Research Grants – Perspectives of an Applicant
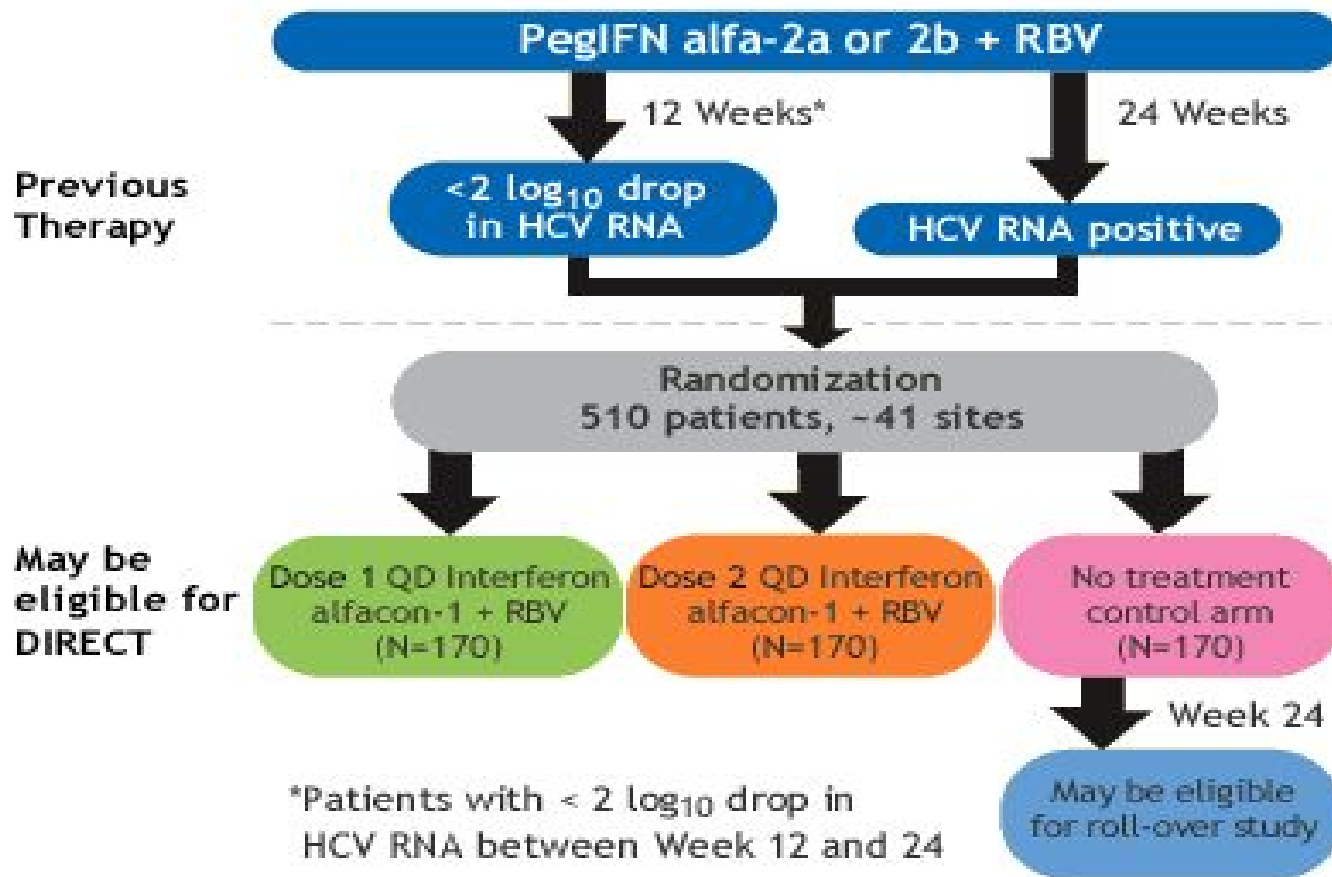
