Three Page Research Strategy

ELIZABETH SECKEL, MA

Grant Writer
Maternal-Fetal Medicine
The Research Plan

Important Question

Expected Payoff
Research Plan must:

• Explain the research question(s)
  • *what* will be done

• Highlight the novelty and/or importance of the project
  • *why* it should be done

• Describe the methods and techniques that will be employed
  • *how* it will be done
Making a strong case…

https://www.atlasobscura.com/places/hussaini-hanging-bridge

https://commons.wikimedia.org/wiki/index.php?curid=1520007
Making a strong case…

Plan
Layout
Articulate
Narrate
Share

Organizing the Research Plan – Rachel Spark, PhD
Plan ahead

Commitment to the Process

• To write the application

• To get critical review from knowledgeable colleagues

• To accept and respond positively to criticism
Plan ahead

Make sure you’re starting with an agency relative problem:

“Does this study address an important maternal/child health problem?”

Yes _____ No _____ (If No, skip the rest of this form and contact MCHRI Administration)
Borderline (needs discussion) _____
Plan ahead

Create a roadmap

1. Big problem
2. Relevance to funding agency
3. Focused subproblem
4. New opportunity
5. Approach
6. Impact
Plan ahead

MCHRI Research Plan Worksheet

1. What is the general problem you are tackling, i.e. the big picture?
2. How is your research relevant to maternal and child health?
3. What specific problem will you address, i.e. the focused question?
4. What is novel about your proposal?
5. How will you accomplish your proposed research?
6. What is the expected payoff, i.e. what will your research bring to the field?
7. How will this proposal help you advance your career?
Plan ahead

Further Resources

- Tips for Planning Your Proposal – Overview Outline
- Strategies and Tips for Proposal Success – Michael Levitt, PhD
- Elements of Scientific Storytelling – Jennifer Stonaker, PhD
Making a strong case...

Plan
Layout
Articulate
Narrate
Share
Layout

Headings for MCHRI’s Research Plan
• Specific Aims
• Project Timeline
• Relevance to Maternal & Child Health
• Background and Significance
• Preliminary Studies
• Research Design and Methods
• Career Development
• Potential Pitfalls & Contingency Plans
• Future Steps
Layout

Research Design and Methods

Organize each aim into consistent subsections:

• Introduction/Motivation
• Methods
• Expected Outcomes

OR

• Knowledge Gap
• Strategy
• Outcomes
Section headings are presented at the left margin entirely in bolded, capitalized letters. The first line of each paragraph that is subordinated to a section heading is indented one tab. Subsequent lines return to the left margin, as shown here.

Subsection Headings

Subsection headings are bolded, with the first letter of each main word capitalized.

Sub-subheadings

This level of subordination is indicated by putting the sub-subheading not bolded but underlined.
OBJECTIVE

Timely identification of infection in pregnant women during labor is critical in order to make significant advances in reducing the global burden of perinatal adverse outcomes associated with maternal sepsis. In this effort, we will compare lactate levels between infected and non-infected pregnant women in the peripartum period, a crucial time for developing infection and infection-associated morbidity and mortality.

BACKGROUND AND SIGNIFICANCE

Pregnant and peripartum women are an intrinsically vulnerable population for infection as their immune response is suppressed to protect the immunologically distinct fetus from the maternal inflammatory response [1-3]. Further physiological, immunological and mechanical changes over the course of pregnancy increase their susceptibility to infections compared with non-pregnant women, with the onset of labor disrupting even more crucial physiological barriers against bacterial infection [4]. Despite maternal sepsis being the third leading direct cause of maternal mortality [5], normal levels of sepsis biomarkers in the peripartum period have yet to be established.

HYPOTHESIS

Due to the normal physiologic inflammation of the peripartum period, we hypothesize that median levels of lactate in non-infected pregnant women will be elevated above the normal levels of non-infected adults, and that median lactate levels of infected pregnant patients will be further elevated, thus providing more accurate lactate levels for diagnosis of infection in peripartum pregnant women.

SPECIFIC AIMS

Aim 1: Compare median lactate levels of infected to non-infected women in the peripartum period.
Aim 2: Establish preliminary data for normal (reference range) levels of lactate in pregnant women in the peripartum period.

