

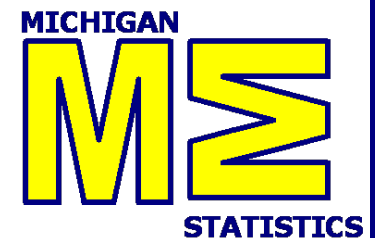
Micro-randomized Trial Designs for Research Using mHealth Technologies



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The Methodology Center
advancing methods, improving health



Outline

- Just-in-Time Adaptive Interventions
 - MD2K Smoking Cessation & HeartSteps
- Micro-Randomized Trial
- Sample Size Considerations

JITAIs: Just-in-Time Adaptive Interventions

- Intervention design that takes advantage of response heterogeneity by individualizing intervention to the specific and changing needs of individuals
- That is,
 - delivered when needed
 - & where-ever needed



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

Example

Reducing Sedentary Behavior by Office Workers

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



(Dantzig et al., 2013)

Just-in-Time 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

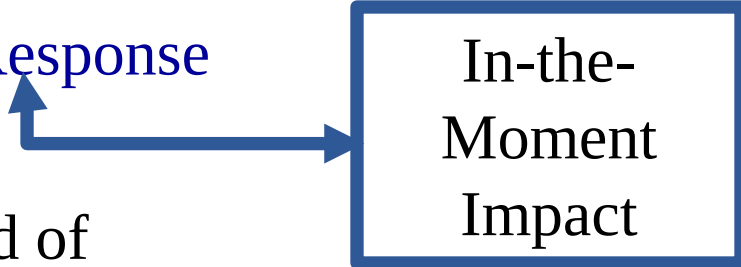
(5) Decision Times

Just-in-Time Adaptive Intervention

5 Elements

The adaptation is guided by consideration of

(1) Distal Outcome and Proximal Response



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graph LR; A[In-the-Moment Impact] --> B[(1) Distal Outcome and Proximal Response]
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In-the-Moment Impact

The adaptation process is composed of

(2) Tailoring Variables,

(3) Decision Rules and

(4) Intervention Options

The adaptation is triggered at

(5) Decision Times



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graph LR; C[Real-Time] --> D[(5) Decision Times]
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Real-Time

IN PROGRESS!



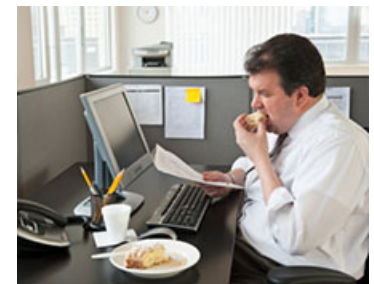
MD2K Smoking Cessation Coach

- o Wearable wrist/chest bands provide multiple physiological sensor streams...; craving, burden,.....
- o Supportive stress-regulation interventions available on smartphone 24/7
- o In which contexts should the wrist band provide a reminder to practice stress-regulation exercises?

IN PROGRESS!

HeartSteps Activity Coach

- o Wearable band senses activity and sleep quality; phone sensors measure busyness of calendar, location, weather,
- o In which contexts should smartphone ping and deliver tailored activity ideas?



Distal Outcomes

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

- Substance use cessation; maintain increased activity level; maintain adherence to meds; reduce rate of cardiovascular events...

Distal Outcomes

HeartSteps Activity Coach: Activity over study duration (42 days).

MD2K Smoking Cessation: Time to relapse

Decision Times

Typical decision times in JITAIs:

- o Intervals in time (every x seconds, every x minutes, every x hours)
- o 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 Times

HeartSteps Activity Coach: Approximately every 2-2.5 hours.

MD2K Smoking Cessation: Each minute during 10 hour day

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

Proximal Response

HeartSteps Activity Coach: Step count over next hour.

