Building Just-In-Time Adaptive Interventions in Mobile Health: The Role of Micro-Randomized Trials

SBM workshop March 30, 2016

Presenters: Inbal Nahum-Shani, University of Michigan
Predrag Klasnja, Group Health
Susan Murphy, University of Michigan
Bonnie Spring, Northwestern University
David Conroy, Penn State University

Moderator: Daniel Almirall, University of Michigan
Workshop Goals and Presenters

Just-in-time Adaptive Interventions (JITAI)s
  Inbal Nahum-Shani, University of Michigan

Case Study 1: HeartSteps
  Predrag Klasnja, University of Michigan

Micro-Randomized Trials (MRT)
  Susan Murphy, University of Michigan

Case Study 2: Sense2stop
  Bonnie Spring, Northwestern University
  David Conroy, Pennsylvania State University
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From Adaptive Interventions (AIs) to Just-In-Time Adaptive Interventions (JITAIs)

Inbal (Billie) Nahum-Shani
Institute for Social Research
University of Michigan
Outline

- Adaptive Interventions (AIs)
  - Definition
  - 5 elements

- Just In Time Adaptive Interventions (JITAIs)
  - A form of adaptive intervention
  - Same elements as AIs
  - But the adaptation serves a different goal

“Suddenly ‘Time’ and ‘Timing’ are everywhere”

(Ancona et al., 2001; AMR)
Review of AIs

- Treatment design
  - Seeking to accommodate heterogeneity in response to treatment
  - Intervention options are adapted to the unique and changing status of individuals

- Example (Marlowe et al., 2008; 2009; 2012)
  - Adaptive drug court program for drug abusing offenders
  - The goal: Minimize recidivism and drug use
    - Operationalized by graduating from the drug court program
Adaptive Drug Court Program

As-needed court hearings + standard counseling

Low risk

Bi-weekly court hearings + standard counseling

High risk

Non-responsive

Non-compliant

As-needed court hearing + ICCM

Non-compliant

Jeopardy contract: “zero tolerance”
Adaptive Drug Court Program

As-needed court hearings + standard counseling

Low risk

Bi-weekly court hearings + standard counseling

High risk

Non-responsive

As-needed court hearing + ICCM

Non-compliant

Bi-weekly court hearing + ICCM

Non-compliant

Non-compliant

Jeopardy contract: “zero tolerance”
Every 30 days

*If* drug-positive urine specimens ≥ 2

*Then,* intervention = {Intensify treatment}

*Else if* drug-positive urine specimens < 2

*Then,* intervention = {Maintain treatment intensity}
Decision Rule

Every 30 days

*If* drug-positive urine specimens $\geq 2$

*Then*, intervention = \{Intensify treatment\}

*Else if* drug-positive urine specimens $< 2$

*Then*, intervention = \{Maintain treatment intensity\}

1. Tailoring Variable:
   Patient information used to make treatment decisions
Decision Rule

Every 30 days

If drug-positive urine specimens ≥ 2
Then, intervention = {Intensify treatment}

Else if drug-positive urine specimens < 2
Then, intervention = {Maintain treatment intensity}
Decision Rule

Every 30 days

\textit{If} drug-positive urine specimens \( \geq 2 \)

\textit{Then}, intervention = \{Intensify treatment\}

\textit{Else if} drug-positive urine specimens < 2

\textit{Then}, intervention = \{Maintain treatment intensity\}
Every 30 days

If drug-positive urine specimens ≥ 2
    Then, intervention = {Intensify treatment}
Else if drug-positive urine specimens < 2
    Then, intervention = {Maintain treatment intensity}

4. Decision Point:
   A time in which treatment options should be considered based on patient information
Every 30 days

\textit{If} drug-positive urine specimens $\geq 2$

\hspace{1cm} \textit{Then}, intervention = \{Intensify treatment\}

\textit{Else if} drug-positive urine specimens $< 2$

\hspace{1cm} \textit{Then}, intervention = \{Maintain treatment intensity\}

\textbf{5. Outcomes:}

Distal $\rightarrow$ Long-term goal of intervention:

