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**Developing Scientific Research
Proposals (Grant Writing)**

2003 Epidemiology and Biostatistics Summer Session



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Session 3

**Background and
Significance**

Preliminary Studies

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Research Application

VHA

- I. Research objectives and specific aims
- II. Background and Work Accomplished
- III. Significance
- IV. Methods
- V. Protection of human subjects
- VI. Project management plan

NIH

- I. Specific aims
- II. Background and Significance
- III. Preliminary studies
- IV. Research design
- V. Analysis by aim
- VI. Sample size
- VII. Logistics
- VIII. Limitations
- IX. Summary

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Background, Significance and Preliminary Studies

1. Background provides the reader with general context and points out gaps in knowledge
2. Significance tells the reader why the proposed research is important
3. Preliminary Studies demonstrate your abilities to carry out the work proposed
4. Summary -- describe how this research will help to solve the problem

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Background

Begin with a clear statement of the problem

- What is the problem?
- Why is it a problem?
 - common disease
 - serious consequence if undetected
 - high burden for population
 - high costs for health care system

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Example

Biracial Cohort

In 1999 there were approximately 200,000 new cases and 40,000 deaths from prostate cancer. Annual costs associated with the diagnosis and treatment of prostate cancer exceed \$13 billion annually.

Prevalence, costs and practice patterns in veterans are not known. However, if estimates from non-VA settings are utilized, up to one million veterans at a cost of \$2 billion annually could be affected.

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Example

Acupuncture for Back pain

Back pain is one of the most important health problems in the United States and other developed countries. It has been estimated that more than 50% of adults are bothered by back pain each year (Sternbach, 1986) and 70% to 80% of adults are afflicted by it at some time in their lives (Frymoyer, 1988).



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Example

Back symptoms are the leading cause of visits to orthopaedic surgeons and the second leading reason for visit to all physicians (Cypress, 1983; Hart, 1995). Until recently, "medical back problems" was the second most common medical diagnosis-related group (DRG) for all hospital discharges. Among surgical DRG's, back and neck procedures ranked only behind cesarean sections and tubal ligation (Graves, 1987; 1987 National Hospital Discharge Survey, NCH unpublished data).



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Example

Back pain is the most costly ailment of working-age adults, with 1985 earnings and productivity losses exceeding \$5 billion for men alone (Salkever, 1985). It has been estimated that total annual costs of back pain (direct medical costs plus lost productivity and compensation) in the United States are between \$50 and \$100 billion per year (Frymoyer, 1991).



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Review of the Literature

Compare, contrast and critique what others have done

- Organize your literature review
- Use focused literature approach rather than presenting unselected articles
- Assume some readers are experts while others know very little
- Direct the reader to the gap your study will fill.

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Organizing the Literature

- Basic research
- Epidemiologic research
- Trials
- Meta-analyses
- Ongoing other studies which are relevant

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Example

Vitamin E and Prostate Cancer

Basic and animal research support the possibility that vitamin E may reduce the growth of prostate tumors.

In vitro and *in vivo* experiments show that the free-radical quenching activity of vitamin E can decrease cancer growth.¹⁵ Vitamin E may also enhance the immune system.¹³ Vitamin E has been shown to slow the growth of human prostate tumors *in vitro*, as well as in rats receiving various doses of chemotherapeutic agents.^{23,24,42}

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Example

Limited observational data, while not entirely consistent, support the possibility that vitamin E reduces the risk of prostate cancer incidence or mortality. Three case-control studies (conducted in Serbia, Greece, and Uruguay) observed inverse associations between dietary vitamin E and prostate cancer risk,⁴³⁻⁴⁵ with statistically significant reductions of 40% or greater.

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Example

The most compelling data suggesting that vitamin E may reduce the risk of prostate cancer come from the Finnish Alpha Tocopherol/Beta Carotene (ATBC) Cancer Prevention Trial. The ATBC was a randomized, double-blind, placebo-controlled trial of α -tocopherol (50 mg daily) and β -carotene (20 mg daily) among 29,133 male smokers.

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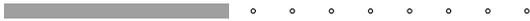
Organizing the Literature

- Use tables and figures to summarize studies
- Liberally use headings, subheadings and sub-subheadings to lead the reader through the logic of your literature review.

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Organizing the Literature





What are the GAPS?

- What don't we know about this topic?
- How would it help to fill in this gap?
- Specifically how will this study fill that gap?





Example

Acupuncture for Back Pain

Despite the fact that acupuncture has been used to treat pain for more than two millennia, its effectiveness remains unclear. A 1990 meta-analysis of acupuncture for chronic pain concluded, "no studies of high quality seem to exist," and therefore, "no definitive conclusions on the efficacy of acupuncture in the treatment of chronic pain can be drawn." (ter Riet, 1990).



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Significance

- Why is this work important?
- Who will it help?
- Is there something new and creative with revolutionary potential? Will it open up a new research avenue?
- Will knowledge gain lead to reduced morbidity, mortality, costs, etc.?
- Is the study worth the money?

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Example

Biracial Cohort Study

Apart from skin cancer, prostate cancer has become the most common cancer in the United States and is the leading cause of cancer death among elderly US men. Prostate cancer remains a major source of morbidity, mortality, and resource consumption for the VA. The VA is committed to enhancing the health of veterans through prevention and optimal management of prostate cancer and remains dedicated to research in these areas.