MD2K Smoking Cessation: Stress over next x minutes

Intervention options

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



- 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

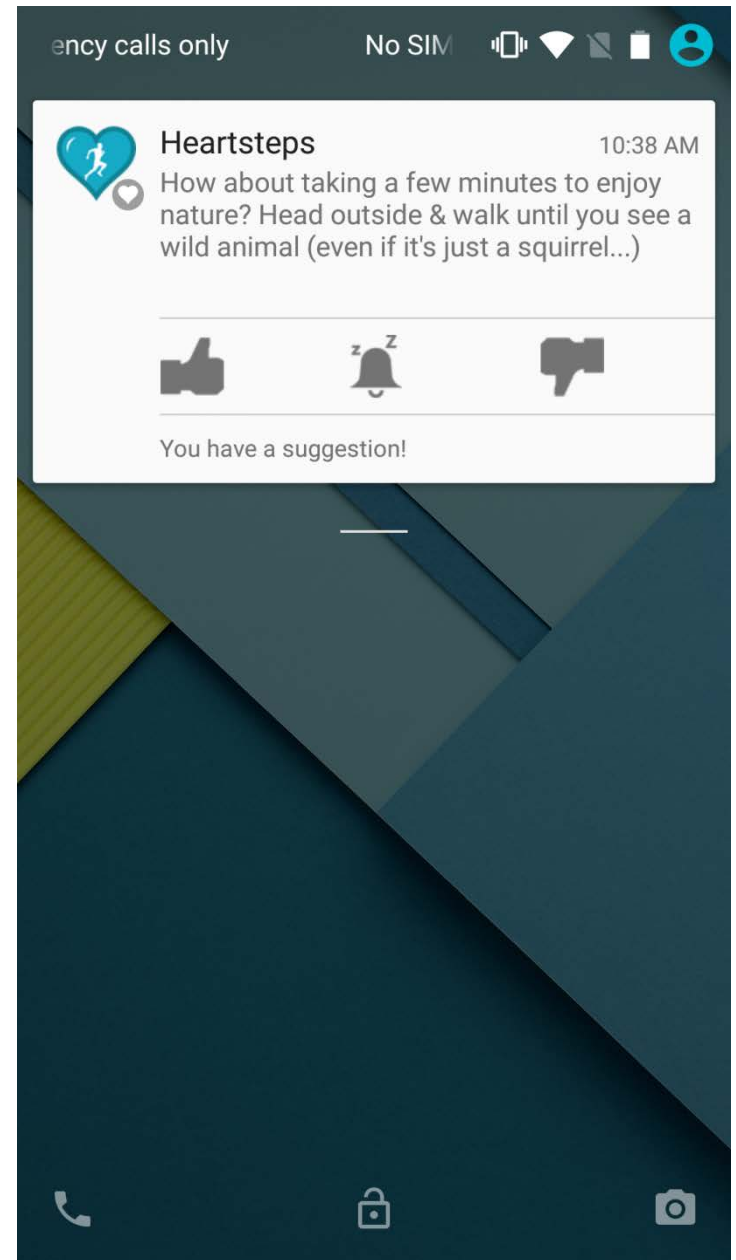
Intervention options

HeartSteps Activity Coach: Whether to provide a tailored activity recommendation: yes/no

MD2K Smoking Cessation: Whether to provide a reminder on the wristband to practice stress-regulation exercises: yes/no

Tailored Activity Recommendation

No Message or



Tailoring variables

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

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

Potential Tailoring Variables

HeartSteps Activity Coach: prior activity level, weather, location, busyness of calendar, adherence, step count, self-reported utility, time of day

MD2K Smoking Cessation: current stress classification, mood, location

Decision Rules

Link tailoring variables to intervention options at decision times

- A decision rule is implemented at each decision time
- A JITAI often includes many different decision rules
- Development of decision rules is guided by an integration of data 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

- Just-in-Time Adaptive Interventions
 - MD2K Smoking Cessation & HeartSteps
- Micro-Randomized Trial
- Sample Size Considerations

Micro-Randomized Trial

Randomize between actions at decision times →
Each person may be randomized 100's or 1000's of times.

- These are sequential, “full factorial,” designs.
- Design trial to detect main effects.

Extension of A/B testing & Single Case Designs

Micro-Randomized Trial Elements

1. Record outcomes: Distal (scientific/clinical goal) & Proximal Response
2. Record observations (potential tailoring variables)
3. Randomize among intervention options at decision times
4. Use data after trial ends to assess intervention effects, moderation, construct decision rules

Why Micro-Randomization?

- Randomization allows us to disentangle why a user received an intervention from the effect of the intervention
- Sequential randomizations will enhance replicability and effectiveness of data-based decision rules.

HeartSteps (42 day study)

- Focus on whether to provide a tailored activity recommendation at the decision times.
- 210 decision times for the activity recommendations.

Randomization Probability

Tailored Activity
Recommendation?

Yes	$\frac{2}{5}$
No	$\frac{3}{5}$

Micro-Randomized Trial

First Question to Address: Do the intervention options affect the proximal response?

--Test for *main effects* of the intervention
(aka, test for a signal!)

