Pilot Studies
Nuts and Bolts

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What is a Pilot Study?

- Early study of a new idea designed to obtain preliminary data to support a larger study
  - Usually small
  - Goals often focus on feasibility and logistics
  - Outcomes often surrogates
  - Typically unfunded or funded intramurally
  - Requires a lot of work - protocol, IRB approval, data forms, recruitment, data entry, analysis…
- Distinguish from pre-testing of methods, questionnaires, measures

Clear Reasons to Do a Pilot Study

- Demonstrate feasibility
  - Determine if you can do it
- Improve logistics
  - Determine the fastest, easiest, most cost-effective way to do it
- Estimate cost
- Demonstrate to funders
  - that you can do it within budget!

Possible Reasons to Do a Pilot Study

- Decide whether to do larger study
- Estimate parameters for designing larger study
  - Rate of outcomes in placebo group
  - Variability of outcome measure
  - Effect size

Yoga to Prevent Diabetes

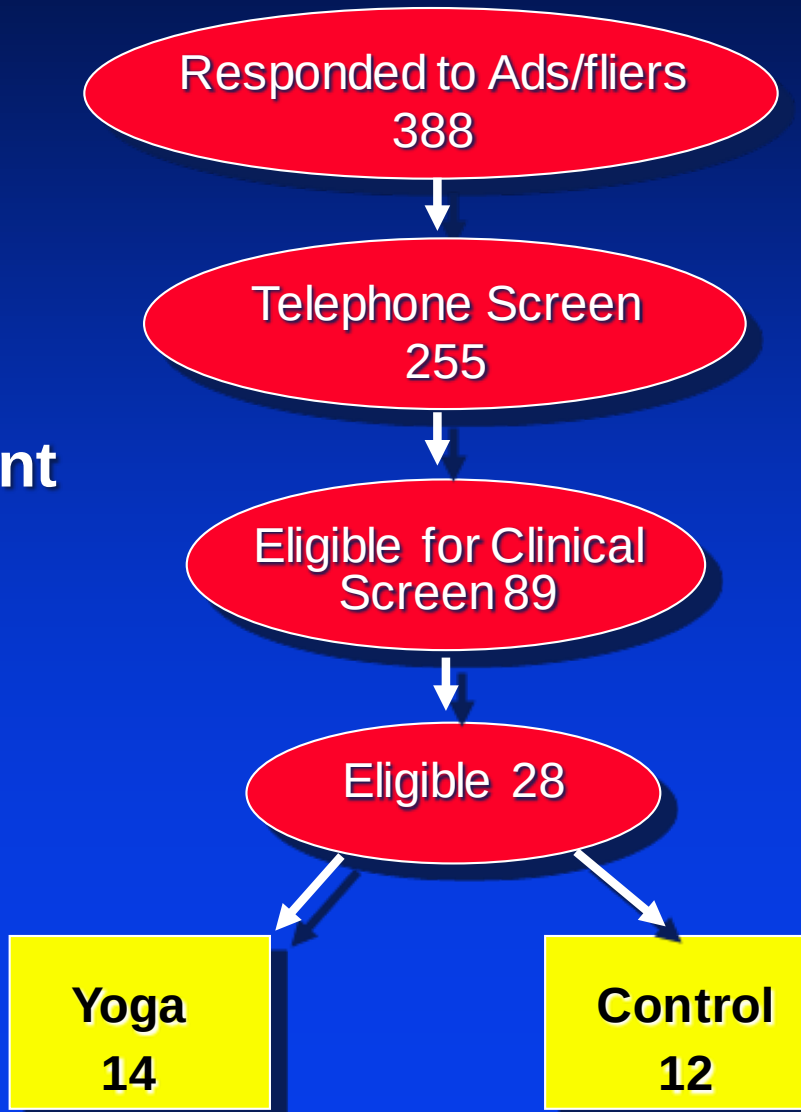
- Evidence suggests yoga decreases stress, improves metabolic risks
- Possible larger study
  - randomized trial of yoga vs. control in adults with metabolic syndrome
  - outcome - new diabetes

Yoga Pilot Study Design

- Randomized trial in persons 30-65 yo with metabolic syndrome
- Intervention - 10 yoga poses taught in group classes x 10 weeks + home practice
- Outcomes – fasting glucose, insulin, lipids, insulin sensitivity, heart rate variability, measures of stress, BMI, diabetes etc.