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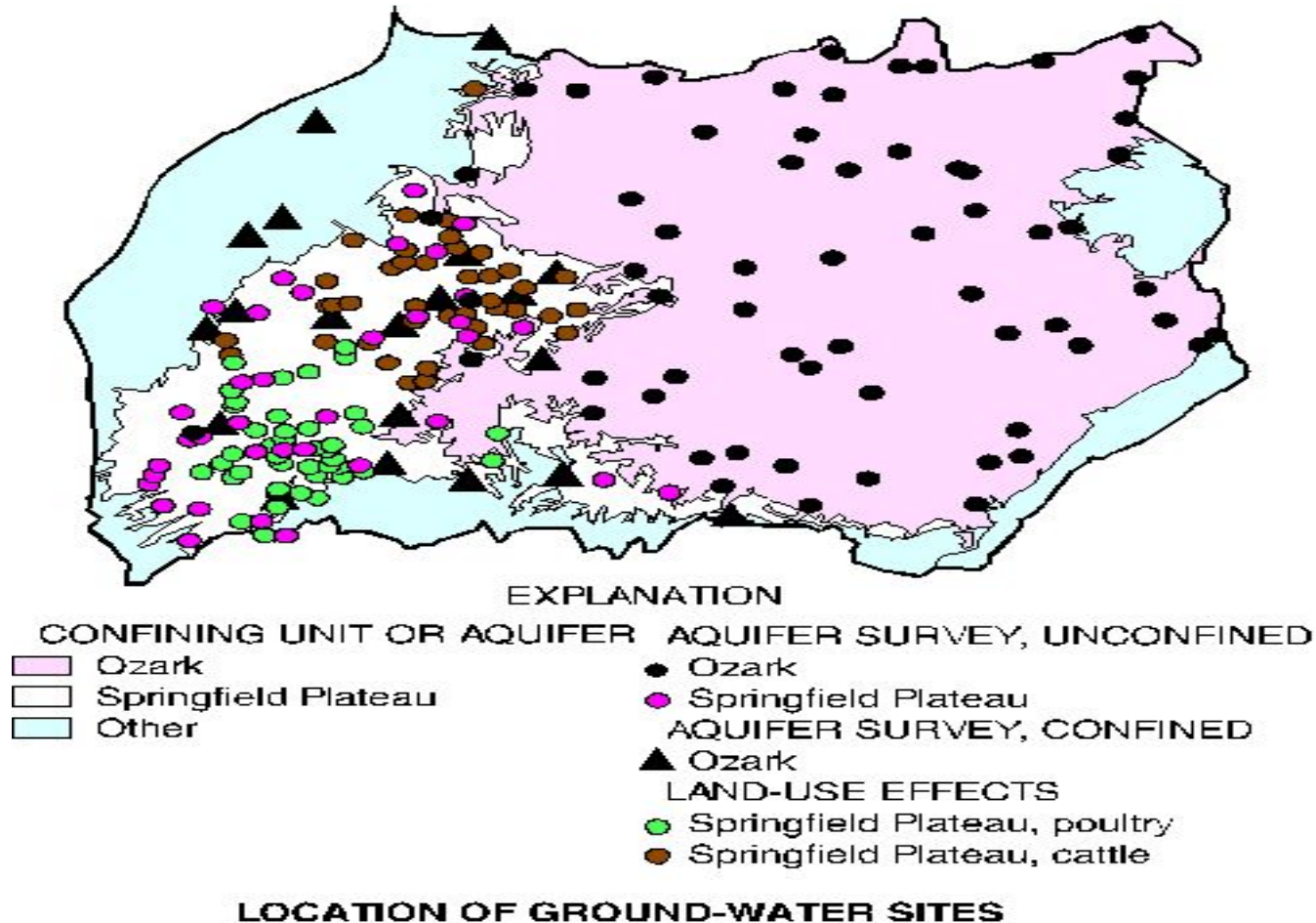- University of Washington

