

**Micro-randomized Trials
in
Mobile Health**



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SBM Master Lecture
04.02.16





Outline

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

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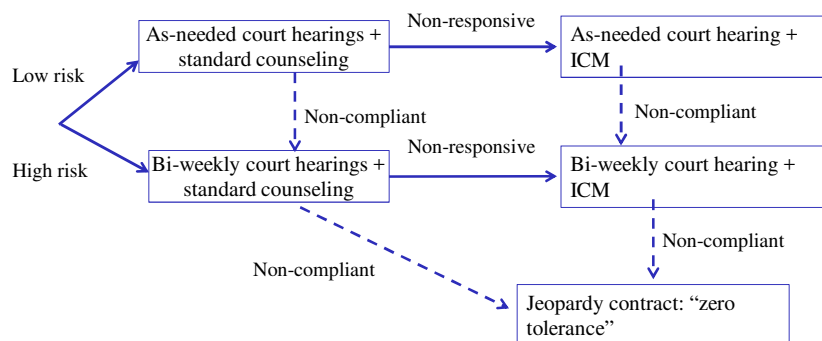
Adaptive Interventions

- Intervention design that takes advantage of systematic response heterogeneity by individualizing intervention options to individuals
- Example: Adaptive drug court program for drug abusing offenders

Marlowe et al., 2008; 2009; 2012

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Adaptive Drug Court Program



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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)

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Example

Reducing Sedentary Behavior by Office Workers

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



(Dantzig et al., 2013)

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Commonalities?

- Both adaptive interventions and JITAIs are time-varying and adaptive
- However in JITAIs technology plays a critical role
 - Information can be obtained when/where needed
 - Interventions can be delivered when/where needed

Just-in-Time Adaptive Intervention 5 Elements

The adaptation is guided by consideration of

(1) Proximal Response and Distal Outcome



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 Points



Real-Time

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Distal Outcomes

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
 - Current craving, stress
- 3) Engagement with mobile app/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)



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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, current mood or craving, location, social context
- Adherence & burden

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Decision Points

Typical decision points in JITAIs:

- 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.

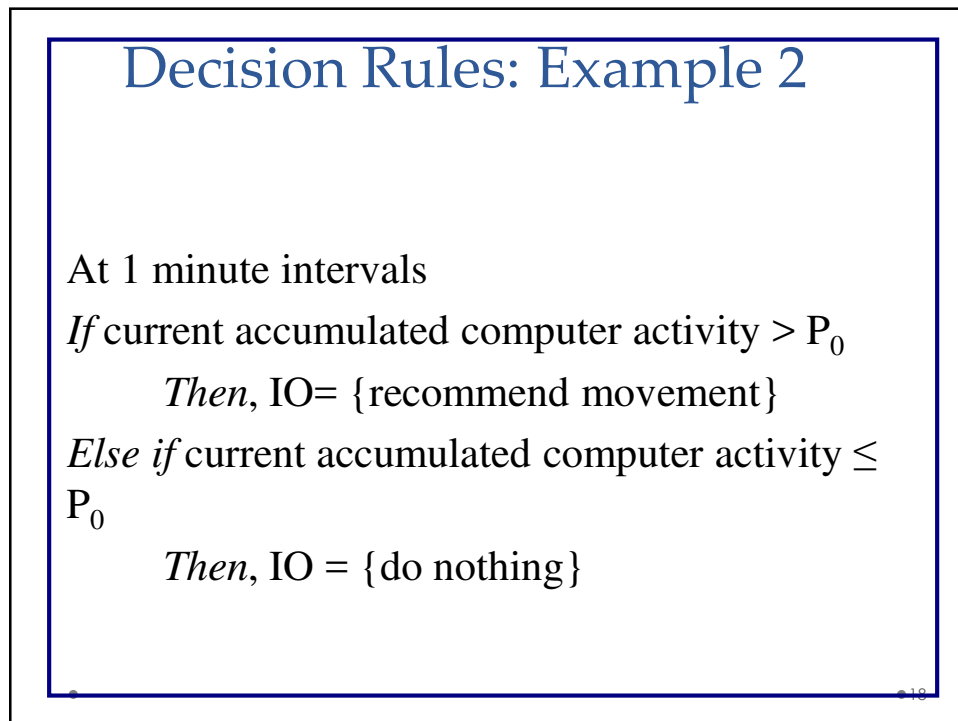
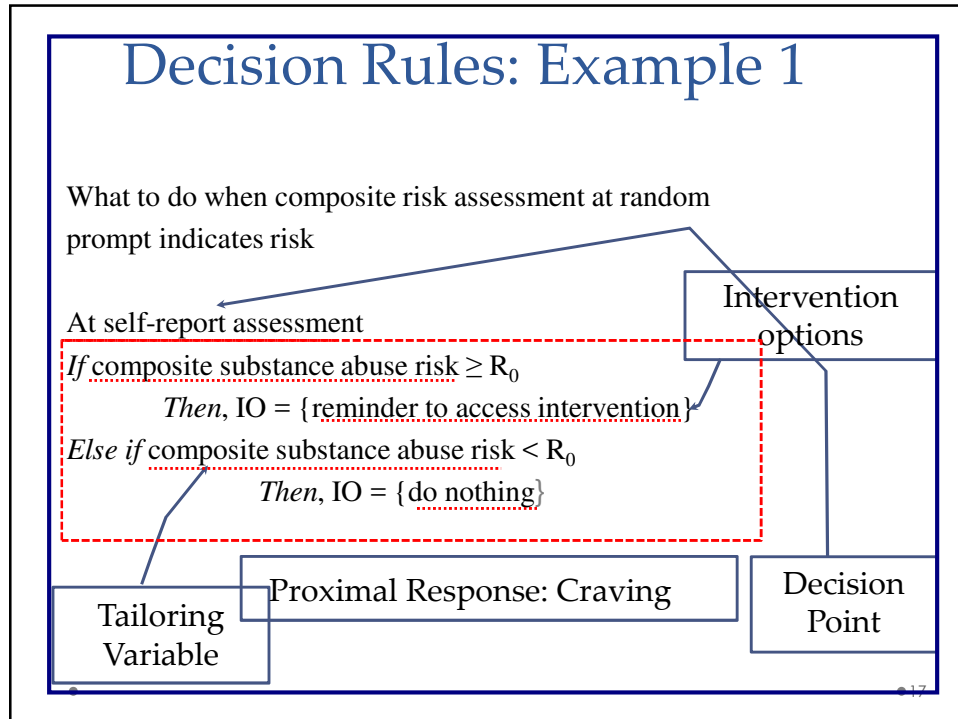
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Decision Rules