Feasibility

- **Recruitment**
  - **Sources of participants**
  - **N of participants**
  - **% eligible**
  - **% willing to enroll**
  - **Time and cost of recruitment**



Feasibility

- Interventions and measures
  - Can obese persons perform the postures?
  - Will there be side effects?
  - Can participants do insulin clamp, 2-h GTT, other tests and questionnaires?
- Adherence and follow-up
  - Will participants stay in the study and practice at home?

Logistics and Cost

- What staff are needed?
- How should the flow of visits be organized?
- How long do visits take?
- Can participants answer questionnaires while completing GTT?
- How much will the trial cost?
- Where will participants park?

Yoga Pilot Study Findings

- **Trial is feasible**
  - Able to recruit and randomize
  - Participants able to do 9 Yoga postures
  - Adherence excellent
    - *13.7 classes attended (goal 14)*
    - *100 min practice/week (goal 90)*
- **Logistics improved**
  - One posture (Downward Dog) dropped
  - Added video for home practice
  - Visit time reduced
- **Cost reasonable**

Yoga Pilot Study Results

Variable	Difference	P-value	Favors
Weight, kg	2.3	0.36	Y
BMI, kg/m^2	0.9	0.30	Y
Waist, cm	0.0	0.99	-
SBP, mmHg	9.2	0.07	Y
DBP, mmHg	4.6	0.10	Y
Perceived Stress Scale	0.4	0.12	Y
Energy Level	-0.8	0.008	Y
Psych Well-being	-0.3	0.06	Y
Depression (CES-D)	0.2	0.45	Y
Self-rated health	-0.3	0.35	Y
Insomnia (% none)	30.0	0.01	Y

Yoga Pilot Study Results

Variable	Difference	P-value	Favors
Insulin Sens Index	0.3	0.56	C
Fast. Glucose	-2.1	0.53	C
2-hour Glucose	0	0.99	-
HDL- cholesterol	2.0	0.50	C
Triglycerides	14.2	0.55	Y
ALT	-2.5	0.58	C

YIKES!

Yoga Pilot Bottom Line

- Full-scale Yoga study funded by NCCAM and now completed!

Should Pilot Studies Include Randomization?

- Maybe not…
  - Nonrandomized studies can generally be smaller, faster and cheaper
  - Obtain more data on intervention if all participants receive it
- Maybe…
  - If need to know if randomization is possible
  - If need to know anything about the control group (adherence, placebo rate, etc)
  - If trying to estimate between group effects

Do Pilots Need Control Groups?

- Feasibility, logistics and cost
  - controls generally not needed
- Effect and sample size estimates
  - controls helpful, esp. if need to control for placebo effect
- Phase I trials (evaluate short-term safety)
  - generally uncontrolled
- Phase II trials (evaluate range of doses)
  - generally randomized and controlled

How Do You Estimate Sample Size for a Pilot Study

- Sample size often set by tradition
  - Lab studies - 3
  - Many phase I trials start with 3, add 3
  - Pilots for feasibility often 10 - 20
  - Pilots to estimate effect size can be large
- Sample size often dictated by (limited) resources and time

Should You Publish Pilot Results?

- Restorative yoga in adults with metabolic syndrome: a randomized, controlled pilot trial. Cohen BE, Chang AA, Grady D, Kanaya AM. Metab Syndr Relat Disord. 2008, 3:223-9.
- PubMed search for "pilot" in title, last 12 months, in English
  - 2649 publications!

