Micro-randomized Trials in Mobile Health

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CHEAR, 10.27.15
Outline

• Adaptive Interventions and Just-in-Time Adaptive Interventions

• HeartSteps

• Micro-Randomized Trial

• Sample Size Considerations
Adaptive Interventions

• Intervention design that takes advantage of response heterogeneity by individualizing intervention options to the specific and changing needs of individuals

• Example: Adaptive drug court program for drug abusing offenders

Marlowe et al., 2008; 2009; 2012
Adaptive Drug Court Program

Low risk
- As-needed court hearings + standard counseling
  - Non-responsive
  - Non-compliant
- Bi-weekly court hearings + standard counseling
  - Non-responsive
  - Non-compliant
  - Non-compliant
  - Jeopardy contract: “zero tolerance”

High risk
- As-needed court hearing + ICM
  - Non-compliant
- Bi-weekly court hearing + ICM
  - Non-compliant
  - Non-compliant
Adaptive Intervention: 5 Elements

The adaptation is guided by consideration of
(1) Distal Outcome and Proximal Response

The adaptation process is composed of
(2) Tailoring Variables,
(3) Decision Rules and
(4) Intervention Options

The adaptation is triggered at
(5) Decision Points
JITAI: Just-in-Time Adaptive Interventions

• A JITAI is an adaptive intervention
• That is
  ◦ delivered when needed
  & where-ever needed

(Kaplan & Stone, 2013; Spruijt-Metz & Nilsen, 2014)
Example

Intervention to reduce heavy drinking and smoking by young adults

- Participants prompted 3/day by mobile device for assessments
  - Smoking urge, self-regulation demands, drinking behaviors
- Urge-surfing interventions delivered by the mobile device only if participant reports an urge to smoke.

(Witkiewitz et al., 2014)
Example

Reducing Sedentary Behavior by Office Workers

- Software on the computer measures uninterrupted computer time via mouse and keyboard activity
- Smartphone delivers message to encourage a walking activity *only* if 30 min. of uninterrupted computer activity occurs

(Dantzig et al., 2013)
Commonalities?

• Both adaptive interventions and JITAIIs are time-varying and adaptive

• However in JITAIIs technology plays a critical role
  o Information can be obtained when/where needed
  o Interventions can be delivered when/where needed
Just-in-Time Adaptive Intervention
5 Elements

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In-the-Moment Impact

Real-Time
The goal is to improve a longer-term, distal, outcome

- Substance use cessation; maintain increased activity level; maintain adherence to meds

To improve the distal outcome, the intervention options are formulated to target proximal responses
Proximal Responses

*Mediators* that may be critical to achieving the long-term goal

1) Short term targeted behavior
   - Substance use over x hours
   - Physical activity over x minutes
   - Adherence over next hour
2) Short term risk
   - Momentary craving, stress
3) Engagement in intervention/Intervention burden
Intervention options

- Intervention options:
  - Behavioral strategies, cognitive strategies, self-monitoring, social linkages, motivational,…
  - Whether to provide an intervention or whether to prompt self-monitoring
  - How to provide an intervention option
  - “Provide nothing” option

- Theoretically/scientifically driven (Klein et al., 2011)
Tailoring variables

*Tailoring variables are moderators* that inform which intervention option is best when, where and for whom.

- Often past proximal responses: stress, activity
- Risk & protective factors: busyness of calendar, momentary mood or craving, location, social context
- Adherence & burden
Decision Points

Typical decision points in JITAIis:

- Intervals in time (every x seconds, every x minutes, every x hours)
- When user requests help (presses “help” button)

Frequency is guided by the dynamics of the tailoring variables and “in-the-moment nature” of the intervention effect.
Decision Rules

Link patient information to intervention options at decision points

• A decision rule is implemented at each decision point
• A JITAI often includes many different decision rules
• Development of decision rules is guided by an integration of empirical evidence, theory and clinical experience.
Summary of JITAI elements

1. Outcomes
   o Distal (scientific/clinical goal) & Proximal Response
     (guided by mediational theories pinpointing the necessary
     processes needed to achieve the distal outcome)

2. Intervention options
   o Guided by the proximal responses

3. Tailoring variables
   o Guided by theory concerning moderation.

4. Decision points
   o Guided by the dynamics of tailoring variable and in-the-moment nature of the effect of the intervention option.

5. Decision rules
Outline

- Adaptive Interventions and Just-in-Time Adaptive Interventions
  - HeartSteps
  - Micro-Randomized Trial
  - Sample Size Considerations
HeartSteps

- Goal: Develop a Just-in-Time Adaptive Intervention for Encouraging and Maintaining Physical Activity
HeartSteps

Distal Outcome:
Activity over the 42 day study.

Proximal Response:
Proximal activity (step count) over next hour.
HeartSteps

Intervention Options:
Whether to provide an intervention: yes/no

1) Provide **Momentary Lock-Screen Activity Recommendation**?