\hspace{1cm} \textit{Program graduation} (14 consecutive weekly negative drug urine specimens)

Proximal $\rightarrow$ Short-term goal of decision rules:

\hspace{1cm} \textit{Abstinence} in the course of intervention (mediator)
Adaptive Intervention: Elements

- Decision Points
- Tailoring Variable
- Decision rule
- Intervention Options
- Monitoring
- Individualizing
- Delivering
- Outcomes: Proximal + Distal

Guide Adaption Process
Adaptive Intervention: Elements

Decision Points ← Trigger
Tailoring Variable ← Monitoring
Decision rule → Individualizing
Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide

Adaptation process

[Diagram showing time units: Minutes, Day, Week, Month, Months]
In the Drug Court Program

Decision Points ← Trigger

Tailoring Variable ← Monitoring
Decision rule → Individualizing
Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide

Monthly Drug-Positive US

(-) Ongoing Abstinence (+) Graduation

Risk

Minutes Day Week Month Months
In the Drug Court Program

Minutes   Day   Week   Month   Months

Decision Points ← Trigger

Tailoring Variable ← Monitoring
Decision rule → Individualizing
Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide

Monthly Drug-Positive US

(-) Ongoing Abstinence (+) Graduation

Risk
In the Drug Court Program

Decision Points ➔ Trigger

Tailoring Variable ➔ Monitoring
Decision rule ➔ Individualizing
Intervention Options ➔ Delivering

Outcomes: Proximal + Distal ➔ Guide

Monthly Drug-Positive US ➔ Treatment Intensity ➔ Ongoing Abstinence ➔ (+) Graduation

Clinic
### In the Drug Court Program

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Day</th>
<th>Week</th>
<th>Month</th>
<th>Months</th>
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<tbody>
<tr>
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</tbody>
</table>

#### Decision Points

- Tailoring Variable
- Decision rule
- Intervention Options

#### Monitoring

#### Individualizing

#### Delivering

#### Trigger

- Intensify only if non-response

#### Clinic

#### Outcomes: Proximal + Distal

- Monthly Drug-Positive US

**Guide**
In the Drug Court Program

Tailoring Variable
Decision rule
Intervention Options

Outcomes: Proximal + Distal

Monthly Drug-Positive US

Decision Points
Trigger

Monitoring
Individualizing
Delivering

Intensify only if non-response
Clinic

Monthly

Every month
In the Drug Court Program

Decision Points

Tailoring Variable  Decision rule  Intervention Options

Monitoring  Individualizing  Delivering

Outcomes: Proximal  +  Distal

Guide

Monthly
Drug-Positive US

Every week

Intensify only if non-response

Clinic

Every month

Minutes  Day  Week  Month  Months
What if Hypothetically...

Decision Points

Tailoring Variable ← Monitoring
Decision rule ← Individualizing
Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide

- (+) Craving
- (+) Graduation
- (-) Daily drug-use episodes
- (-) Ongoing Abstinence

Day
Week
Month
Months

Minutes

Risk
What if Hypothetically…

Decision Points ← ───────────────── → Trigger

Tailoring Variable ← ─────────── Monitoring
Decision rule ← ─────────── Individualizing
Intervention Options ← ─────────── Delivering

Outcomes: Proximal + Distal → Guide

Craving (⁺) → Daily drug-use episodes

Minutes  |  Day  |  Week  |  Month  |  Months
--------|-------|--------|---------|--------
What if Hypothetically…

As soon as craving occurs, in the natural environment, the cycle begins:

**Decision Points**
- **Trigger**
- **Monitoring**
- **Individualizing**
- **Delivering**

**Tailoring Variable**
- **Decision rule**

**Intervention Options**
- **Outcomes: Proximal** + **Distal**
- **Guide**

**Craving**
- **Craving-Regulation Intervention**
- **Daily drug-use episodes**
### What if Hypothetically

<table>
<thead>
<tr>
<th>Minutes</th>
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</tbody>
</table>

#### Decision Points

- Tailoring Variable
- Decision rule
- Intervention Options

#### Trigger

- Monitoring
- Individualizing
- Delivering

#### Outcomes: Proximal + Distal

- **Guide**

---

Prompt only if craving is high

As soon as craving occurs, in the natural environment

- Craving

- Day 1
What if Hypothetically...

