Clinical Trial Methodology: Micro-randomized Trials

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45 minutes  30 slides
• **Data Science & mHealth**
  
  – We want to address questions such as:
    “Are the treatments, delivered via a mobile device, effective?” and
    “When, where and in which context is it most effective to deliver treatments via a mobile device?”
  
  – How might we collect high quality data to address these questions? (clinical trial design)
  
  – How do we use data to address these questions? (data analysis methods)
Key Terms

• Just-in-Time Adaptive Interventions (JITAI)
  – Intervention Design for mHealth—specifies when, where and in which context is it most effective to deliver (“push”) a treatment

• Randomized Trials
  – Factorial trials (used to build interventions)
    • Micro-randomized trial (a type of factorial trial for building JITAIs)
  – RCT (used to evaluate a built intervention)
Next two heartsteps studies will involve individuals who have had a recent heart attack. This is a simplified version of heartsteps so that I can explain the issues with clarity.
Case Study

**HeartSteps**

- 5 Decision Times per Day (Pre-work, midday, midafternoon, end of work, evening)

- **Treatments** (aka, intervention options or “EMIs”)
  - Activity recommendations tailored to time of day, day of week, weather, location
  - Designed to impact user in the near-term

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Place (home – work – other)
Time of day (morning – lunch – midPM – evening – after dinner)
Day (weekday – weekend)
Weather/Activity venue (outside – inside – outside snow)
Case Study

HeartSteps

– 5 Decision Times per Day
– Treatments are Tailored Activity Recommendations

– Observations

• Wearable bracelet records step count
• Sensors on phone record location, weather, busyness of calendar, time of day, day of week....
• Self report on usefulness of recommendations, nightly report on stressfulness of day
*HeartSteps*

- 5 Decision Times per Day
- Treatments are Tailored Activity Recommendations
- Observations via wearable sensors and self-report

- **Proximal Response**
  - step count in 1 hour following each decision time

- **Distal Response**
  - step counts over 42 days (scientific/clinical goal)
The JITAI decision rules specify when, where and in which context is it most effective to deliver (“push”) a treatment.
**Case Study**

**First Example: Decision Rule A**

At each decision time:

<table>
<thead>
<tr>
<th>Calendar Busy?</th>
<th>Weather?</th>
<th>Good</th>
<th>Bad</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td>Deliver Activity Recommendation</td>
<td>Do Not Deliver Activity Recommendation</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>Deliver Activity Recommendation</td>
<td>Deliver Activity Recommendation</td>
</tr>
</tbody>
</table>
Place (home – work – other)
Time of day (morning – lunch – midPM – evening – after dinner)
Day (weekday – weekend)
Weather/Activity venue (outside – inside – outside snow)

So that’s 90 buckets. In addition, for most conditions we also had both sedentary & active activity suggestions. Sedentary messages were suggestions for stretching or quick (1-2 minutes) of activity; active messages were at least 5 minutes of activity. Taking those into account, we had closer to 150 buckets of messages.
An HeartSteps Activity Recommendation
HeartSteps

— We’d like to develop a decision rule that tells us whether we should deliver a tailored activity recommendation.
  • i.e. when, where and in which context is it most effective to deliver a treatment?

— Decision rule A is an example of a decision rule that we might develop.

Don’t deliver if weather is bad and calendar is busy.
Case Study

HeartSteps

The Micro-Randomized Trial

(a type of factorial trial for building JITAlTs)

Should we push treatments?
HeartSteps

- First Question: Do the tailored activity recommendations affect the proximal response, i.e., step count?
  - This question determines the required number of participants.
- Second Question: Does the busyness of the user’s calendar, day of week and the weather impact the effectiveness of the activity recommendations on step count? *(informs JITAI decision rules)*
- Many more questions........
Discuss why we randomize

HeartSteps

- Micro-Randomized Trial: At each decision time randomize participants to “tailored activity recommendation” versus “nothing”
  - 5 decision times per day, 42 day study = 210 randomizations
  - Randomize to tailored activity recommendation with probability .4
Case Study