2) Provide **Daily Activity Planning**?
HeartSteps

Decision times:
1) **Momentary**: Approximately every 2-2.5 hours
2) **Daily**: Each evening at user specified time.

Potential Tailoring Variables:
weather, location, busyness of calendar, adherence, step count, self-report: usefulness, burden
Momentary Lock-Screen Recommendation

No Message or
Outline

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Micro-Randomized Trial

Randomize between appropriate intervention options at decision times → Each person may be randomized 100’s or 1000’s of times.
Micro-Randomized Trial Elements

1. **Record** outcomes
   - Distal (scientific/clinical goal) & Proximal Response

2. **Record** potential tailoring variables

3. **Randomize among** Intervention Options at decision points

4. **At End of Trial** use Resulting Data to assess moderation, construct decision rules
Why Micro-Randomization?

• Randomization (+ representative sample) is a gold standard in providing data to assess the causal effect of an intervention option.

• Sequential randomizations will enhance replicability and effectiveness of data-based decision rules.
HeartSteps (42 day study)

• Focus on whether to provide an activity recommendation at the decision times.

• 210 decision times for the activity recommendations.

<table>
<thead>
<tr>
<th>Lock-screen activity Recommendation?</th>
<th>Randomization Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>$\frac{2}{5}$</td>
</tr>
<tr>
<td>No</td>
<td>$\frac{3}{5}$</td>
</tr>
</tbody>
</table>
Micro-Randomized Trial

First Question to Address: Do the intervention options have an effect on the proximal response?

--Test for proximal main effects of the intervention
Micro-Randomized Trial

A JITAI involves time varying potentially intensive intervention delivery → potential for accumulating habituation and burden

→

Allow proximal main effects of the intervention components to vary with time
Sample Size for a Micro-Randomized Trial

Determine sample size to detect a time-varying proximal main effect of the Lock-Screen Activity Recommendation on subsequent activity
Availability & The Main Effect

- Interventions can only be delivered at a decision time if an individual is available.

- The proximal main effect of treatment at a decision time is the difference in proximal response between available individuals assigned a lock-screen message and available individuals who are not assigned a lock-screen message.
Proximal Main Effect

Main effect of activity message on proximal response is likely time-varying $\beta(j), j=1,\ldots,J$
Sample Size Calculation

• We calculate a sample size to test:

\[ H_0 : \beta(j) = 0, \ j = 1, 2, \ldots, 210 \]

• A simple approach is to target a \( \beta(j) \) which is quadratic with intercept, \( \beta_0 \), linear term, \( \beta_1 \), and quadratic term \( \beta_2 \)

and test \( \beta_0 = \beta_1 = \beta_2 = 0 \)
Sample Size Calculation

Because we target an approximately quadratic proximal main effect, assessment of the effect of the lock-screen message uses not only contrasts of *between person responses* but also contrasts of *within person responses*.

--We can expect that the required sample size (number of subjects) will be small.
Sample Size Calculation

• Our test statistic uses estimators from a “generalization” of linear regression.

• The test statistic is quadratic in the estimators of the $\beta$ terms.

• To calculate a sample size we need to specify a clinically/scientifically important effect to detect.
Specify Alternative for Sample Size Calculation

SPECIFY:

• Standardized main effects:
  – proximal effect on first day,
  – average proximal effect over trial duration

• Day of maximal proximal effect.
HeartSteps (42 day study)

Standardized effects:

- initial effect: 0
- average standardized effect over trial duration: ?
- day of maximal effect: 28
<table>
<thead>
<tr>
<th>Standardized Average Main Effect over 42 Days</th>
<th>Sample Size For 70% availability or 50% availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.06</td>
<td>81 or 112</td>
</tr>
<tr>
<td>0.08</td>
<td>48 or 65</td>
</tr>
<tr>
<td>0.10</td>
<td>33 or 43</td>
</tr>
</tbody>
</table>
Micro-Randomized Trial

1) Be conservative in planning the trial!
   1) Under-estimate the amount of time participants are available for the intervention component.
   2) Under-estimate the average proximal effect
Micro-Randomized Trial

2) Power to detect proximal main effect is robust to interactions and to delayed effects (e.g., burden)

3) Secondary data analyses concern time varying effect moderation and data analyses to construct data-driven decision rules for the JITAI
Micro-Randomized Trials: When are they (not) useful?

- **NOT USEFUL:** When malleable circumstances are rare: Want to learn the best type of alert to prevent suicide attempt
- **USEFUL:** When malleable circumstances change rapidly: Stress, urges to smoke, adherence, physical activity, eating
- **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.
HeartSteps Collaborators:  P. Liao, A. Lee, C. Anderson, P. Klasnja, A. Tewari & Inbal Nahum-Shani

Sample size calculator:  
https://jisun.shinyapps.io/SampleSizeCalculator