Funding for Pilots

- UCSF
  - Research Allocation Program (RAP)
  - Training programs, mentors
- NIH - R03, R21, U34, K awards
- Other
  - Foundations
  - Philanthropy
  - Pharmaceutical companies
- PI discretionary funds

Summary: Pilot Studies

- Crucial to the development and testing of novel ideas and interventions
- Necessarily small and under-powered
- Have different or additional goals
- Are recognized as a specific study design by NIH, local funders, journals
- But little attention to design, methods and interpretation of pilot studies

Nuts and Bolts

- Contracts and Budgets
- Study team
- Space
- Start-up
- Money Matters
- Recruitment
- Forms
- Closeout

Contracts

- Required if trial supported by industry
- Must be approved by UCSF Industry Contracts & company's legal division
  - lots of puzzling legalese
  - you should understand and revise, esp. scope of work
  - best to start with UCSF template, revise and submit to company
- Between UCSF Regents and company
  - signed by PI

Elements of a Contract

- Scope of work
- Timetable for deliverables
- Budget and timing of payments
  - get a bolus up front
  - don't link payment to deliverables out of your control
- Ownership of data and publishing rights
- Rules for breaking contract
- Confidentiality, indemnification
- Patents and inventions

Budgets

- **NIH-style (NIH, VA, AHRQ, PCORI CDC)**
  - **prepared far in advance**
  - **governed by strict rules**
    - ***funds restricted to categories***
    - ***permission for carry-over required***
    - ***certain expenses not allowed***
    - ***subject to government audit***
- **Pharmaceutical company budgets**
  - **prepared just before trial starts**
  - **negotiable**
  - **much more flexible**

Money Matters

- Pre-award manager (Research Management Services)
  - help prepare budget and "face" pages
  - help with budget justification
  - make sure you follow rules/timelines
- Post-award manager (Dept/Division)
  - pay salaries, buy equipment and supplies
  - monthly report of expenditures
  - projections over life of trial

Who is the Study Team?

- Principle investigator
- Project director/clinic coordinator
- Recruiter
- Data manager
- Programmer/analyst
- Statistician
- Quality control supervisor
- Administrative assistant
- Financial/personnel manager

How to Hire the Study Team

- Work with your department or unit personnel (HR) staff
  - write a job description
  - decide on job series, step, salary
  - post the job at UCSF and advertise
  - review resumes
  - interview
  - select

Where to Find the Study Team

- Other studies
- UCSF employees
- Recent graduates, students
- Friends and colleagues
- Craig's List
- Chronicle, web

Team Leadership

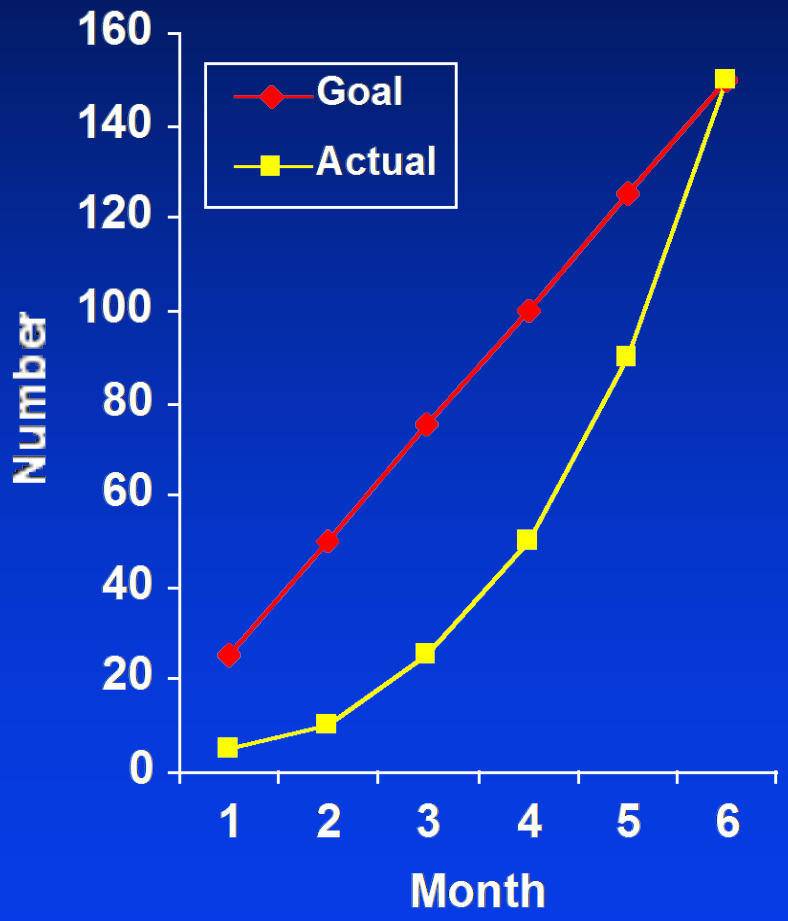
- Management training useful
- You are responsible and the boss
- Keep your staff happy
  - involvement in the science
  - salary, working conditions
  - level of responsibility
- Set an example
- Promote good staff interactions
- Some staff should be fired