As soon as craving occurs, in the natural environment

Every few minutes

Decision Points

Tailoring Variable

Decision rule

Intervention Options

Outcomes: Proximal + Distal

Trigger

Monitoring

Individualizing

Delivering

Guide

Craving

Based on Craving status

As soon as craving occurs, in the natural environment
We need A Therapist in the Pocket

To…

- Monitor craving level of craving every few minutes or so
- Use this information to decide whether/how to intervene
- Deliver the intervention as soon as high craving occurs
  - In the person’s natural environment
A Phone in Your Pocket

- Continuously monitor the person’s status and context
  - Wide range of embedded sensors: e.g., accelerometer, camera, GPS, microphone, and the touchscreen sensors.
  - Other wearable sensors: e.g., hand movement sensors, electrocardiogram, galvanic skin response sensors.
  - Ecological Momentary Assessment (EMAs)
- Deliver the intervention as soon as needed, in the natural environment of the person.

Advances in mobile and wireless technology enable the delivery of adaptive interventions that aim to provide Just-In-Time support.
So what is a JITAI?

- Adaptive intervention – includes adaptation
- Goal of the adaptation is to:
  - Provide the right type of support
  - At the right time
  - While minimizing waste (disruptions)
- Timing is salient in support effectiveness
  - Timing => ‘event-based’ -- unexpected (Ancona et al., 2001)
  - Time is salient when it’s running out (Wessman & Gorman, 1977).
- Conditions that define the ‘right time’ change rapidly, over short time-frames
  - ... a few days, hours, minutes, seconds
Why JITAI Is In Health Behavior Interventions?

- Need to address health-related events/conditions that
  - Change rapidly,
  - Unexpectedly,
  - And in the person’s natural environment.

- While minimizing disruptions to the daily life and routine of the participant.
Example #1

- B-Mobile for reducing sedentary behaviors
  - Mobile app automatically monitored and categorized behavior as either sedentary or not.
  - Promotes for walking breaks are delivered only if an individual experienced 30 minutes of sedentary behaviors.

(Thomas & Bond, 2015)
Example #1

Every minute

If minutes of continuous sedentary behavior ≥ 30

Then, IO = {prompt for a 3 minute walking break}

Else if minutes of continuous sedentary behavior < 30

Then, IO = {Nothing}

Opportunity to raise awareness and shape walking

Distal outcome: reducing sedentary behavior
Proximal outcomes: Daily walking (total minutes)
Example #2

- Mobile-BASICS: targeting heavy drinking and smoking
  - Mobile phone administered
  - Participants prompted 3/day for assessments
    - Smoking urge, affect, drinking behaviors
  - Urge-management interventions delivered only if an individual reported an urge to smoke at assessment times.

(Witkiewitz et al., 2014)
Example #2

At random prompt for self-report
If response to prompt=Yes

Then
If Urge ≥ U₀

Then, IO = {Urge surfing}

Else if Urge < U₀

Then, IO = {Nothing}

Else, if response to promote=No

Then, IO = {Nothing}

Distal outcome: smoking cessation
Proximal outcomes: # of cigarettes smoked per day
Example #3

- iCrave for weight management
  - Mobile app containing a button that participants can press whenever they experience craving for unhealthy snacks
  - A visualization task is provided as soon as they press the button.
  - Next, participant is prompted to make a choice between: (1) not eating at all; (2) a healthy snack; or (3) an unhealthy snack.
  - A congratulating message is provided only if the participant selects to not eat at all.