RESEARCH APPROACH

Sample Size: Assuming lactate follows a log-normal distribution, a two-sample t-test of log(lactate) can be used to compare medians on the original scale [11].
Layout

RESEARCH APPROACH

Aim 1: Dissect the genetics of early placental dysfunctions.

Our access to hTPCs derived from euploid and aneuploid placentas, along with the advent of CRISPR-Cas9 systems, opens the ability to discover the genetic basis for placental dysfunction in a human-based in vitro system.

Aim 1a: Investigate the genetics of early placental anomalies in trisomic hTPCs.

Knowledge gap: The mechanisms by which aneuploid cells disrupt placental development are not well understood. Addressing this knowledge gap provides a powerful means to uncover genes and pathways involved in placental dysfunction and diseases of pregnancy.

Strategy: Using CRISPR/Cas9 gene editing or lentiviral transduction, the euploid hTPC lines will be engineered to have down regulation or overexpression of key genes identified in the trisomy transcriptome analysis (Sebastiano and Winn Labs). We will overexpress or downregulate genes in the euploid hTPCs that are altered across all trisomies and trisomy hTPCs, e.g. increasing Itchy E3 Ubiquitin Protein Ligase (ITCH) and Insulin-like Growth Factor Binding Protein 3 (IGFBP3) expression and decreasing Fatty Acid Binding Protein 7 (FABP7) and Hepatocyte Growth Factor (HGF) (Fig. 2B). Genes that are overexpressed in a specific trisomic chromosome (i.e. FLT1 for T13, ANKRD12 for T18, and PLAC4 for T21) will then be examined at the transcriptional and phenotypic level to determine if and which of the chromosome specific dose gene effects drives placental dysregulation.

Phenotypic assessment of hTPCs: hTPCs are maintained in culture in progenitor state using methods previously described [10]. As in prior work, hTPC lines will be differentiated with activin inhibition [11] and alterations in differentiation markers characterized (i.e. by decrease in E-cadherin and ITGA5, along with an increase in expression of HLA-G, ITGA1, and VE-cadherin) [12-15].

Assessment of TB proliferation, migration and invasion: After initial experiments with the IncuCyte system to determine plating density and timing to optimize results for hTPCs, each hTPC line (n=3 for each genotype) will be phenotypically assessed in a similar fashion to data presented in Fig. 3.

Data for proliferation, migration or invasion will be presented as mean +/- SD from defined static time points or as the ED50 for kinetic data. Comparisons among groups will use parametric or nonparametric analysis for multiple comparison as needed, with significance set at p <0.05.

Outcomes: These experiments will reveal the altered genes and molecular pathways that account for specific aspects of impaired TB differentiation and function.
Layout

Further Resources

• *Are You Justified? Text Alignment in Your Grant Proposal* – Grant Writers’ Seminars and Workshops Blog
• Funding agency’s instructions!
Making a strong case…

Plan
Layout
Articulate
Narrate
Share

https://www.atlasobscura.com/places/hussaini-hanging-bridge
https://commons.wikimedia.org/wiki/index.php?curid=1520007
Articulate

Have a clear structure

Write a few bullet points under each heading to get started
Articulate

Every paragraph in your application should make one point only.

Present the stand-alone thoughts in an order that creates a progression of logic to lead the reviewer through your story.

The ideal grant is one that leads reviewers through it without them knowing that they are being led.
Articulate

Don’t assume knowledge

Share your proposal with colleagues in other disciplines
Articulate

Avoid excessive emphasized text
This study measured the responses of forearm blood flow (FBF) and forearm vascular resistance (FVR) after isometric handgrip exercise (IHE) and related them to plasma norepinephrine (NE) and epinephrine (E) in 12 normotensives (N) and 14 primary hypertensives (PH). IHE was performed at 30% of maximum voluntary contraction using a calibrated dynamometer. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), FBF, FVR, NE, and E were measured in the resting arm before and after IHE. Pre-exercise SBP and DBP were higher in PH than in N. FVR was similar in PH and N. NE was higher in PH compared to other matched normotensives. After IHE, SBP and DBP were increased 18% and 19%, respectively, in PH and 16% and 25% in N. HR, NE and E were increased in PH and N. Group differences were not significant. Pre and post IHE FBF was similar in both groups. FVR increased in both groups. The findings indicate that skin and muscle arteriolar resistance at rest and during stress in PH with enhanced sympathetic tone are not different from N, and suggest that other hemodynamic abnormalities, perhaps increased cardiac output and splanchnic resistance, mediate the excessive neural tone and raise blood pressure.
Articulate

When to use abbreviations:

To replace a term that is long or unwieldy and appears many times in the grant.

