Writing Superior, Clear and Innovative Specific Aims

R² Workshop

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The Cornerstone of a Research Proposal

• What are the objectives of the work?

  ▪ Master Plan of your research.

  ▪ Simple and easy to read.

  ▪ Dense, full-of-jargon, poorly-written Specific Aims will not help the review of your proposal, even if the science is sound!

  ▪ Is a useful summary for obtaining early feedback on your proposal
The Science of Specific Aims

• Unmet scientific need

• Includes project goals, hypotheses to be without fine detail

• Original ideas

• Novelty of design

• Fills a gap in the existing scientific story
The Art of Specific Aims

• Be crystal-clear in your writing!
  – State the conceptual framework
  – Limit scientific jargon
  – Non-experts in the field should understand the aims and why they are important
The Marketing of Specific Aims

• Review committee considerations
  – Not all members read every word of the proposal
  – Many read just the specific aims

• Statement of aims preceded by several paragraphs
  – National and big picture science
  – Clinical and translational importance
The Formula for Specific Aims

1. Introductory Paragraph

*Opening sentence* containing extremely creative thoughts. This will grab the attention of your reader.

State what is *known* about this issue.

State what is *unknown* about this issue.

State why is this lack of knowledge is important.
Formula, cont’d

2. **What, Why Whom Paragraph**

State the overall, long-term goal of your mission. This represents any future projections or the continuum of your line of research.

State the overall objective of this application. This is a step to achieving your long term goal.

Steps along the continuum for this research that must be achieved, regardless of how hypothesis tests.

Clearly state your central hypothesis. All vague and unfocused fishing expeditions for information will not adequately fulfill your research mission and appears as an invalid study design.

State your rationale for your hypothesis, or how did you come up with the central hypothesis.

Briefly explain why your research design are the best possible solution for the topic at hand.
Examples

• The overarching goal of this proposal is to estimate associations between prenatal exposure to mixtures of correlated endocrine disrupting chemicals (EDCs) and child neurodevelopment.

• The goal of our research is to determine the mechanism of X (or Y, or Z).

• The overall goal of our research group is to define the role of …
Mounting evidence suggests that prenatal exposure to these EDCs may be associated with adverse child neurodevelopment, yet previous studies are limited by small sample sizes, inconsistencies in developmental measures, and differences in the timing of exposure and outcome assessments\textsuperscript{1,2}. More importantly, previous research has been hindered by a fundamental methodological problem: the challenge of estimating the neurodevelopmental impact of complex mixtures of highly inter-correlated EDC chemicals, with varying concentrations of constituents and potentially different effects across populations. Only recently have investigators begun developing and applying methods to study the effects of complex environmental chemical mixtures, and these methods have yet to be applied to the study of EDC effects on neurodevelopment. This is a critical research gap, as exposures to EDCs are ubiquitous in the US and other developed countries. The validation of methods for evaluating effects of chemical mixtures has been identified as a high priority by NIEHS and the National Academy of Sciences\textsuperscript{3,4}. 
3. **Specific Aims**

Detail your specific aims that will test your central hypothesis, citing primary and secondary endpoints.

Write in the ACTIVE voice.

Use verbs:

- to explain
- to examine
- to investigate
- to estimate
- to compare
Example

Specifically, we propose to:

Estimate the independent and combined associations between prenatal exposure to mixtures of correlated EDCs metabolite concentrations and age 6-7 year neurodevelopmental endpoints in the SELMA cohort based on the results of a comparative modeling strategy.

Compare the results of four different analytic strategies to model exposure-outcome associations in the SELMA cohort;

Select the strategy(s) that best meets criteria of congruence between discovery and confirmation phases and correct identification of etiologically important components in the simulation phase.

Apply the selected analytic strategy(s) from Aim 1 to a New York City cohort (CCCEH) to ascertain whether these methods are applicable in a heterogeneous population with different EDC exposure concentrations.
Formula, cont’d

4. Payoff paragraph
Briefly explain why this application is innovative
State plainly and simply the general positive impact that your study will have on science.