(Hsu et al, 2014)
Example #2

Decision Point: the person is in the best position to determine whether s/he is experiencing craving [“Pull”]

When pressing the support button on the app
Offer visualization task

Then,

If selection = Not to eat at all

Then, IO = {Congratulations}

Else if selection = Eating

Then, IO = {Do nothing}

Distal outcome: Weight loss/management
Proximal outcome: Unhealthy snacking episodes
What's in Common?

- The status of the participant changes rapidly, unexpectedly, ecologically.

**Rapidly & Ecologically**
- Scientist-specified
- Patient initiated

**Decision Points**
- Tailoring Variable
- Decision rule
- Intervention Options

**Trigger**
- Monitoring
- Individualizing
- Delivering

**Outcomes:** Proximal + Distal

- Guide
- Rapid, Ecological
  - Active
  - Passive
What's in Common?

- The status of the participant changes rapidly, unexpectedly, ecologically.
- Personal and Contextual conditions
- Represents states of risk or opportunity

Decision Points ↔ Trigger

Tailoring Variable ↔ Monitoring
Decision rule → Individualizing
Intervention Options ↔ Delivering

Outcomes: Proximal + Distal → Guide

Smaller time scale
What's in Common?

Decision Points ↔ Trigger

Tailoring Variable ↔ Monitoring
Decision rule → Individualizing
Intervention Options ↔ Delivering

Outcomes: Proximal + Distal → Guide

- The status of the participant changes rapidly, unexpectedly, ecologically.
- Personal and Contextual conditions
- Represents risk or opportunity

“do nothing”

Smaller time scale

- As soon as these conditions occur
- In the person’s natural environment
So what's the problem?

- Open scientific questions
  - What personal and/or contextual conditions represent risk or opportunities with respect to the proximal outcomes.
  - How rapidly these conditions are likely to change?
  - What intervention options could address or capitalize on these conditions; hence affect the proximal outcomes?
  - What personal and/or contextual conditions represent risk that intervention provision be wasteful/disruptive?
Questions?
Building Just-In-Time Adaptive Interventions in Mobile Health: The Role of Micro-Randomized Trials

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HeartSteps: A JITAI for encouraging regular, opportunistic physical activity

Predrag “Pedja” Klasnja
University of Michigan & Group Health Research Institute
HeartSteps Goals

• Help individuals increase—and sustain—their physical activity levels

• Increase activity by supporting not just structured exercise but also *opportunistic* physical activity—activity that people can do throughout the day
HeartSteps Target Population

• HeartSteps 1.0: Sedentary adults with regular schedules (full time jobs, graduate students)
• HeartSteps 2.0: Patients with heart disease who are finishing phase II cardiac rehabilitation
Why a JITAI?

• Opportunities for physical activity and salience of PA goals vary by situation
• Phones know users’ location, state of calendar, weather, and current and recent activity, and can thus know what activities are currently possible and appropriate
• A JITAI can support opportunistic activity by
  • Suggesting specific, doable, and appropriate activities people can do in their current situation throughout the day, as context changes
  • Increasing repertoire of cognitively-accessible activities people can do in different contexts
Pull Interventions

Made available to users on the phone but accessed at will

- Graphs and charts for self-monitoring
- Coping strategies, educational materials
- “Help” button to receive coping support
Pull Interventions

• Allow inclusion of many components
• Put user in control of access
• Low burden

But…

• Depend on users to know when to access them and remember to do it
Push Interventions

Delivered based on time, context, user’s state and activities

- Reminders
- Suggestions, tips, motivational messages
- Prompts to set goals, complete EMA…
- Rewards for goal attainment
Push Interventions

• Can use sensing and user modeling to determine right delivery time
• Don’t rely on user’s awareness of times of need or remembering to access

But…

• High burden
HeartSteps Design Goal

Develop a JITAI that includes the right combination of...