Outline

- Why does NIH sponsor statistical methods grants?

- What are the key elements of a grant?

- How are grants reviewed?

- What happens when a grant is scored?

- When should you submit a grant?

Why does NIH sponsor statistical methods research?

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EXPLANATION

CONFINING UNIT OR AQUIFER
- Ozark
- Springfield Plateau
- Other

AQUIFER SURVEY, UNCONFINED
- Ozark
- Springfield Plateau

AQUIFER SURVEY, CONFINED
- ▲ Ozark

LAND-USE EFFECTS
- Springfield Plateau, poultry
- Springfield Plateau, cattle

LOCATION OF GROUND-WATER SITES

NIH sponsor: Implications

- Focus on research whose **relevance** to real biomedical problems is clear.

- Focus on research related to **priorities** identified by the institutes.

- Find a **connection** to **local** (e.g. your institution) medical research that can motivate and illustrate your statistical work.

- Locate a couple of **data sets** that you can use as concrete examples to illustrate your methods. These data actually often guides the determination of which institute would **fund** the research (e.g. NCI, NHLBI, NIAID).

What are the key elements of a grant?

- Forms and instructions (PHS 398)

    ▷ `http://grants.nih.gov/grants/forms.htm`

- Cover, budget, biosketch

- Content of **Research Plan** (per guidelines) [**25 total pages**]:

    ▷ Specific Aims [**1 page**]

    ▷ Background and Significance [**2-3 pages**]

    ▷ Preliminary Studies [**6-8 pages**]

    ▷ Research Design and Methods [**what's left $\leq$ 25 pg.**]

    ▷ Human Subjects

Elements: Specific Aims

General Introductory Text:

"Longitudinal studies in medicine are faced with new analysis challenges due to continually advancing measurement and database technologies. Specifically, innovations in molecular assays, medical imaging, and psychological assessment have generated numerous new putative markers of disease progression. Also, advances in electronic data recording now allow longitudinal investigations to collect high-dimensional outcome data measured at a fine time resolution. The overall goals of this proposal are to develop regression methodology, graphical summaries, and software tools for analyzing modern longitudinal biomedical data. The specific aims are: "

Elements: Specific Aims

The Aims:

1. **Repeated measures and time-dependent accuracy.**
   Biomarkers are measurements that characterize specific aspects of
   patient health status. Examples include viral load or CD4 cell
   counts in HIV, FEV1 in cystic fibrosis, or serum proteins such as
   CA-125 in ovarian cancer. With a clinical event time, T_i, such as
   time until disease or death, analysis of biomarker data will focus
   both on the predictive distribution $P[T_i > t \mid Y_i(s)]$ where $Y_i(s)$
   represents the measured biomarker at time s (or a function of its
   history), and on the time-dependent accuracy of the biomarker as
   defined by characteristics of the marker distribution conditional on
   event time, $P[Y_i(s) > c \mid T_i = t]$, for various "threshold" values,
   c. This aim will:

- (1.1) Develop semi-parametric ROC methods that characterize covariate-specific *incident* accuracy using a regression quantile approach to estimate $P[Y_i(s) > c \mid T_i = t, X_i]$.

- (1.2) Develop semi-parametric predictive methods that characterize $P[T_i > t \mid Y_i(s), X_i]$ where the marker may be measured at a general time $s < t$.

- (1.3) Develop ROC methods using partly conditional survival estimation (Aim 1.2) and marginal regression quantile estimation to characterize covariate-specific *cumulative* accuracy defined by $P[Y_i(s) > c \mid T_i < t, X_i]$ and $P[Y_i(s) > c \mid T_i \geq t, X_i]$.