Why should the reviewers care
Why you should get funded
Why is it important for the general population
Example

Results will inform future researchers and policy makers about possible developmental risks associated with prenatal exposure to EDCs across populations of children.
Hurricane Sandy Grant
Major climatic events, such as hurricanes, appear to be increasing due to the consequences of global warming. Such events are likely associated with increased psychological stress. On October 29, 2012 Superstorm Sandy, a major hurricane, devastated the mid-Atlantic region of the United States, particularly the New York City/New Jersey area. Along the coastline, houses and businesses were destroyed and residents were evacuated; as of February 2013 some residents were still displaced. In Manhattan, few residents were displaced; those who were quickly returned. However, the storm resulted in serious perturbations to mass transportation, which led to income loss for many. Further, the storm also resulted in long-lasting power outages and shortages of basic supplies such as bread, milk and gasoline.
Pregnant women are considered a vulnerable population. There is increasing evidence that acute psychosocial stressors may be associated with adverse pregnancy outcomes, such as decreases in birth weight and decreases in gestational length. Such outcomes may be the result of acute biological responses to stressors, such as increased production of hormones such as cortisol and increased inflammatory processes. Previous studies in pregnant women following natural disasters find associations with depressive symptoms, anxiety and post-traumatic stress syndrome, and with birth weight, preterm delivery and intrauterine growth restriction; inferences from these are limited, however, because baseline measures of perceived stress were not available and sample sizes were limited.
One recent novel hypothesis relates psychosocial stress and experiences of adverse life events to decreases in leukocyte telomere length (LTL). LTL is associated with chronic diseases, particularly atherosclerotic heart disease, in adulthood and decreased longevity. Little is known regarding the determinants of LTL at birth, which is likely the largest predictor of LTL in adulthood. Given the paucity of literature, it is of interest to determine whether exposure to acute stressors in pregnancy is associated with decrements in LTL at birth.
We were fortunate to be in the process of recruiting 1000 mother-father-newborn trios for a study of prenatal determinants of leukocyte telomere length at birth (R01 HD071180) at the time of Superstorm Sandy. The trios come from prenatal clinics at Columbia University Medical Center in Manhattan and Christiana Health Care Center in Delaware. The protocol for the parent study is remarkable for: comprehensive evaluation of fetal growth by ultrasound from early in pregnancy to parturition; comprehensive measurements of maternal lifestyle, behavior, and health; and the archiving of biological specimens from mothers and newborns. In this R21 application we build upon this study and propose to evaluate the effects of Superstorm Sandy on pregnancy outcomes and LTL in newborns. Because of the timing of recruitment, we are able to evaluate several “exposure windows”, that is no exposure (i.e. birth before the storm), exposure in each trimester and in the three months prior to pregnancy. We also are fortunate to have an unexposed site to serve as a “place” control. For several important reasons, the proposed study improves upon previous work on stress and pregnancy: first, we have both time and place controls and second, we have baseline assessments of stress, social support, anxiety, depression, and resilience. Further, we have sufficient sample size to test our hypotheses. Finally, we are already administering a questionnaire to participants asking about their experiences and stress during the storm.
The specific aims are:

1. To examine associations between exposure to Superstorm Sandy and a) decreased length of gestation, b) reduced birth weight, c) reduced birth weight for gestational age, d) decreased head circumference, e) decreased birth length. Secondary aims will examine the associations between exposure in specific trimesters and outcomes and between exposure and dichotomous outcomes such as preterm birth and small for gestational age (SGA).