• pull interventions
• push components, *delivered at the right times* to encourage activity throughout the day, as context changes
HeartSteps 1.0: JITAI for Regular Walking

Pull components:

- Feedback on steps
- Daily "what motivates me" message
- Library of previous activity suggestions
Push Intervention Components

• Actionable, contextually-relevant suggestions for walking
• Planning of when, how, and where one will be active next day

Intended outcome: steps
Suggestions

Suggestions tailored on:
• time of day
• weekday vs. weekend
• location
• weather

Two types of suggestions:
• to walk
• to interrupt sitting
Message Examples

Have a long conference call today? Walking in place or pacing while you talk can keep you engaged and increase your step count!

There's no better way to spend a weekend evening than taking a walk around the neighborhood! Are you up for it?

It's important to hydrate. If you walk to the water fountain now, you can refill your bottle while also stretching your legs!
Example Decision Rule for Tailored Activity Messages

5 times a day (morning commute, lunch time, mid-afternoon, evening commute, post-dinner):

If raining/snowing=No and walkable temperature=Yes
   Then, IO = {message for an outdoor walk, tailored to user’s current location (home/work/other), time of day, day or week, and weather}

Else if raining/snowing=Yes or walkable temperature=No
   Then, IO = {message for indoor activity, tailored to location, time of day}
Proximal Outcome for Suggestions

Goal of proximal outcome selection
Determine if the suggestions are having direct intended effects (theoretical fidelity)

Ideal outcome
Did the person do suggested activity?

Chosen outcome
Step count in 30 minutes from intervention offering/randomization
Planning

Two types of planning:
• Generate a new plan
• Select a plan from a list of previous and suggested plans

Proximal outcomes:
• Step count the next day
• Self-report if plan followed
How hectic was your day today?

Not at all hectic

Very hectic

Did any of the following make it difficult for you to be active today? (choose all that apply)

- Poor weather
- No time/too busy
- No place to be active
- Illness or injury
- Sore muscles

Next
Questions We Want to Answer

- Do contextual suggestions have a proximal effect at all? (do they get people to walk during the day?)
- Do people get tired of them after a while? I.e., does their effect change over time?
- If suggestions have an effect, when should we be sending them?
  - Do they work better during certain parts of the day?
  - Do they work better when weather is good vs. bad?
- Do contexts in which suggestions work change over time?
- How do people’s perceptions of suggestions (as captured via their thumbs-up/down responses) change over time?
- How does context moderate suggestion perceptions?
Pilot Study Methods

• Six-week study with 40 sedentary adults
• Both components micro-randomized:
  • Suggestions randomized 5 times a day:
    • No suggestion, activity suggestion
  • Planning randomized every night:
    • Planning /no planning
• Data captured during the study:
  • Steps, location, weather, calendar, phone application use, user burden, answers to daily questionnaires
Pilot Study Goals

• Assess time-varying proximal effects for each intervention component
• Understand for whom, when, and in what circumstances components have an effect
• Understand how components affect user burden

Determine decision rules for adaptive version of HeartSteps

  Augment current decision rules with additional information (e.g., context, frequency) about when to—and when not to—send suggestions
Questions?
Building Just-In-Time Adaptive Interventions in Mobile Health: The Role of Micro-Randomized Trials

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Micro-randomized Trial Design

Susan Murphy, University of Michigan
Interesting Scientific Questions

- Do the intervention options (e.g. yes/no tailored activity suggestion) impact the proximal outcome (e.g. step count over next 30 min.)?
- Does the context (location, current stress, weather, social setting) impact the effectiveness of the intervention options on the proximal outcome?
- Example: Should we provide a tailored activity suggestion when the user has recently been physically active?
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 and multiple times per day.

• These are sequential, “full factorial,” designs.

Extension of A/B testing & Single Case Designs
Micro-Randomized Trial Elements

1. Record outcomes: distal (scientific/clinical goal) & proximal outcome

2. Record potential tailoring variables

3. Randomize among intervention options at decision points

4. At end of trial use resulting data to assess intervention effects, moderation, construct decision rules
HeartSteps

• 5 decision points per day; 42 day study

• Intervention options: Yes/No to providing a tailored activity suggestion

• 210 decision points for the Yes/No tailored activity suggestions.

