIVE)

• Observational study, time-series
• No control group
• Subject loss can be an issue

EXPERIMENTAL STUDY DESIGNS

• Randomized Controlled Trials
  – Watch out! Strong evidence requires time, resources, and pain!

• Clinical Trials

• Cross-Over

• Quasi-Experimental

• Before-After (Pre-Post)
N OF 1
OTHER QUANTITATIVE STUDY DESIGNS

• Sequential, Multiple Assignment, Randomized Trials (SMARTs)
• Multiphase Optimization Strategy (MOST)
• Factorial (full and partial) ANOVA
• Stepped Wedge
• Interrupted Time-Series
• Regression Discontinuity Design
FOCUS GROUPS

- Eight pharmacists working with community health workers described perceptions, opinions, attitudes towards them helping with medication adherence.
- Qualitative data for analysis

OTHER QUALITATIVE STUDY DESIGNS

• Phenomenological
• Ethnographic
• Grounded Theory
• Historical
• Case
• Action Research

• Methods: interviews, observation, focus groups, document review
<table>
<thead>
<tr>
<th>Table 1. Comparison of quantitative and qualitative research approaches</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General framework</strong></td>
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<tr>
<td>Quantitative: Seek to confirm hypotheses about phenomena</td>
</tr>
<tr>
<td>Instruments use more rigid style of eliciting and categorizing responses to questions</td>
</tr>
<tr>
<td>Use highly structured methods such as questionnaires, surveys, and structured observation</td>
</tr>
<tr>
<td>Qualitative: Seek to explore phenomena</td>
</tr>
<tr>
<td>Instruments use more flexible, iterative style of eliciting and categorizing responses to questions</td>
</tr>
<tr>
<td>Use semi-structured methods such as in-depth interviews, focus groups, and participant observation</td>
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<tr>
<td><strong>Analytical objectives</strong></td>
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<tr>
<td>Quantitative: To quantify variation</td>
</tr>
<tr>
<td>To predict causal relationships</td>
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<tr>
<td>To describe characteristics of a population</td>
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<tr>
<td>Qualitative: To describe variation</td>
</tr>
<tr>
<td>To describe and explain relationships</td>
</tr>
<tr>
<td>To describe individual experiences</td>
</tr>
<tr>
<td>To describe group norms</td>
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<tr>
<td><strong>Question format</strong></td>
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<tr>
<td>Quantitative: Closed-ended</td>
</tr>
<tr>
<td>Qualitative: Open-ended</td>
</tr>
<tr>
<td><strong>Data format</strong></td>
</tr>
<tr>
<td>Quantitative: Numerical (obtained by assigning numerical values to responses)</td>
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<tr>
<td>Qualitative: Textual (obtained from audiotapes, videotapes, and field notes)</td>
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<tr>
<td><strong>Flexibility in study design</strong></td>
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<tr>
<td>Quantitative: Study design is stable from beginning to end</td>
</tr>
<tr>
<td>Participant responses do not influence or determine how and which questions researchers ask next</td>
</tr>
<tr>
<td>Study design is subject to statistical assumptions and conditions</td>
</tr>
<tr>
<td>Qualitative: Some aspects of the study are flexible (for example, the addition, exclusion, or wording of particular interview questions)</td>
</tr>
<tr>
<td>Participant responses affect how and which questions researchers ask next</td>
</tr>
<tr>
<td>Study design is iterative, that is, data collection and research questions are adjusted according to what is learned</td>
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</tbody>
</table>
CHOOSING A STUDY DESIGN

• Discuss with mentor!
• Apply PICOT and FINER
  – State of science, Time, Resources, Limitations/bias, Patient risk
• Consult with CCTS Design and Analysis Core
IRB AND HIPAA
THE I STANDS FOR...

• Irritating?
• Impossible?

• It is necessary if Human Subjects Research

• If not sure, there’s a form for that: “Determination of Whether an Activity Represents Human Subject Research”
TRAINING REQUIRED

• New investigator training
• HSPP HIPAA training (not the same as clinical HIPAA training!)

• It’s all online:
• http://research.uic.edu/compliance/irb/education-training
WHAT IS THE IRB?

• Committee composed of cross-section of community where research performed
• Protect rights and well-being of human subjects
• At least 5 members (per DHHS) and includes non-scientists, community members

• Want to know more?
• Contact the IRB and sit in on a review!
PROTOCOL CATEGORIES

• Exempt
  – Education, existing data (publically accessible), food tasting

• Expedited
  – No more than minimal risk

• Full
  – Full board review required
IRB COMMUNICATION

- Initial application
- Continuing review (each year)
- Protocol deviation
- Protocol amendment
- Adverse event
- Closure (final report)
HIPAA

• Health information that can be traced back to a particular individual (protected health information – PHI) is strictly forbidden for research unless the individual provides authorization

• HIPAA waiver may be appropriate in chart reviews
  – A study on hypertension could involve abstracting blood pressure data on 100 patients without recording other information that could identify them or link back to those patients
IRB TRICKS AND SECRETS

• Look at similar previous applications
• Keep consent forms simple with low-literacy level (use template)
• Talk to IRB personnel ahead of time about concerns
• Have mentor review application
• Create protocol following IRB’s template

• Don’t let yourself be frustrated!
• The IRB will always win!

