Developing Scientific Research Proposals (Grant Writing)

2003 Epidemiology and Biostatistics Summer Session

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Session 4

Methods by Study Type

Research Application

	VHA		NIH
I.	Research objectives and specific aims	I.	Specific aims
II.	Background and Work Accomplished	II.	Background and Significance
III.	Significance	III.	Preliminary studies
IV.	Methods	IV.	Research design
V.	Protection of human subjects	V.	Analysis by aim
VI.	Project management plan	VI.	Sample size
		VII.	Logistics
		VIII.	Limitations
		IX.	Summary

Before Getting Started

- Carefully know what you are going to do before you start writing
- Talk to experts and collaborators, have meetings, make informed decisions
- Sketch out the design, think through the details
- Outline the major sections and subsections

Writing Tips

Get organized, stay organized:

- Use Sections (subsections, subsubsections, subsubsubsections)
- Use Tables for lists of variables, ideas, procedures
- Use Figures for complex procedures

Writing Tips

- Give enough, but not too much detail:
- Tie decisions to specific aims
- Justify decisions (balance science with feasibility)
- Use generally accepted methods whenever possible and appropriate

Writing Tips

- Carefully describe new or controversial approaches, and give data to support their use
- Put questionnaires in appendices
- Focus on science, not process!

Experimental Design

General questions about data to address:

- Are the data you propose to collect going to allow you to address the specific aims?
- Can you collect these data?

Outline of Methods Section

Components:

- Overview
- Overall Design
- Study Population
- Recruitment

Outline of Methods Section

Components:

- Measurements (Exposures, Outcomes, other variables, etc.)
- Specimen collection
- Follow-up plan
- Data management

Outline of Methods Section

Components:

- Quality Assurance
- Analysis plan
- Sample Size
- Power

Outline of Methods Section

Components:

- Human subjects issues
- Limitations
- Infrastructure

Outline of Methods Section

Additional components for trials:

- Intervention / Treatment
- Other Measures: Compliance, side effects
- Data and safety monitoring

Overview

Give complete synopsis of study in one paragraph

- What kind of study (design)
- Who (participants)
- Procedures (recruitment, treatment)
- Data collected (key variables)
- Analysis (specific aims)
- Power (sample size)

Design

Study Types

- Descriptive
- Case-Control
- Cohort
- Nested case-control
- Trial

Design

Descriptive Study

- Surveys, cross-cultural comparisons, temporal trend
- Exposure and outcome data generally collected simultaneous
- Example: Seven Countries Study

Design

Descriptive / Survey

- Advantages: Low cost, often short time frame
- Disadvantages: Limited ability to adjust for confounding, often limited number of exposures and outcomes
- Generally reserved for hypothesis generation

Design

Case-control

- Definition of case and source
- Definition of controls and source
- Exposure data collected retrospectively
- Example: Boston Area Health Study of MI cases and community matched controls

Design

Case-control

- Advantages: Shorter time frame and lower cost than a cohort study, can study many exposures in detail
- Disadvantages: Can study only one disease outcome, subject to selection and recall bias
- Example: Pancreatic cancer and coffee

Design

Cohort

- Recruitment effort is not trivial
- Exposure data collected or available before outcomes
- Endpoints collected over time
- Examples: Framingham Heart Study, Nurses Health Study

Design

Cohort

- Advantages: Minimizes selection and recall bias, can study many outcomes and many exposures simultaneously
- Disadvantages: Can be expensive and of long duration, power can be lower than expected (healthy volunteers)

Design

Nested Case-Control

- Design can have features of cohort studies or of classical case-control studies.
- Careful attention to these issues should be made when describing the study to avoid confusion.
- Examples: PHS: CRP and MI; NHS; Breast Cancer and fat intake.

Design

Trials / Experimental

- Design is generally simple but can be complex (e.g., factorial)
- Recruitment issues can be complex
- Treatment (agent, dose, blinding, program, theoretical model)
- Randomization (simple, blocked, adaptive)

Design

Trials / Experimental

- Follow-up
- Consent issues
- Monitoring
- Examples: Physicians Health Study, VA HIT

Design

Trials / Experimental

- Advantages: Minimizes bias and confounding, can accurately measure effect sizes
- Disadvantages: Logistically difficult, long time frame, expensive

Study Population

Define the ideal study population based on the science

- Representation: Age, Sex, Race/ethnicity
- Health status: Can they participate, will they live long enough to contribute information?
- Exposures: Should you over-sample?
- Special inclusion/exclusion criteria

Recruitment Strategy

Design the recruitment strategy with an eye toward feasibility.

- Where will the subjects come from?
- How much effort will be expended in recruitment?
- What are the response and willingness rates?

Source

Survey research

- Random-digit dialing
- Mass mailing
- Defined population lists

Source

Case-control studies

- Physician referral, disease registries, pathology reports, hospital records
- Random-digit dialing, neighborhood, hospital

Source

Cohort studies

- Population-based lists (drivers, voters)
- Defined populations (military, school, large industry, unions, licensed professionals)
- Health-related lists (HMO, insurance, Medicare)

Source

Trials

- Physician referral
- Advertising
- Lists

Recruitment Strategy

Approach

- Letter
- Phone
- Physician
- Door-to-door
- Advertising

Recruitment Strategy

Response/participation/randomization rates

- Quantitative estimate
- Access to sufficient numbers?
  - multi-site study
  - more years to recruit
  - relax inclusion/exclusion criteria
  - decrease participant burden
  - pay money

Recruitment Strategy

Do you need multiple sites?

Site Selection

- Organize site recruitment
- Consider application process
- Evaluate prior experience
- Consider potential recruitment pool
- Consider minority recruitment sites