Link individual 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.

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Summary of JITAI elements

1. Outcomes
 - Distal (scientific/clinical goal) & Proximal Response (guided by mediational theories pinpointing the necessary processes needed to achieve the distal outcome)
2. Intervention options
 - Guided by the proximal responses
3. Tailoring variables
 - Guided by theory concerning moderation.
4. Decision points
 - Guided by the dynamics of the tailoring variable and in-the-moment nature of the effect of the intervention option.
5. Decision rules

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HeartSteps

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



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HeartSteps

Distal Outcome:
Activity over the 42 day study.

Proximal Response:
Proximal activity (step count) over next 30 minutes.

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HeartSteps

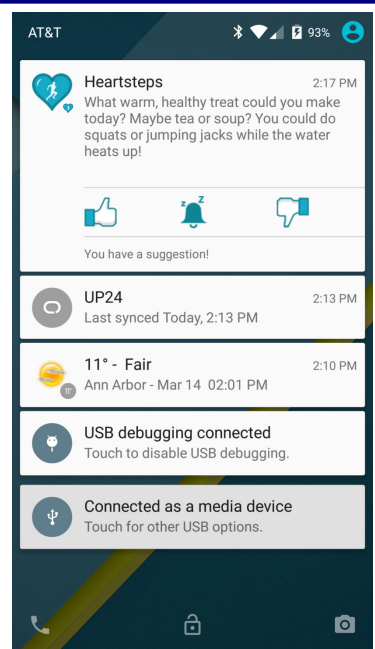
Intervention Options:
Whether to provide Tailored Activity Recommendation? Yes/No

Decision times:
Approximately every 2-2.5 hours

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Tailored Activity Recommendation

No Message or



HeartSteps

Potential Tailoring Variables:

Sensor data: activity recognition (walking, driving, standing/sitting), weather, location, busyness of calendar, adherence, step count
Self-report: usefulness, burden

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Micro-Randomized Trial

Randomize each participant between intervention options at each decision time

→ Each person may be randomized 100's or 1000's of times.

These are sequential, “full factorial,” designs.

Extension of A/B testing & Single Case Designs
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Why Micro-Randomization?

- Randomization (+ representative sample) is a gold standard in providing data to assess the causal effect of an intervention.
- Sequential randomizations will enhance replicability of data analyses (moderation, decision rule development) .

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HeartSteps (42 day study)

- Whether to provide a tailored activity recommendation at the decision times.
- 210 decision times for the tailored activity recommendations.

		Randomization Probability
Tailored Activity Recommendation?	Yes	$\frac{2}{5}$
	No	$\frac{3}{5}$

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Micro-Randomized Trial

These sequential factorial trials are used to build JITAIs...

First Question to Address: Do the intervention options differentially impact the proximal response? AKA: is there a signal here?!

--Test for proximal *main effects* of the intervention options

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Micro-Randomized Trial

Time varying potentially intensive/intrusive interventions → potential for accumulating habituation and burden

→

Allow main effect of the interventions on proximal response to vary with time

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Availability & the Main Effect

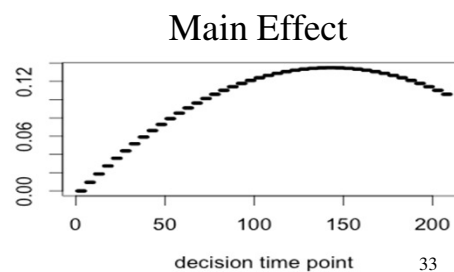
- Intervention options can only be delivered at a decision point if an individual is *available*.
- The effect of an activity message at a decision point is the difference in proximal response between *available* individuals assigned an activity recommendation and *available* individuals who are not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

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Main Effect

Main effect of activity recommendation on proximal response is likely time-varying $\beta(t)$, $t=1, \dots, T$

- What does $\beta(t)$ this main effect mean?



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 effects, moderation, construct decision rules

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Sample Size Calculation

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

$$H_0 : \beta(t) = 0, t = 1, 2, \dots, T$$
- Size to detect a low dimensional, smooth alternate H_1 .
 - Example: H_1 : $\beta(t)$ quadratic with intercept, β_0 , linear term, β_1 , and quadratic term β_2 and test

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

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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.
- Given a specified power to detect the smooth alternative, H_1 , a false-positive error prob., and the desired detectable signal to noise ratio, we use standard statistics to derive the sample size.

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Sample Size Calculation

Alternative hypothesis is low dimensional
 → assessment of the effect of the activity recommendation uses contrasts of *between participant responses* + contrasts of *within participant responses*.

--The required number of participants will be small.

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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.
- Average availability

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HeartSteps (42 day study)

Standardized effects:

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

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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

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Micro-Randomized Trial

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

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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

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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.
- USEFUL: Proximal response can be unobtrusively sensed or unobtrusively self-reported.

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