2. **Longitudinal categorical data and likelihood inference.**
   Recent "marginalized models" have extended the previously
   limited likelihood-based regression options for categorical
   longitudinal data by combining a marginal mean model with the
   dependence features of traditional random effects or transition
   models. Flexible methods that admit both serial association and
   subject-level random intercepts will be needed in practice because
   both forms of correlation are often present. Extensions of
   marginalized models for the analysis of ordinal data, for analysis
   with case-crossover type designs, and to analysis with endogenous
   covariates are needed. The goals of this specific aim are:

   - (2.1) Develop binary and ordinal response data likelihood-based
     regression methods that admit both short-range serial dependence
     and long-range correlation.

   - (2.2) Investigation of study design options such as "case-series"
     sampling where only covariates for subjects with at least one

positive outcome, $Y_i(t) = 1$, are sampled.

- (2.3) Develop likelihood-based methods for regression analysis with either exogenous or endogenous time-varying covariates.

3. **Software for longitudinal data analysis.**
   The transfer of technology from theory to practice is limited by the availability of user friendly public software. This aim will take both existing statistical programs and new algorithms developed as part of this grant and create accessible publically available software for the analysis of longitudinal data.

Some Comments on these Specific Aims

- Overall theme

- Detailed sub-aims for each major aim

- Connected to modern issues (biomed, stat)

- Connected to specific scientific examples

Elements: Background

- From NIH instructions (PHS 398):

  ▷ "State concisely the importance and health relevance of the research"

  ▷ "...identify the gaps that the project is intended to fill"

- What did Heagerty do?

  ▷ For each aim I organized as follows:

  * Background (medical and statistical)
  * Gave (2) specific example data sets
  * Stated the "statistical challenges" (e.g. **research need**)

Elements: Preliminary Studies

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- Describe your previous work that is relevant to the proposal.

- Describe your collaborations with scientists in your motivating applied area.

- Provide relevant published or accepted papers in Appendix.

- Connect your **past** (accomplishments) with your **future** (the direction of the proposal).

Elements: Research Design and Methods

- Provide as much detail as you can.

  ▷ Overview

  ▷ Estimation

  ▷ Asymptotic properties

  ▷ Applications and/or simulations
    (show that the proposed work has the promise of being successful)

- Detail in methods, simulations, and data analysis.

- Describe well-planned, concrete, systematic strategy for how to proceed with each aim (timeline).

- Note: for the pages: corr(preliminary, research design) < 0 — so usually must compromise.

Review: Innovation

How are grants reviewed?

- Reviewed in "study section" by statistical peers.

  ▷ BMRD – see `http://www.csr.nih.gov` for roster

- Criteria:

  ▷ **Significance** – importance, impact?

  ▷ **Approach** – strategy, likely success?

  ▷ **Investigator** – background?

  ▷ **Innovation** – novel and creative?

  ▷ **Environment** – appropriate resources?

What happens when a grant is scored?

- Approximately 3 months after submission you get a numerical score:

1.0-1.5	virtually flawless
1.5-2.0	significant, easy fix
2.0-2.5	promising, need to consider critiques seriously
2.5-3.0	areas of weakness
3.0-5.0	serious issues

- You will get written reviews (approx 3) that provide detailed assessment.

- You will get a percentile score which is used to determine funding.

- Funding is determined later...

- If not funded – revise the grant and resubmit (only twice).

Grant is funded!

When to submit a grant?

- NIH: 2 / 6 / 10 = Feb, June, Oct

- When you feel like you have a clear research **agenda**.

- When your career can benefit from the **resources**.

- When your career can benefit from the **peer validation** of your research agenda.

Resources

- NIH forms

  `http://grants.nih.gov/grants/forms.htm`

- CSR Study Section BMRD

  `http://www.csr.nih.gov` – search here

- NCI funded statistical grants

  `http://statfund.cancer.gov` – search abstracts

- ENAR2006 Junior Investigator Workshop (Davidian, Betensky)

  `http://health.bsd.uchicago.edu/rathouz/ENARJrWorkshop/`

- New Investigator

  `http://grants.nih.gov/grants/new_investigators/index.htm`