An abbreviation should be used often enough that a reviewer does not forget the meaning.
### Articulate

- **Limit use of the verb “to be”**
  - Instead of: \( X \) is an indication that \( Y \)
  - Write this: \( X \) indicates \( Y \)

- **Limit prepositional phrases**
  - Instead of: \( The \) instrument in the lab is necessary
  - Write this: \( The \) lab instrument is necessary

- **Use direct, active-voice sentences**
  - Instead of: Provides justification for
  - Write this: Justifies

- **Avoid noun forms of verbs (nominalizations)**
  - Instead of: \( The \) application of these techniques can
  - Write this: Applying these techniques can
Articulate

Express confidence in your ability to accomplish aims

*It’s what you WILL do, not what you will TRY to do*
Articulate

Further Resources

- Tips for Grant Writing – Michaela Kiernan, PhD
- Writing in the Sciences – Kristin Sainani, PhD
- Writing for Reviewers – Liz Seckel, MA
- Summary of words to avoid in grant applications – Grant Writers’ Seminars and Workshops Blog Series
Articulate

Make certain all figures are legible and have detailed legends

Further Resources

• A Picture Speaks a Thousand Words – Sarah Heilshorn, PhD
• Visualizing Your Data – Sarah Heilshorn, PhD
Making a strong case…

Plan
Layout
Articulate
Narrate
Share

https://www.atlasobscura.com/places/hussaini-hanging-bridge
https://commons.wikimedia.org/w/index.php?curid=1520007
Narrate

Tell your story!

- Specific Aims
- Project Timeline
- Relevance to Maternal and Child Health
- Background and Significance
- Preliminary Studies (if available)
- Research Design and Methods
- Career Development
- Potential Pitfalls and Contingency Plans
- Future Steps

"My project is simply this. I want to find out once and for all whether there's any truth in the belief that money can't buy happiness."

© Eoin O-Sullivan
Specific Aims

• This is one of the most important sections in any grant application

• It is by far the most difficult section to write well

• Write this section FIRST

• It must quickly engender robust enthusiasm for your idea

• It serves as the template for the rest of your proposal

• The flow of logic must be compelling
Narrate

- Is the question important?
- What specifically will be done?
- What is the overall goal?
- What is the expected payoff?
Narrate

Use the answers to the key questions to organize your Specific Aims
Specific Aims

1) Is the question important?
   • Attention grabbing first sentence
   • Bring reviewers up to speed
   • Frame the knowledge gap/need
Specific Aims

1) Is the question important?

2) What is the overall goal?
Specific Aims

1) Is the question important?

2) What is the overall goal?
   - Big-picture goal
   - Objective of this proposal
   - Best bet / hypothesis
   - Supportive preliminary data
Specific Aims

1) Is the question important?

2) What is the overall goal?

3) What specifically will be done?
   - Aims
   - Working hypotheses
   - Methods
Specific Aims

1) Is the question important?

2) What is the overall goal?

3) What specifically will be done?

4) What is the expected payoff?
   - Return on investment
   - Related to goals of the funding announcement
Specific Aims

1) Is the question important?
   • Grabbing attention
   • Bringing your reviewer up to speed
   • Framing the knowledge gap/need

2) What is the overall goal?
   • Big-picture goal
   • Objective of this proposal
   • Best bet / hypothesis
   • Supportive preliminary data

3) What specifically will be done?
   • Aims
   • Working hypotheses
   • Methods

4) What is the expected payoff?
   • Return on investment
   • Related to goals of the funding announcement
SPECIFIC AIMS

Despite extensive evidence of postpartum depression’s prevalence and negative sequelae for both mother and child, many women who are at-risk for postpartum depression fail to receive mental health screening and treatment. One study found that only 12% of women with postpartum depression had received psychotherapy and even fewer (3.4%) received psychopharmacologic treatment by 4 months postpartum. Poor postpartum patient access to mental health services is due to a variety of factors, including high cost, limited providers resulting in long wait times for clinic appointments, limited time, logistics of childcare in the early postpartum period, and stigma. Mobile health interventions, such as smartphone applications (“apps”), can overcome some of these barriers by offering an affordable price point, ease of access, and 24/7 availability.