2. To examine associations between exposure to Superstorm Sandy and LTL in newborns and to examine whether associations, if any, are modified by baseline levels of perceived stress, social support, anxiety, depression and resilience.
Our results have the potential to inform emergency responders and clinicians how best to support and potentially mitigate the effects of psychological stress among pregnant women during and after a major natural disaster. This study will also set the stage for studies to inquire whether exposure to stressful events during the fetal period has long lasting effects on behavior and cognition in children.
Linear Progression of Logic for a Strong Specific Aims Section

GAP

OBJECTIVE

CENTRAL HYPOTHESIS

SPECIFIC AIMS

EXPECTED OUTCOMES

www.usuhs.mil/medschool/faculty/ppt/writingspecificaims.pptx
Finally…

– Propose good science
– Write well
– Get feedback
Specific aim 1: Identify the states with the most effective PDMPs.

I will use a multiple-group interrupted time series analysis (ITSA) to estimate the effect of PDMP on a vector of outcomes. Compared to a single-group ITSA, a multi-group ISTA can account for exogenous policy shifts that affect both the exposed and the unexposed populations (e.g., the FDA’s promotion of abuse-deterrent formulations). Rather than focus on a single outcome variable at this stage, I will define my outcome variable as a vector of outcome measures (85), including, for example, opioid- and benzodiazepine-related overdose rates; rates of NMUPD; rates of prescriptions for opioids, benzodiazepines, and stimulants; and rates of neonatal abstinence syndrome. Furthermore, I will employ several comparison groups to both 1) investigate the sensitivity of the effect estimates to different counterfactual populations and 2) identify differences in the distribution of potential component causes that might contribute to any differences in the effect estimates observed across the counterfactual populations. Example comparison groups will be identified using the nearest geographic neighbor, propensity-score weighting techniques (86), and a synthetic controls approach (87).
1.DF, EPI, Student (continued)

Specific aim 2: Develop a novel method to weight the effects of state PDMPs to the national level to estimate the number of NMUPD and drug overdoses that could be reduced if the most beneficial PDMPs were scaled up to the national level.

This aim will extend previous work using weights to generalize observed estimates from a randomized study sample to a specific target population (79-84). Although in expectation random assignment balances the distribution of potential confounding factors between the control group and the treatment group, it is well known that trial populations often are incongruent with target populations (88-90). This incongruence between observed trial estimates and expected population estimates are a function of stringent eligibility criteria and individual self-selection into trials (89-91). And while randomization, in expectation, can overcome three assumptions necessary for association to equal causation (exchangeability, positivity, and consistency), trial procedures can introduce selection bias and limit external validity.
Specific aim 2 (continued):
Because it is assumed that randomization ensures internal validity in clinical trials, extant methods have employed weights to maximize external validity, or generalizability, of trial estimates to the target population. However, in the absence of any expectation of internal validity, such as with policy analysis from observational data, Specific aim 2 will require both a theoretical step and an analytical step. First, for the theoretical step, I will need to identify how the assumptions necessary for internal validity might change when using weighted observational data from a source population to generalize to the target population. For this step, I will focus on these assumptions when using different quasi-experimental methods that often require weaker assumptions than standard regression methods to estimate causal effects, such as regression discontinuity designs, difference-in-differences, and interrupted times series designs (92). Next, I will determine what additional assumptions will be necessary to transport effects from a state population to the general US population, such as equal distribution of effect modifiers in both populations under study. For the final step, I will employ an ecosocial framework to identify the potential causal mechanisms, identify important effect modifiers, and develop a method to weight estimates from a state population to the general US population.
2.IM, EPI, Student

Task-Shifting in HIV Care and Treatment in Rural sub-Saharan Africa through

There is a severe shortage of health professionals in low-income settings such as sub-Saharan Africa, which is the region most-severely burdened by the HIV/AIDS epidemic. Several HIV programs have used non-clinical staff and volunteers such as peer educators and community health workers (CHWs) to achieve positive health outcomes, particularly the early identification of HIV infected individuals and their linkage and retention into care. This is in-line with the 90-90-90 targets for 2020 set by UNAIDS to end AIDS by 2030, which aim to have 90% of all people living with HIV knowing their status, 90% of all people living with HIV receiving antiretroviral therapy (ART), and 90% of all receiving ART achieving viral suppression.
Evidence on the effectiveness of CHWs in administering HIV care and treatment in resource-limited settings is mixed. Most studies which have assessed task-shifting (the delegation of tasks to less specialized health workers) in HIV care and treatment have focused their evaluation on clinical staff and not on community-based staff. Many studies have assessed HIV outcomes in communities serviced by both clinical and community-based staff, making attribution of HIV outcomes to lower health cadres difficult. The effectiveness of CHWs has been evaluated in individual HIV programs but has not been compared across comparable populations. Proper attribution of HIV outcomes to lower health cadres is important for health systems management and human resource for health (HRH) planning.
2.IM, EPI, Student (continued)

