OAIC Symposium on Pilot Study Development

Claude D. Pepper
Older Americans Independence Centers of Johns Hopkins University and University of Maryland, Baltimore

Objectives for Symposium

- To outline the training, knowledge and skills necessary for designing and performing high quality pilot studies.
- To provide an overview of crucial statistical and design issues necessary to develop a successful pilot study.
- To provide examples of OAIC funded pilot studies that illustrate skills needed to design and implement a successful pilot.

Pilot Study Session Program

- The Optimal Pilot Study: An Overview
  - Jeremy Walston, MD (JHU OAIC)
  - Andy Goldberg, MD (UMD OAIC)
- Real Life Pilot Experience
  - Steve Prior, PhD, UMD
  - Devon Dobrosielski, PhD, JHU
- Summary Discussion
  - John Sorkin, PhD, UMD
  - Karen Bandeen-Roche, PhD, JHU

Pilot Study: Definition

- A preliminary investigation intended to collect data to prepare for a larger, more definitive study.
- Generally small in size, scope, duration and budget.
- A Dictionary of Epidemiology (John M. Last, 3rd Edition): A small-scale test of the methods and procedures to be used on a larger scale if the pilot study demonstrates their feasibility (i.e., that these methods and procedures can work).

Rationale for Pilot Studies

- High quality pilot data are essential for developing focused research questions and rationale for developing definitive studies.
- Pilot data strengthens grant applications for external funding.
- A pilot study allows you to know what things go wrong so you can fix them before you start the larger, definitive study.

Some Objectives of Pilot Studies

- Integrity of study protocol
- Testing of data collection forms or questionnaires
- Randomization procedure
- Recruitment and consent
- Acceptability of intervention
- Selection of most appropriate outcome measure
- Sample size calculation

Additional Objectives
■ Protocol testing and refinement
■ Test and identify appropriate logistics
  ▪ Participant burden
  ▪ Approaches to recruitment
  ▪ Baseline testing and methods (standardized and reproducible)
  ▪ Intervention
  ▪ Structure of follow-up

Types of Pilot Studies

Intervention Evaluation
■ Test feasibility of intervention
■ Phase I and II drug trials
■ Test new technology
■ Test a procedure

Idea Generation
■ Develop hypotheses
■ Explore initial hypotheses
■ Explore associations

Method Development
■ Develop instruments or measures
■ Establish forms, procedures, data systems, working relationships
  ▪ Taylor et al. Pilot study of the incidence and progression of degenerative Parkinson disorders in Aberdeen, United Kingdom: Methods and Preliminary Results. Movement Disorders 2006;20:976-982
■ Test methodologies

Clinical Trial Preparation
■ Test feasibility of recruitment
■ Estimate sample size for full scale trial

Types of Pilot Studies

Revisited…
■ A pilot study allows you to know what things go wrong so you can fix them before you start the larger study.
  -Strengthens hypothesis and aims
  -Provides sample size estimates
  -Informs experimental design, methodological issues
  -Provides insight into limitations, potential pitfalls
**Not Objectives of a Pilot Study**

- Conduct definitive hypothesis testing
- Refine/finalize the specific aims for the definitive study
- Generate a definitive answer to the research question
- Therefore, always choose depth over breadth and be certain your research question is well-defined and unlikely to change in a meaningful way.

**Can I Publish the Results of My Pilot Study?**

### Yes!

- Number of pilot studies published in 2000-2001 in top journals
  - BMJ = 11
  - Lancet = 17
  - JAMA = 7
  - NEJM = 3
- Randomized pilot studies appear in meta-analyses as primary studies in some Cochrane systematic reviews

**Challenges in Designing and Writing a Pilot Study Protocol**

**Too Ambitious**

- Goal is to generate estimates of key outcomes of interest.
  - Don’t bundle too much into an early stage project.
  - Don’t try to answer too many questions.
- Differentiate feasibility with a few primary outcomes from mechanistic with predetermined hypothesis-driven outcomes.
- Collect sufficient, meaningful preliminary data to permit informed sample size calculations.
  - Means and SDs for quantitative variables (or proportions for categorical data) in intervention and control groups.
  - Estimate magnitude of effect that is likely to be observed in a definitive trial.

---

**Can I Publish the Results of My Pilot Study?**

### JHU OAIC:


### UMD OAIC:

we will need examples of successful pilots that have helped to launch careers from both of our OAICs.

Andy, I would suggest that you start here.
Proposal Length

- Short - most pilot proposals 3-6 pages
  - Requires concise writing
  - Subject-Verb separation, making for complex sentences is a common problem
    - “Maturation of B cells, which includes rearrangement and expression of immunoglobulin genes as well as selection for cells with functional immunoglobulins and against self-reactive B cells, takes place in the bone marrow.”

Specific Aims

- Not definitive hypothesis testing or objective
  - Still requires well defined, purposeful objective(s)
  - Embedded in a larger good idea or leading to a good, innovative idea/project
  - Necessarily limited in number and scope - Keep these focused and feasible

Significance

- Emphasize the importance of area of inquiry and potential product in small space.
  - Scholarship has to be sharp and to the point, the key articles by the key people.
  - Rationale for the pilot clearly defined.
  - Theoretical model may or may not be necessary.

Should Pilot Data Be Included in a Pilot Study Application?

