CLINICAL RESEARCH IN HEART FAILURE: OPPORTUNITIES FOR EARLY CAREER

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Necessary Skills for a Clinical Research Career

• Ability to identify a good research project
• Establishing a research team
• Ability to design a protocol
• Knowledgeable about IRB submission
• Success enrolling
• Familiar with data collection and analysis
• Skill in writing: papers and grants
• Dealing with journals
Identify a good research question

- Scientifically relevant - “hot”
- Feasible to study – and not overpopulated
- Fundable
- In an area that will have long-term interest for you
- Intriguing to both you and your clinical and research colleagues
- Lends itself to some smaller less ambitious projects as well as long-term larger questions

Importance of this cannot be emphasized enough!
Identify a good research project

- Spend time thinking
- Identify several projects
- Run ideas past experienced physician-scientists
- Think about
  - Time frame needed to carry out project
  - Resources necessary
  - Scope
Timeline

• Fellow to Instructor or Assistant Professor
• Assistant Professor to Tenured Associate Professor
Hedge your Bets

- Academic success requires a continuous pipeline of projects and publications.
- Small secondary projects not dependent on funding are key to maintaining the pipeline.
- High-impact papers from your prior level of training, supervision of a student, resident or fellow in a systematic review, meta-analysis or small original research project can be worked on in parallel with your first grant proposal(s).
- Consider identification of several avenues of investigation, ideally related or similar.
- Identify every funding opportunity and apply for them all.
Establish a research team

• The successful physician-scientist cannot do this alone.
• Spend time thinking about what your research team will look like –
  • Large/small?
  • Bench research or clinical epidemiology?
• Hire your first research assistant or laboratory technician as soon as possible
  • What qualifications are necessary?
  • Think about how you will spend your time, and what this person could do to accomplish the things you don’t have time for
  • IRB application skill, protocol design, grant applications, technical skills, people skills
Designing a research protocol

• Before you get your first job, you must learn to put a protocol together effectively.
• Before you write your first grant, you must learn to put a protocol together thoughtfully.
Research Protocol Development Form

Your name: ________________________________

(Note: not all sections are applicable to all studies, e.g., observational studies or evaluation of a diagnostic test.)

Study Title:

Research Question:

Study Hypothesis:

Independent (Intervention) Variable(s):

Dependent (Outcome) Variables(s):

Extraneous (Potentially Confounding) Variables (list multiple):

List inclusion and exclusion criteria for your study:

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<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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Study Design (e.g., RCT, cohort, cross-sectional):

Research Protocol Development Form (2)

Name: ____________________________

Sampling (yes or no; method to be used):

Randomization? (if yes, how?):

<table>
<thead>
<tr>
<th>Study Measurements (e.g. HDL, PO2, pain)</th>
<th>How measured (ABG machine, VAS, etc.)</th>
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<td>Baseline/initial</td>
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Post Intervention

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<th>When (timing)</th>
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Are the Primary Study Measurements or Scales Validated? (if so, how?):

Sample Size Calculation (discuss with research preceptor or statistician as needed):

How many patients will you need to perform your study and adequately answer your question?

These calculations generally require information about:

1. The desired alpha (usually 0.05) ______ and desired beta (usually 0.1 or 0.2) ______

2. The type of data of the dependent (outcome) variable:
   a. If categorical data, the expected prevalence of the outcome: ______________________
   b. If quantitative data, the expected variance (e.g. SD) in the variable:____________________

3. The amount of difference (effect size) in the primary outcome measure that you wish to detect in your study: ______________________

How many study subjects are estimated to be needed in each group and total?

Common Protocol Mistakes

- No primary hypothesis
- No primary outcome variable
- No sample size or power calculations
- Hypothesis not testable by proposed experiments
IRB submission

• There is an art to this. Learn the art.
• Speak to members of the IRB. They know the workings of your committee and the common pitfalls.
• Learn the standard language that is necessary for all clinical research protocols.
• Learn your IRBs “hot buttons”
Success Enrolling
Data collection

• Know what you are going to collect before your start.
• Spend time on case report forms.
• Scour the literature – what other factors might you have neglected that are important in this area of investigation?
Data analysis

• Enlist the help of a biostatistician early, ideally prior to beginning data collection.
• In clinical research, a t test is rarely adequate.
• Learn something about biostatistics. Particularly if you are interested in correlations or associations, the biostatistics are quite complex.
• At the NIH, all human research protocols (R01) have a biostatistical reviewer
Writing: Papers and Grants

• To be successful in academic research, you must learn to write concisely and clearly.
• If you do not want to spend your career writing, this is not the career for you.
Dealing with Reviewers - Journals

• Is my paper accepted?
  • Acceptance
  • Rejected but would be considered with minor revisions
  • Rejected but would be considered with major revisions
  • Kind rejection
  • Firm rejection
  • Rejected by editors without peer review
Dealing with Reviews – NIH and others

• Summary statement
  • Summarizes the discussion that provides the basis for your impact score
  • Not an exhaustive critique
  • Does not list every point reviewers found problematic
  • Not a document stating what you need to do to get a better score

• The Program Director is Always Available to Assist
Dealing with Reviews – NIH and others

- The reviewer is always right - Assume comments are helpful
- Assume more flaws exist in the application than cited
- Be grateful not defensive
- Be open-minded and learn – look for overarching themes
- Determine if the application is worth fixing
  - Major flaws
  - Lack of reviewer enthusiasm
  - Fixable problems
What if the Reviewer is Wrong?

**Panel 1:**
This design will never work in the real world.

**Panel 2:**
That design is already widely used in the real world.

**Panel 3:**
I can come back later if you need time to concoct additional uninformed criticisms.

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What if the Reviewer is Wrong?

- Poor presentation
- Grantsmanship
  - Poor presentation results in reviewers:
    - Missing a point
    - Misunderstanding
    - Concluding you are a careless scientist
    - Concluding there is lack of involvement of mentor or collaborators
Major Flaws in Research Grant Awards

- Work has already been done
- Hypotheses not supported by data
- Methods are not suitable
- Insufficient statistical power
- Lack of past productivity or insufficient evidence of collaborative interaction of investigators
- Poor resources or facilities
Major Flaws in Training/Career Awards

- Mentor lacks relevant expertise
- Mentor overcommitted
- Training plan lacks sufficient detail to develop candidate
- Research project is weak
NEVER LET SUCCESS GET TO YOUR HEAD. NEVER LET FAILURE GET TO YOUR HEART.