We have a unique opportunity to compare HIV outcomes in populations that are serviced by different healthcare cadres but are otherwise comparable. Kenya recently decentralized the management of its HRH to county governments. Many NGOs in Siaya County handed over their CHW programs to the local governments as they transitioned out of their funding cycles, particularly coinciding with the end of the millennium development goals (MDGs) era and the transition into the sustainable development goals (SDGs) era. There is a move towards integrating the operation of CHW programs, but the government does not yet have the capacity to take up CHWs in all districts, leaving some communities not serviced by CHWs and without access to health facilities, while other communities may have several health facilities in close proximity, that are serviced by clinical staff.
2. IM, EPI, Student (continued)

This provides a prime opportunity to conduct a natural experiment by following a longitudinal cohort of patients and providers to compare HIV and staff performance outcomes in an ethnically homogenous population that primarily differs in access to clinical versus community-based health providers. The objectives of this proposal are to measure the performance of clinical versus community-based providers of HIV care and treatment and to compare patient health outcomes across the coverage areas of different types of health providers in Siaya County, Kenya. The performance of nurses and CHWs will be measured by HIV proficiency testing exercises and ART administration tests, and patient follow-up rates will be measured by frequency of household visits to eligible patients. Data from household and facility level registers will be used to measure proportions on ART, virally suppressed and median CD4 counts for HIV positive patients of the corresponding CHWs and nurses. The specific aims are:
2. IM, EPI, Student (continued)

(1) To measure the performance of CHWs vs. facility-based nurses in HIV diagnosis, ART administration and patient follow-up

(a) We hypothesize that CHWs are as proficient as nurses in HIV diagnosis and in ART administration, but that CHWs are more proficient than nurses in patient follow-up

(2) To compare the following health outcomes for HIV positive patients of CHWs vs. nurses: proportions on ART, virally suppressed and median CD4 counts

(a) We hypothesize that after a year of follow-up, a higher proportion of HIV positive patients of CHWs will be on ART, have higher rates of viral suppression and higher median CD4 counts than patients of nurses.
2.IM, EPI, Student (continued)

(3) To compare proportions on ART, virally suppressed and median CD4 counts of patients of CHWs and nurses to a control group of patients in households not covered by CHWs and with limited access to health facilities in the county

(a) We hypothesize that after a year of follow-up, a higher proportion of HIV positive patients of CHWs will be on ART, have higher rates of viral suppression and higher median CD4 counts than patients without access to healthcare.

Our results have the potential to inform governments and development stakeholders on the efficiency of less clinically skilled health cadres in HIV care and treatment to achieve the 90-90-90 goals. They also have a potential for health systems strengthening, as they will inform CHW programmers and HRH planners on the efficiency of integrated CHW programs, which can be applied to other disease areas that utilize the same CHWs.
3. BR, EPI, Student

I am in the early stages of working on specific aims for my doctoral dissertation in Epidemiology and would love to get feedback as part of the workshop. These are my current draft aims:

**Aim 1:** Systematically review the scientific literature related to individual microfinance loans and health outcomes in men, women and children.

**Aim 2:** Evaluate the association between microfinance loans and change in psychological distress in Indonesia over 14 years of follow-up.

**Aim 3:** Examine the relationships between loan characteristics and subsequent health outcomes amongst microfinance borrowers in Indonesia, including lender type, amount, repayment period, interest rates and loan purpose.
Thank you!

Research Resources

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