Space

- Considerations
  - accessibility, parking
  - design and décor
  - privacy
  - clinical needs, special tests
  - safety measures
  - cost
- CTSI Clinical Research Service
- Medical or other on campus space

Recruitment

- Hire an experienced recruiter/service
- Provide adequate time and money
- Monitor results
- Make changes
  - different approaches
  - more centers
  - longer recruitment
  - change eligibility

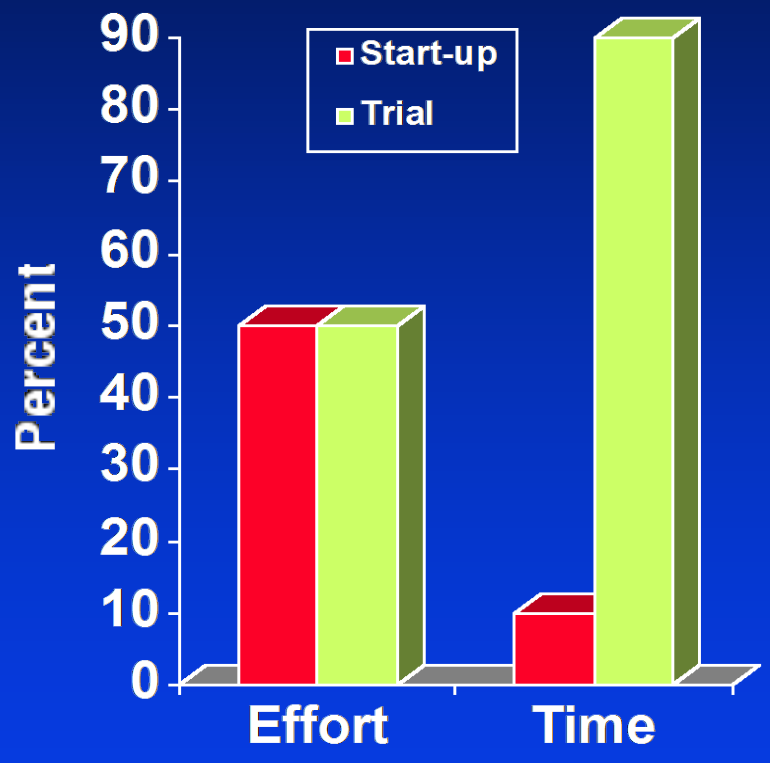


Plan Multiple Approaches to Recruitment

- Referral from providers
- Targeted mailing (age, gender, disease)
  - *UCSF, Kaiser, DMV, HCFA, registries, etc.*
- Advertise
  - hospital, clinics, special sites, churches
  - radio, newspaper, TV, internet
  - celebrities, leaders
- Social Media – Google, Facebook
- *CTSI Participant Recruitment Service*

Follow IRB, HIPPA and confidentiality rules

Start-up



- Protocol
- Operations Manual
- Forms
- IRB approval
- Hiring
- Training
- Database design
- Database validation

Closeout

- Final visit and post-trial plans
  - –make final measurements
  - –say goodbye and thank you
  - –inform of test results
  - –inform of treatment status
  - –inform of trial results
  - –?make clinical recommendation

Summary

- **Trails are costly and complicated**
  - **get advice from experienced colleagues**
  - **get materials used in prior trials**
  - **use UCSF services**
    - ***financial, legal, IRB/CHR***
    - ***CTSI Clinical Research Service***
      - Space, phlebotomy, study staff
    - ***CTSI Consultation Services***
      - **Design, ethics, statistics, database management, regulatory issues**
    - ***CTSI Recruitment Service***