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Example

The prevalence of prostate cancer in this aging male population, the great willingness of patients in the VA Healthcare System to participate in research projects, the existence of accessible national and local administrative and clinical databases, and the existence of an extensive multi-center research infrastructure, provide a unique opportunity to study prostate cancer at a relatively low cost.

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Example

The establishment of low-cost preventive strategies would be of great benefit to veterans and to the VHA. In addition, better understanding of the causes of prostate cancer could lead to enhanced screening and prognostication as well as improved means of treating and preventing prostate cancer.

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Preliminary Studies

Also referred to as:

- Previous Studies
- Work accomplished
- Progress Report

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Preliminary Studies

- Describes your teams experience
- Highlights your prior publications in this area
- Summarizes pilot data that are necessary to demonstrate effect size, feasibility, recruitment rates, etc.
- Supports your design

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Preliminary Studies

Your Preliminary Studies section can answer many questions about your design. Here is a short list:

- Survey instrument validity and reliability
- Laboratory Procedures
- Recruitment method feasibility and validity
- Recruitment rates

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Preliminary Studies

- Retention rates
- Intervention effectiveness
- Exposure prevalence
- Outcome incidence
- Management experience

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Preliminary Studies

- Quality assurance methods
- Scientific competence
- Team productivity
- Infrastructure
- Costs

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Your Team's Experience

Dietary Feasibility Study

Scientists at the CPRP have extensive experience in the design, implementation and evaluation of both individual- and community-level dietary change studies. To best focus our presentation of this work for this proposal, the description is divided into four sections: a) nutrition intervention research; b) multi-center, diet intervention coordinating center experience; c) self-help dietary intervention trials in primary care practice; and d) methodologic research in intervention assessment.



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Your Prior Publications

Supplements and Cancer

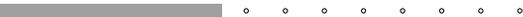
Dr. Patterson has recently published or submitted four manuscripts on the measurement of vitamin supplement use or on correlates of use (80b, 80c, 85a, 85b). One of these studies was an NIH funded study on Methods for Practical and Accurate Assessment of Vitamin Supplements.



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Relevant Experience

...we outline below only our most relevant experience in the conduct of studies of the relation of supplement intake to cancer incidence, in the conduct of large scale studies (cohort and clinical trials), and in the measurement of supplement use and dietary intake. We also give the results of our pilot study on recruitment.



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Studies that Support the Methods

Food Frequency Questionnaire

This questionnaire, developed by Walter Willett, MD, DrPH, and colleagues, is an efficient, reliable, and accurate instrument for categorizing individuals according to their intake of 32 nutrients, including vitamin E, vitamin C, and folic acid.²⁴⁹⁻²⁵¹ Data from the FFQ will be used to categorize the participants according to their baseline intake of various nutrients and then to evaluate whether the effect of each randomized treatment varies according to baseline dietary intake

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Example: Pilot Study

Supplements in Cancer

In preparation for this proposal, we conducted a pilot study to test the proposed recruitment plan, including our ability to recruit a cohort with a large percentage of supplement users, who were willing to complete lengthy questionnaires and to join a study in which they would be followed through health registries (as was explained in the recruitment letter).

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Example: Pilot Study

The cover letter and two questionnaires (Appendix A and B) were mailed to 800 randomly selected age- and county-eligible individuals from a mailing list obtained from a commercial firm, Research and Response. Our response rates were 45% (186 of 414) for women and 38%(147 of 386) for men, including non-response due to undeliverable mail.

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Example: Summary

Diet and Genetic Risk of Lung Cancer

In summary, there is considerable evidence that dietary change self-help materials could be effective public health interventions. However, we recognize that quality research in this area is complex. Reasons include: 1) dietary habits appear to be very difficult to modify; 2) sample sizes must be large, due to a combination of small effect sizes and highly variable measures;



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Example: Summary

and 3) research participants are not generally representative of the target population, because only highly motivated people are willing to comply with burdensome, repeated assessments of nutrient intake. We have recently completed a series of studies that address these problems, by developing more potent low-intensity interventions along with assessment tools that measure dietary change with minimal participant burden.



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Example: Summary

Thus, this proposal is unique in two ways. First, we can generate detailed, personalized motivational and behavioral feedback based on self- and telephone-administered questionnaires, avoiding the very high costs of individualized, professionally-administered dietary assessment and counseling. Second, we can evaluate self-help dietary intervention programs delivered to a defined population, using evaluation techniques that are both valid and feasible for public health research.



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Background Check List

Does the background. . .

- Begin with a clear statement of the problem?
- Compare, contrast and critique what others have done?
- Show how existing work lays the groundwork for your proposal?
- Cite original literature rather than review articles?

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Background Check List

Does the background. . .

- Use a focused literature approach rather than present unselective articles?
- Explain how this study will fill a gap?
- Raise questions the reviewers might ask, then answer them immediately?
- End with a summary?

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Significance Check List

Does the significance section. . .

- Spell out how this work will fill the gaps in knowledge?
- Describe something new and creative with revolutionary potential?
- Point out how this work will lead to a new research avenue?

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Preliminary Studies Check List

Does the Preliminary Studies section. . .

- Demonstrate your expertise?
- Summarize your prior work in this field?
- Summarize pilot data?

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Preliminary Studies Check List

Does the Preliminary Studies section. . .

- Provide evidence of:
 - Recruitment rates
 - Survey instrument validity and reliability
 - Intervention effectiveness
 - Incidence rates for outcomes
 - Quality control measures
 - Adequate infrastructure
 - Experience in data management
 - Feasibility of lab methods

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