DO, OR DO NOT. THERE IS NO TRY.  
– Yoda
BASIC PROTOCOL

• Title
• Investigators (with contact info)
• Introduction summary
• Background and justification
• Objectives and hypotheses
• Materials and methods
• Risks
• Power analysis and statistical plan
• Data management and safeguards for subjects
• References
EXAMPLE CASE 1

• 72 year old Alzheimer patient has given consent to be enrolled into a clinical study involving an investigational drug for memory.

• The patient is unable to give information about the purpose of the study or methods involved.
INFORMED CONSENT

• This case involves informed consent and probably requires a surrogate decision-maker to give consent.

• Surrogate’s decision must be based on the risk-benefit ratio and what is in the best interest of the patient.
EXAMPLE CASE 2

• During a clinical trial of stem cell transplantation, a significant number of patient withdrawals occur.
• This could harm a study statistically if more drop out.
• The PI wants to modify the informed consent document to make discontinuing or withdrawing from the study a mutual decision requiring the participant and researcher to agree.
AUTONOMY

• This violates principle of autonomy.
• Consent must be voluntary, and participant must be able to withdraw from study without impediments, reprisals, or compromising future care.
EXAMPLE CASE 3

- A smoking cessation study includes 10 clinics, 5 intervention and 5 control.
- The study was presented to people in a smoking cessation program with different interventions conducted at the intervention sites.
- They were not informed it was part of a study, to prevent them from altering their responses to surveys (thus altering the results).
FULL DISCLOSURE

Subjects have the right to full disclosure prior to agreeing to participate in a study.
EXAMPLE CASE 4

• After completing a study involving collection of tissue samples, a researcher wants to do additional testing not explicitly described in the initial consent form.
ADDITIONAL INFORMED CONSENT

• Most IRBs require an additional informed consent, or at minimum, a signed addendum to comply with the right for full disclosure.
DATA
COLLECTION

- Paper?
- Excel?
- REDCap?
- Variable definition names
- Keep a code book (dictionary)
STORAGE

• Keep documents in one safe place organized
• Secure documents (lock and key)
• Keep master list with identifiers separate
• Network drive storage (routine back ups)
• Special electronic storage if HIPAA identifiers
• Know the retention policy (when to destroy records)
ANALYSIS

• There are alternatives to Excel!
• Get help!

• Consider:
  – SAS
  – SPSS
  – STATA
  – R
VARIABLES

• Continuous (e.g., HbA1c)
• Discrete (e.g., number of live births)
• Categorical
  – Nominal – no order
  – Ordinal – has order (e.g., stages of melanoma)
HYPOTHESES

• What are we trying to prove here?

• Null hypothesis ($H_0$) negative/default
  – No difference in prevalence of breast cancer between Chinese and American women.

• Alternate hypothesis ($H_A$) research
  – There is a difference in the prevalence of breast cancer between Chinese and American women.
GRANT WRITING
WHY WRITE A GRANT?

• You need money/resources for:
  – Statistician, data manager, research assistant, materials, participant incentives, IT

• If it is low-cost, you probably don’t need it.

• But you probably should know something about it.
GRANT COMPONENTS

• Overview, objectives, aims
• Background, needs assessment, rationale
• Personnel and environment
• Design and methods
• Budget and justification
• Timeline
• Outcomes
• References
YOUR IDEA

• Compelling
• Original (check the literature – this is your background)
• Significant
• Address problem worth addressing (question worth answering)
• Clear
• Attainable by methods
• Feasible with time and resources
• Confirm with mentors and advice on funding source
“Agreed. We fund only those proposals we can understand.”
PRESENTATION
SHARING SCIENTIFIC DATA

• Abstract
• Poster presentation
  – Scholarly Activities Day!
• Oral presentation
• Written manuscript
ABSTRACTS

• Check the call for abstracts early!
  – Months before the meeting
• Regional meeting acceptance easier than national/larger
• Be efficient and descriptive
• Get examples!
POSTERS

• Keep it Simple S***** (KISS)
• Clear, succinct – understood in < 1-2 minutes
• Follow guidelines for size
  o Bullet points preferable
• Make sure text easy to read
• Get examples/templates!
EXAMPLE POSTER
MANUSCRIPTS

• Get examples!

• Guidelines on what to include:

  • RCT  CONSORT
  • Observational studies  STROBE
  • Systematic reviews  PRISMA
  • Quality improvement  SQUIRE
DOM RESOURCE

http://dom-drupal.med.uic.edu/drupal