Our goal is to enable interactive, patient-centered conversations about mental health in the postpartum period, frictionless screening for postpartum depression, and guided self-help content in an interactive cognitive behavioral therapy-based format.

Woebot, an automated conversational agent (“chatbot”) founded by former Stanford clinical psychologist Alison Darcy, is designed to deliver cognitive behavioral therapy in brief, daily conversations within a free instant messenger app accessible via smartphone, desktop, and web browser (see Figure 1). Woebot was developed to have a human-like, friendly “personality” that checks in with users daily, similar to chatting with a friend. Woebot talks to the user about mental health and wellness and sends them videos and other useful tools depending on their mood and needs at that moment. Woebot can be thought of as a choose-your-own-adventure self-help guide which gets more individualized to the user’s needs over time. Woebot can overcome many barriers to care because it is free to download and use, can be used from home without the need to schedule an appointment or find childcare, and is freely available day or night without limitations on usage. In the non-obstetrical setting, Woebot has been shown to significantly reduce symptoms of anxiety and depression in college students after two weeks of use compared to an information-only control group (see Figure 2).

Aim: To determine the extent to which use of an automated conversational agent in the peripartum setting can improve maternal mental health as measured by Patient Health Questionnaire (PHQ-9) and Edinburgh Postnatal Depression Scale (EPDS) scores at 6 weeks postpartum. We will test the hypothesis that the use of Woebot for six weeks postpartum will lead to statistically significant reductions in PHQ-9 and EPDS scores compared to treatment-as-usual controls.

Use of a mental health chatbot in the postpartum setting could significantly improve patient’s symptoms of anxiety and depression following delivery, which can have long-term impacts on their overall health as well as the health of their child. Given the multitude of positive qualities of chatbots, including unlimited care, no-cost, and 24/7 availability, successful implementation could provide a significantly improved mental health experience for postpartum patients.

Amy Judy, MD, MPH, (Stanford University) – MCHRI CE Grant
Narrate

Further Resources

• Specific Aims Outline - Handout
• Writing Your Specific Aims – Crystal Botham, PhD
Narrate

Research Design and Methods

**Introduction/Motivation**

- Brief sentence or two stating aim’s purpose and how it fits into the overall research plan
Narrate

Research Design and Methods

Methods

• Steps of experimental design
• Use separate paragraphs/sections to develop each set of studies
• Succinctly provide only meaningful detail – what can’t be found in a methods manual
• Refer to, don’t detail, anything described in your team’s peer-reviewed publications
Expected Outcomes

- Summarize what you expect your most important results will be
- “At the completion of this part of the project, we expect to have determined…”
- Emphasize how they will contribute to the achievement of your objective
Narrate

Research Design and Methods

- For clinical studies, include inclusion/exclusion criteria and sample size determination

- **A pre-award biostatistical consultation is required** for all human-based studies
  - Available through the Quantitative Sciences Unit: https://redcap.stanford.edu/webauth/surveys/?s=XJ8FW9LALN
  - Contact ASAP!
Narrate

Potential Pitfalls and Contingency Plans

• First indicate why the problem is unlikely

• Then offer alternative strategies -- but

• Do not overemphasize the problems

• Always write these as conditionals (they are only what you “might” or “would” do)
**Narrate**

**Project Timeline**

- Use specific aims/milestones/objectives as indicators of progress

- This demonstrates you have a plan and aren’t winging it

<table>
<thead>
<tr>
<th>Project</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Q5</th>
<th>Q6</th>
<th>Q7</th>
<th>Q8</th>
<th>Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim 1: Develop Material</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Milestone 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Milestone 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aim 2: Test Material</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Milestone 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Milestone 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aim 3: Build Bridge</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Narrate

Preliminary Studies

• Data presented should be carefully selected to support the feasibility of your aims/hypotheses

• Avoid inclusion of extraneous or irrelevant data

• Present data as simply as possible: design each figure or table to convey a single point or idea
Narrate

Background and Significance

• Background
• Critique existing knowledge
• Identify the
  • Knowledge gap
  • Objective
  • Significance
• State how this will advance the field
Narrate

Background and Significance

• Hook the reader with a strong introductory paragraph.

• Common mistake: Using the introduction to showcase comprehensive and exhaustive knowledge without clear thread of thought.