Components of a Micro-randomized Trial

— Decision Times
— Treatments (Randomized at Decision Times)
— Observations
— Proximal Response
— Distal Response
In a Micro-Randomized Trial, you

- Randomize among treatments at decision times
- Record observations (sensor & self-report data)
- Record outcomes
  - Proximal Response & Distal Response
- Use data after study ends to assess treatment effects, inform decision rule development
Time varying treatment (e.g. whether or not a recommendation is delivered at each decision time) implies need for time-varying effects.
### HeartSteps Sample Size (power=.8, significance level=.05)

<table>
<thead>
<tr>
<th>Standardized Effect on Average Step Count over 42 Days</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.06 standard deviations</td>
<td>112</td>
</tr>
<tr>
<td>0.08 standard deviations</td>
<td>65</td>
</tr>
<tr>
<td>0.10 standard deviations</td>
<td>43</td>
</tr>
</tbody>
</table>
A PRESSING ISSUE “AVAILABILITY”

Check to see if correct.
Example JITAI Decision Rule A

At each decision time, if person is available then

<table>
<thead>
<tr>
<th>Calendar Busy?</th>
<th>Weather?</th>
</tr>
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<tbody>
<tr>
<td></td>
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<tr>
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<tr>
<td>No</td>
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</tbody>
</table>

Check to see if correct.
HeartSteps Sample Size

- First Question: Do the tailored activity recommendations affect the proximal response, i.e., step count?
- Intuition

<table>
<thead>
<tr>
<th>Standardized Effect on Step Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Graph showing standardized effect on step count over decision time point" /></td>
</tr>
</tbody>
</table>

Time var
### HeartSteps Sample Size (power=.8, significance level=.05)

<table>
<thead>
<tr>
<th>Standardized Average Effect over 42 Days</th>
<th>Sample Size 50% Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.06 standard deviations</td>
<td>112</td>
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HeartSteps

Further Data Analyses Address:

– Does the busyness of the person’s calendar, the weather, recent ratings of usefulness, recent availability impact the effectiveness of the activity recommendations on step count? (informs JITAI decision rules)

– Many more questions........
Key Questions

- Micro-randomized Trials: When are they (not) useful?

  - NOT USEFUL: When malleable circumstances are rare.
  - USEFUL: When malleable circumstances change rapidly over time.

  - NOT USEFUL: Proximal response cannot be feasibly assessed or predicted.
  - USEFUL: Proximal response can be unobtrusively sensed or unobtrusively self-reported or predicted with precision.

Not Useful: When malleable circumstances are rare. For example the MRT is not useful for deciding what to do when there are early signs of mania in people with a bi-polar disorder; this is because episodes of mania are relatively rare. A second example is when the proximal outcomes targeted by the push intervention cannot be feasibly assessed at frequent intervals (burdensome, intrusive self-reports).

Useful: When malleable circumstances change rapidly over time. For example MRT might be useful in deciding how to help people with serious mental illnesses cope with stress or depressive symptoms; these individuals might experience rapid and frequent changes in symptoms on a day-to-day basis. A second example is when the proximal outcomes targeted by the push intervention can be feasibly assessed at frequent intervals (via unobtrusive sensors or unobtrusive self-report).
I collaborate with
- Researchers who want to build or improve an mHealth just-in-time adaptive intervention (JITAI)

Researchers want to collaborate with “people like me” to
- to design clinical trials and develop the data analytics needed to address important mHealth JITAI design questions

→→→ enhance effectiveness of mHealth interventions
• Collaboration—I need to know

  – What proximal and distal responses do you want the treatments to impact?
    • Stress, urges, adherence, activity, drug use, ......

  – How often might the mobile device deliver a treatment?
    • Types of treatments: Behavioral, cognitive, self-monitoring, motivational, reminders, ......

  – How often can you collect data (via sensors, self-report)
    • Stress, urges, adherence, activity, location, mood, drug use, other behaviors
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