- Yes, if it makes the case for the importance and sound conduct of the pilot and for the particular funding mechanism – e.g., R03, R21

Sample Selection

- By definition, working with small samples
  - Use as rigorous a strategy as possible but recognize the risk of less representative samples.
  - Try to make sure that your pilot subjects cover the entire range of subjects in your full study.
  - Do not slap on the label of pilot study when your sample size is too small.

Approach

- Feasibility
  - Beware of the tendency to propose or do too much.
- Recruitment and retention
  - Propose a realistic recruitment and retention plan.
  - Reviewers know that recruitment difficulties extend to pilot studies.
Sample Size

- How Many Subjects for My Pilot Study?
  - Depends on the objective of the study.
  - Some pilots don’t require formal sample size calculations.
  - Enough observations to provide useful information.
  - 95% Confidence interval approach if you know target for success (e.g. 70% of patients are able to complete the form).

Statistical Analysis

- Be clear about how the data will be interpreted and utilized.
- Analyses mainly descriptive.
- Confidence interval estimation appropriate in some situations.
- If hypothesis testing is done, treat as preliminary and interpret with caution.
- Outcome data useful to calculate sample sizes for larger study.

Review

- How will the review be done?
  - Ranges from NIH where same review criteria used as for R01 to small Foundation where one reviewer uses a 5 point Likert scale
  - Know the review process and criteria
- Who are the reviewers?
  - Find out who will be reviewing your application, if possible

Budget

- Usually for specific expertise (data management, statistics, consultant), supplies, part of study assistant effort.
- Usually not for investigator salaries, full time study coordinators, equipment, travel.
- Pilots help understand resource requirements in full study.

Potential for Extramural Support

- Does the project have a high likelihood of leading to future extramural, larger grant support?
- Be explicit about how/where pilot results will fit with larger grant- place the pilot study in the context of the full-blown study.
- Deciding on K23, R21 or R01 application

Challenges in Conducting a Pilot Study

- Short time frame
- IRB approval - A pilot takes as long as a large study
- Subject recruitment and retention
  - Don’t be deceived by small number of subjects needed
- Personnel problems
  - Research assistant gets sick, co-investigator or statistician moves
- Supply chain problems
  - Animals, reagents, databases hard to get
- Data inconclusive, uninformative
Challenges in Conducting a Pilot Study

- Short time frame
- Changes in laboratory or clinical practice
  - Affects recruitment, measures, interventions
- Equipment breakdown
  - Flow cytometer, multiplex assay system not working?
  - "I never thought about that!"

Research Working Groups Help Pilots Succeed

- Multidisciplinary team of investigators from OAIC Cores.
- Developed to provide resources, monitor progress & accomplishments, problem solve, accelerate progress, access/cultivate collaborations, etc.
- Meet frequently during early phase of pilot to assure the project’s rapid development, submission of regulatory materials & study implementation in a timely fashion.

Final Pilot Study Wisdom

- Is it really a pilot? Over-ambitious vs. underwhelming.
- Right place, wrong time- does it match the RFA, review criteria, and eligibility? Seek advice!
- Write with purpose – make it compelling, feasible.
  - Statistics/power analysis: even a pilot study needs them.
  - “Gotta have some to get some”
- Can you really do all that with just a few bucks?
- Provide a theoretical model and timeline.

Sources of Funding for Pilot Studies

NIA early stage research mechanisms
- R03s – small grants (50k a year, two years)
  - http://www.nia.nih.gov/GrantsAndTraining/FundingOpportunities/R03.htm
  - Includes Human Biospecimen Resources on Aging Research
- R21s – exploratory/developmental grants ($275k over two years)
  - Exploratory/Developmental Research Grant Award
- NIA Center Programs – pilot studies cores
  - Older Americans Independence Centers
  - Demography Centers
  - Resource Centers on Minority Aging Research

Acknowledgment: Dr. Robin Barr – Pilot Studies Workshop, 2008 AGS Annual Meeting

Sources of Funding for Pilot Studies

- K24 (Mid-Career award in Patient-Oriented research)
  - $50,000 a year that can be used to provide pilot funding
- K07 (Academic Leadership Award)
  - A portion of the $100,000 a year may be used for pilot funding
- NIH Clinical and Translational Science Awards (CTSA) often have local small grant or pilot study mechanisms
- Secondary Data Analysis
  - NIA supports the National Archive of Computerized Data on Aging: http://www.natarchive.uc.edu/NACDA/
  - NIA’s Behavioral and Social Research program lists many sources on its website: https://www.nia.nih.gov/ResearchInformation/ExtramuralPrograms/BehavioralAndSocialResearch/Resources.htm

Acknowledgment: Dr. Robin Barr – Pilot Studies Workshop, 2008 AGS Annual Meeting

Sources of Funding for Pilot Studies

AHRQ Small Research Grant Program (R03)
- Priority areas include translating research into practice, patient safety and quality, patient-centered care, payment and organization
- AFAR Research Grants
  - up to $75,000 for a one- to two-year award to junior faculty, broad range of biomedical, clinical topics http://www.afar.org/grants.html
- Robert Wood Johnson Foundation
  - multiple grants in $50,000-100,000/year on wide range of health topics, some applicable to genitales http://www.rwjf.org/grants/
- VA Research - VA Research Foundation small grants
Sources of Funding for Pilot Studies

- Specialty Associations
  - American Heart Association Affiliate grant Programs
  - American Diabetes Association
- State, Local Community or Institutional Small Grants

Acknowledgements

- National Institute on Aging
- Wake Forest University Pepper OAIC Pilot Project Skills Development Program