• Demonstrating how you think and prioritize is far more important than displaying your knowledge.
Narrate

Relevance to Maternal and Child Health

• Describe the relevance of your research to maternal and child health

• Be succinct and use plain language that can be understood by a general audience

• 2-3 sentences max
Narrate

Career Development

• Describe how this funding will advance your career goals

• 2-3 sentences max
Narrate

Future Steps

- Summarize expected outcomes
- Discuss future experiments and approaches
Further Resources

- Russell SW, Morrison DC. The Grant Application Writer's Workbook: National Institutes of Health Version. Grant Writers' Seminars and Workshops, LLC.

- Yang, OO. Guide to Effective Grant Writing: How to Write a Successful NIH Grant Application. NY: Springer.


All available at Lane Library!
Further Resources

- Communicating Your Research Strategy – Sky Brubaker, PhD
- Nuts & Bolts of Writing the Research Strategy – John Boothroyd, PhD
- Research Plan: Developing the Devilish Details – Tim Stearns, PhD
Making a strong case…

Plan
Layout
Articulate
Narrate
Share

https://www.atlasobscura.com/places/hussaini-hanging-bridge
https://commons.wikimedia.org/w/index.php?curid=1520007
Share

Show your draft application to:
  Your collaborators
  A colleague that does not know what you intend to do

After reading your proposal, they should be able to tell you:
  WHAT you intend to do
  WHY it is important
  HOW you’re going to do it.

*If they don’t get it, you must revise your application!*
Scoring and Review Criteria

Review is based on (1) relevance to maternal and child health and (2) NIH Investigator-initiated Review Criteria:

1. **Significance.** Does this study address an important [child health] problem? If the aims are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventions that drive this field?

2. **Approach.** Are the conceptual or clinical frame-work, design, methods, and analyses adequately developed, well integrated, well-reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

3. **Innovation.** Is the project original and innovative? For example: Does it challenge existing paradigms or clinical practice or address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or use novel concepts, approaches, methods, tools, or technologies?
Scoring and Review Criteria

4. **Investigators.** Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

5. **Environment.** Does the scientific environment contribute to the probability of success? Do the studies benefit from unique features of the scientific environment or subject populations or use useful collaborative arrangements? Is there evidence of institutional support?
Applicant Name:  
Reviewer Last Name:  

**Overall Evaluation:** [Score] (Select Score: 1-4) 

<table>
<thead>
<tr>
<th>Score</th>
<th>Overall Evaluation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High (H)</td>
<td>Exceptionally strong with minor weaknesses</td>
</tr>
<tr>
<td>2</td>
<td>Medium-High (MH)</td>
<td>Strong but with some minor weaknesses</td>
</tr>
<tr>
<td>3</td>
<td>Medium-Low (ML)</td>
<td>Some strengths but also some moderate weaknesses</td>
</tr>
<tr>
<td>4</td>
<td>Low (L)</td>
<td>Few strengths and some major weaknesses</td>
</tr>
</tbody>
</table>

**Definitions**

- **Minor Weakness:** easily addressable, does not lessen impact
- **Moderate Weakness:** lessons impact
- **Major Weakness:** severely limits impact

1. **Maternal and Child Health Relevance.** Does this study address an important maternal/child health problem?  
   - Yes [ ]  
   - No [ ]  
   
   If there are any questions or concerns about maternal & child health relevance (e.g. borderline), please mark 'No' and explain in question 4. Will be discussed in the meeting.

2. **Overall Summary & Assessment of Proposal**  
   Please provide a brief summary highlighting the strengths & weaknesses of the application.


4. **Other Comments & Questions to Applicant.** Please note any Maternal & Child Health relevance concerns here.

5. **Conflict of interest (COI) disclosure:**  
   - I have directly worked on or have been involved in this project [ ]  
   - I have no conflict of interest that I am aware of [ ]
Share

Further Resources

- MCHRI Postdoc Program Review Sessions Jan. 16th
- Each other!!
Write for Reviewers
“Agreed. We fund only those proposals we can understand.”
Further Resources

Further Resources

- [A Reviewer’s Perspective](#) – Jeffrey Koseff, PhD
- [Thinking Like a Reviewer](#) – Lamia Wahba, PhD
- [NIH mock study section](#) – NIH Office of the Director
Thank you for listening