PILOT STUDIES

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Trial Development Models

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WHAT IS A PILOT STUDY?
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WHAT A PILOT STUDY IS NOT
A Wake-Up Call

Caution Regarding the Use of Pilot Studies to Guide Power Calculations for Study Proposals

Helena Chmura Kraemer, PhD; Jim Mintz, PhD; Art Noda, MS; Jared Tinklenberg, MD; Jerome A. Yesavage, MD

Arch Gen Psychiat 2006;63:484-9
WHAT A PILOT STUDY IS NOT
The Wake-Up Call

Pilot studies produce unstable estimates of efficacy.

They are not the basis for determining:

--The sample size of a trial;
--If a trial should be conducted.

“Studies worth performing are aborted.
Studies not aborted are underpowered.”

Kraemer et al., 2006
HOW DO YOU DETERMINE SAMPLE SIZE?
Find Clinically Significant Target

Figure 1. Identification of a clinically significant target for an anger treatment to reduce CHD. Figure 1a shows a natural cut-point at which CHD is increased. Figure 1b shows a graded association between anger and CHD where judgment is needed.
HOW DO YOU DETERMINE SAMPLE SIZE?

Preserve Clinical Significance

![Graph showing the relationship between mean anger in the treatment arm and total sample size. The graph illustrates how sample size changes as the mean anger in the comparator arm increases.]
HOW DO YOU DETERMINE WHETHER A TRIAL SHOULD BE CONDUCTED?

**Significance**

<table>
<thead>
<tr>
<th>Disease:</th>
<th>Current Treatment:</th>
<th>New Treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affects many</td>
<td>No current treatment</td>
<td>Shows promise in preliminary work</td>
</tr>
<tr>
<td>Affects a subgroup</td>
<td>Not very effective</td>
<td>Targets novel risk factor</td>
</tr>
<tr>
<td>Is increasing</td>
<td>Uncertain effectiveness (clinical equipoise)</td>
<td>Targets novel pathway</td>
</tr>
<tr>
<td>Is increasing in a subgroup</td>
<td>Effective but adherence is poor</td>
<td>Less costly than standard</td>
</tr>
<tr>
<td>Is not decreasing</td>
<td>Systematically developed and refined</td>
<td>Fewer side effects</td>
</tr>
<tr>
<td>Is costly</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Credibility**

--Grounded in science of behavior change.
--Systematically developed and refined

**Plausibility**

Proof of Concept (N=4)

Clinically significant target

% Adherence

Baseline

8 Weeks Active Treatment
WHAT IS A PILOT STUDY?

CONSORT Guidelines

CONSORT 2010 statement: extension to randomised pilot and feasibility trials

Sandra M. Eldridge¹, Claire L. Chan¹, Michael J. Campbell², Christine M. Bond³, Sally Hopewell⁴, Lehana Thabane⁵, Gillian A. Lancaster⁶ and on behalf of the PAFS consensus group
PILOT VS. FEASIBILITY PILOTS

CONSORT Guidelines
WHAT IS A PILOT STUDY?
CONSORT Guidelines

Predecessors to a future clinical trial
Aim is feasibility. Whether a future trial:
  Can be done;
  Should be done; and, if so,
  How.
A smaller scale of the future clinical trial.
IMPORTANCE OF A PILOT STUDY
Studies Implementation

<table>
<thead>
<tr>
<th>TREATED</th>
<th>CONTROLS</th>
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</thead>
<tbody>
<tr>
<td>GOAL</td>
<td>Attendance at dance class ≥ 3 days/week</td>
</tr>
<tr>
<td>ACHIEVED</td>
<td>33%</td>
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Robinson, Stanford GEMS
IMPORTANCE OF A PILOT STUDY
Inability to Implement Results in a Null Trial

Robinson, Stanford GEMS
## PRODUCT OF FEASIBILITY PILOT STUDY

<table>
<thead>
<tr>
<th>Source</th>
<th>Accessible/ Week</th>
<th>Eligible (55%)</th>
<th>Willing (70%)</th>
<th>Passed Screen (90%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruitment Site #1</td>
<td>9</td>
<td>5.0</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>Recruitment Site #2</td>
<td>7</td>
<td>3.9</td>
<td>2.7</td>
<td>2.4</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td><strong>16</strong></td>
<td><strong>8.9</strong></td>
<td><strong>6.2</strong></td>
<td><strong>5.6</strong></td>
</tr>
</tbody>
</table>

**Expected Rate:** 5.6/week  
**Number Subjects Needed:** 30  
**Number Weeks Needed:** \(\frac{30}{5.6} = 5.4 \text{ weeks}\) (double the estimate)

**Time Needed for Recruitment:** 5.4 Weeks \(\times 2 = 12 \text{ Weeks}\)
WHO CARES ABOUT A PILOT STUDY?

Investigators: To implement a trial they designed.

Reviewers: Reassurance that the trial is feasible.

The Research Community: Only if the results offer generalizable lessons.
SUMMARY

Science is progressive.
Pilot studies are integral to progression

Figure 1. The ORBIT Model for Behavioral Treatment Development

Czajkowski, Powell et al., 2015; Powell, Freedland & Kaufmann (in press)