Time-varying Main Effects

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



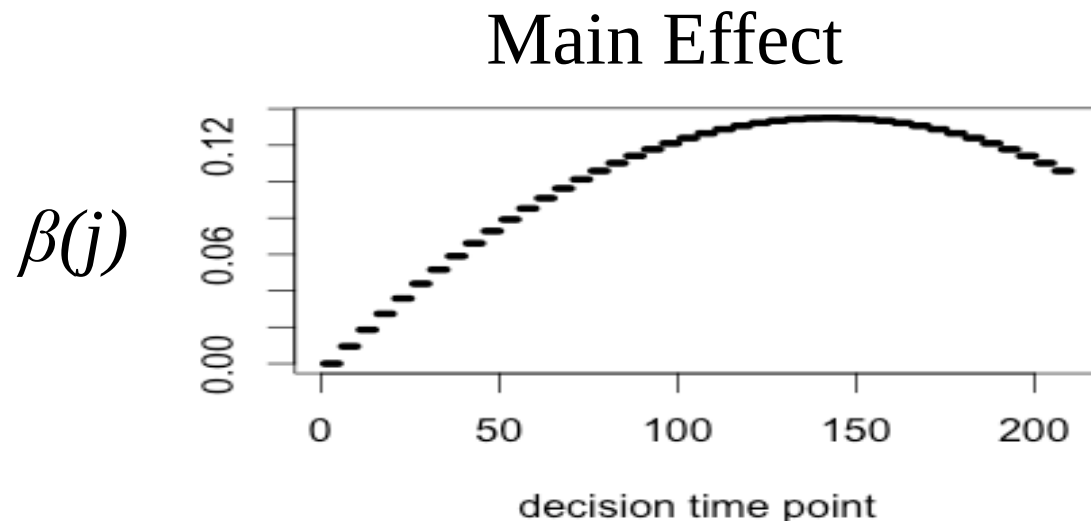
Allow main effects of the intervention options to vary with time

Availability & The Main Effect

- Interventions can only be delivered at a decision time if an individual is *available*.
- The proximal main effect of tailored activity recommendation at a decision time is the difference in proximal response between *available* individuals assigned a recommendation and *available* individuals who are not assigned a recommendation.

Main Effect

Main effect of tailored activity recommendation on proximal step count is likely time-varying $\beta(j)$, $j=1,\dots,J$



Micro-Randomized Trial

First Question to Address: Do the intervention options affect the proximal response?

--Test for *main effects* of the intervention (aka, test for a signal!)

Proposal

Determine the number of participants so that micro-randomized trial can detect a main effect of the intervention on proximal response

The main effect is a time-varying main effect $\beta(t)$, $t=1,\dots,T$

The main effect is a causal effect.

Sample Size Calculation

- We calculate the number of participants to test H_0 : no effect of the intervention, i.e.,

$$H_0 : \beta(t) = 0, t = 1, 2, \dots, 210$$

- Size to detect a simple low dimensional alternate H_1 .

– Example: $H_1: \beta(t)$ quadratic with intercept, β_0 , linear term, β_1 , and quadratic term β_2 and test

$$\beta_0 = \beta_1 = \beta_2 = 0$$

Sample Size Calculation

Alternate hypothesis is low dimensional → assessment of the effect of the tailored activity recommendation uses contrasts of *between person responses* + contrasts of *within person responses*.

--The required number of participants 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 β terms.
- To calculate a sample size we need to specify a clinically/scientifically important effect size to detect.

Specify Alternative for Sample Size Calculation

SPECIFY:

- Standardized main effects:
 - Main effect on first day,
 - average main effect over trial duration
- Day of maximal main effect.

HeartSteps (42 day study)

Standardized main effects:

- initial main effect: 0
- average standardized main effect over trial duration: ?
- day of maximal main effect: 28

HeartSteps Sample Sizes

Power=.8, α =.05

**Standardized Average
Main Effect over
42 Days**

**Sample Size
For
70% availability or
50% availability**

0.06

81 or 112

0.08

48 or 65

0.10

33 or 43

Micro-Randomized Trial

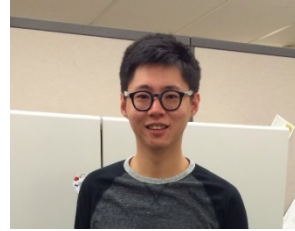
- 1) Be conservative in planning the trial!
 - 1) Under-estimate the amount of time participants are available for the intervention component.
 - 2) Under-estimate the average main effect.

Micro-Randomized Trial

- 2) Power to detect 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.



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Sample size calculator:

<https://jisun.shinyapps.io/SampleSizeCalculator>