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## Clinical Trial Methodology: *Micro-randomized Trials*

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45 minutes 30 slides



## Guiding Principles

- 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)



## Case Study

### *HeartSteps*

- Goal is to build a JITAI to increase physical activity by sedentary adults
- Decision Times (times at which a treatment might be delivered)
  - Pre-work, midday, midafternoon, end of work, evening
    - Select these times based on the dynamics of the outcome and/or the “in-the-moment” intended impact of the treatment.

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

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



## Case Study

### *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)



## Case Study

### *Components of a Just-in-Time Adaptive Intervention*

- Decision Times
- Treatments
- Observations
- Proximal Response
- Distal Response
- The JITAI decision rules that input observations and output treatment

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:

Weather?

		Good	Bad
Calendar Busy?	Yes	Deliver Activity Recommendation	Do Not Deliver Activity Recommendation
	No	Deliver Activity Recommendation	Deliver Activity Recommendation



## Case Study

### *Second Example: Decision Rule B*

- For each combination
  - weather (good, bad),
  - location (home, work, elsewhere),
  - time of day (morning, midday, midafternoon, end of work, evening)
  - there is a bucket of activity recommendations.
- If decision rule A indicates that we should deliver a recommendation then decision rule B selects a recommendation from the appropriate bucket of activity recommendations.

Place (home – work – other)

Time of day (morning – lunch – midPM – evening – after dinner)

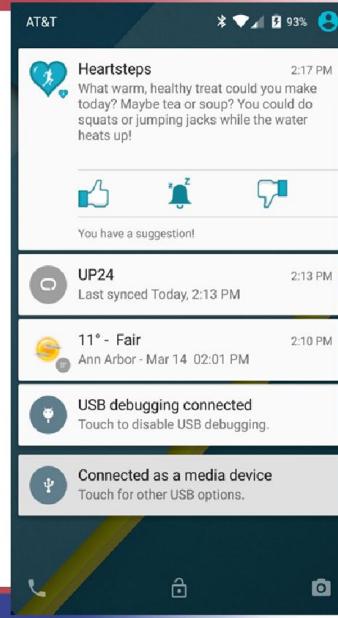
Day (weekday – weekend)

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.

## Case Study

### An HeartSteps Activity Recommendation





## Case Study

### *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 JITAls)

Should we push treatments?



## Case Study

### *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.....



## Case Study

### *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

Discuss why we randomize



## Case Study

### *Components of a Micro-randomized Trial*

- Decision Times
- Treatments (**Randomized at Decision Times**)
- Observations
- Proximal Response
- Distal Response



## Case Study

*In a Micro-Randomized Trial, you*

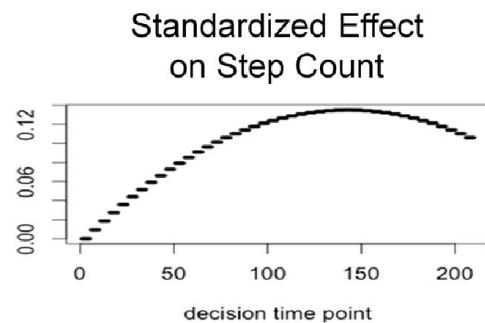
- Randomize among treatments at decision times
- Record observations (sensor & self-report data)
- Record outcomes
  - Proximal Response & Distal Response
- Use data after study ends to assess treatment effects, inform decision rule development



## Case Study

### HeartSteps Sample Size

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



Time varying treatment (e.g whether or not a recommendation is delivered at each decision time) implies need for time-varyin effects.



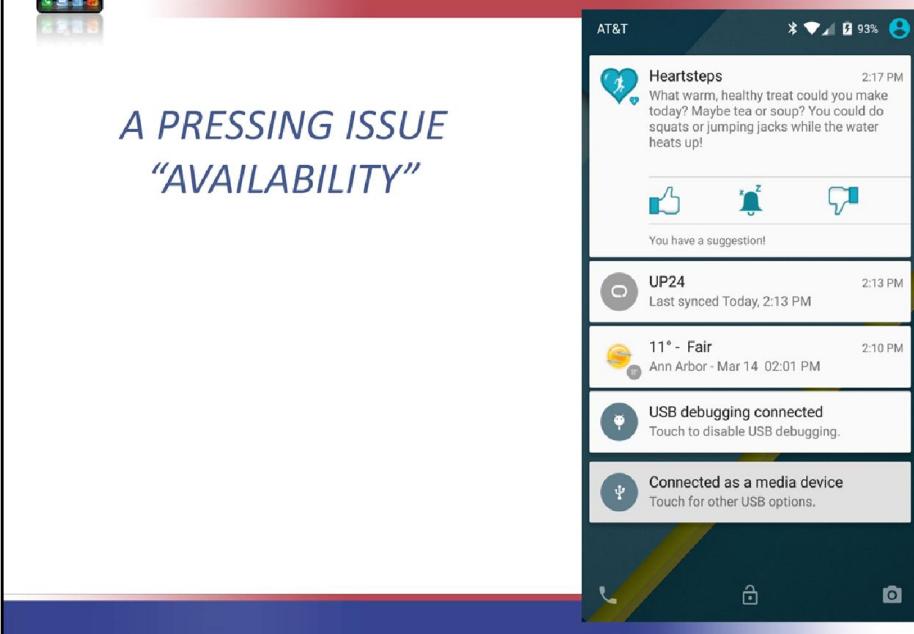
## Case Study

*HeartSteps Sample Size (power=.8, significance level=.05)*

<b>Standardized Effect on Average Step Count over 42 Days</b>	<b>Sample Size</b>
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0.06 standard deviations	112
0.08 standard deviations	65
0.10 standard deviations	43

## Case Study



Check to see if correct.



## Case Study

### *Example JITAI Decision Rule A*

At each decision time, **if person is available then**

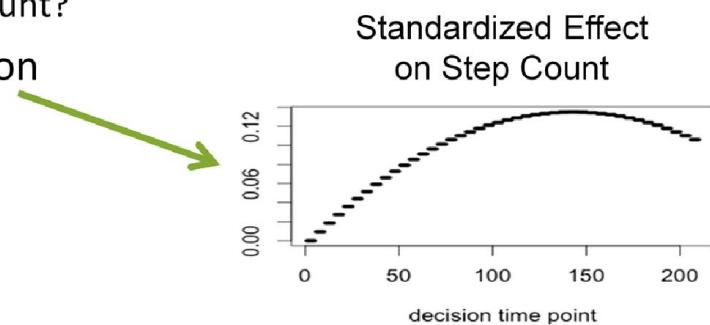
**Weather?**

		Good	Bad
Calendar Busy?	Yes	Deliver Activity Recommendation	Do Not Deliver Activity Recommendation
	No	Deliver Activity Recommendation	Deliver Activity Recommendation

Check to see if correct.

### HeartSteps Sample Size

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



Time var



## Case Study

*HeartSteps Sample Size (power=.8, significance level=.05)*

<b>Standardized Average Effect over 42 Days</b>	<b>Sample Size 50% Availability</b>
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0.06 standard deviations	112
0.08 standard deviations	65
0.10 standard deviations	43



## Case Study

### *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.
    - 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.

**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).



## Reaching Out to Experts – Who and Why?

### ► 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



## Key Questions

- 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



## Contact Information

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