<table>
<thead>
<tr>
<th>Tailored Activity Suggestion?</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: Does the intervention option (e.g. tailored activity suggestion) affect the proximal outcome (e.g. step count over next 30 min.)?

- Test for a main effect.
  - Determine the sample size to address this question.
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

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

- The proximal main effect of a tailored activity suggestion at a decision time is the difference in proximal outcome between available individuals assigned an activity suggestion and available individuals who are not assigned an activity suggestion.
Time-varying Main Effect

Effect of tailored activity suggestion on step count is likely time-varying – denote by $\beta(j), j=1, \ldots, 210$
Sample Size Calculation

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

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

• Size to detect a simple low dimensional alternate $H_1$.

  • Example: $H_1: \beta(t)$ quadratic with intercept, $\beta_0$, linear term, $\beta_1$, and quadratic term $\beta_2$ and switch to

$$H_0: \beta_0 = \beta_1 = \beta_2 = 0$$
Sample Size Calculation

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

--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 $\beta$ 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.
Specify Alternative for Sample Size Calculation

SPECIFY:

- Standardized main effects:
  - Main effect on first day, 0
  - Average main effect over trial duration ?
- Day of maximal main effect. 28
# HeartSteps Sample Sizes

Power = .8, $\alpha = .05$

<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>
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</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 option.
   2) Under-estimate the average 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 conditions 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 outcome cannot be feasibly assessed or predicted.
- **USEFUL:** Proximal outcome can be unobtrusively sensed or unobtrusively self-reported or predicted with precision.
Questions?
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Sense2stop: A JITAI for Addressing States of Vulnerability to Smoking Relapse

Bonnie Spring, David Conroy, Kevin Moran
Center for Behavior and Health
Northwestern University
Outline

• **What:**
  - is MD2K?
  - is the Sense2stop smoking cessation study?

• **Why:**
  - is the study needed clinically/scientifically?
  - this problem warrants a JITAI?

• **How:**
  - will the study design answer the question?

• **Next:**
  - where will we go from here?
What is MD2K? – NIH U54EB020404 (PI Santosh Kumar)
Who is the MD2K Smoking Study Team?

Bonnie Spring

Kevin Moran

Gwen Ledford

David Conroy

Mustafa Al’Absi

Dave Wetter

Inbal (Billie) Nahum-Shani

Susan Murphy

Santosh Kumar
The Problem

• Most (93%) unaided smoking cessation attempts fail in 1st week
  ➢ 95% of lapses (slips, few puffs) followed by relapses
  ➢ We encourage patients to call when tempted to smoke. …but they rarely do

• Stress predicts lapse/relapse=> increasing state of risk?
  ➢ Empirically supported treatments exist for stress.
  ➢ Good intervention target to prevent lapse/relapse?

• But is stress a useful tailoring variable: basis for decision rule about when to trigger intervention?

  WE DON’T KNOW…..

  Sense2stop study will figure out
Why JITAI?

• Stress = a time-varying state that occurs rapidly, unexpectedly, episodically in the person’s natural environment

• The goal is to help recently quit smokers regulate stress so they won’t slip back to using smoking to do so

• Performing brief effective exercises can buffer/blunt real-life life stress

• ***But people fail to use them***

• Should we prompt recently quit smokers to perform brief stress-regulation exercises so they can blunt their rising relapse risk when they experience stress?

When should we prompt them?
Two Alternative Hypotheses

• Stress as a state of heightened relapse risk:
  ▪ Person needs to be prompted (reminded) to perform stress management as soon as stress occurs in the natural environment to contain the rising vulnerability and prevent lapse.
  ▪ No need to bother the person when s/he is not stressed.
  ▪ Provide a prompt only when the person is under stress

• No-Stress as a state of opportunity to master skills:
  ▪ Stress → limited cognitive capacity;
  ▪ Under stress, people have little capacity to pay attention and master new skills
  ▪ Provide a prompt to practice stress management skills only if the person is not under stress
Scientific Questions

1. Will a brief ecological reminder intervention to engage in a stress regulation exercise reduce near-term future risk of stress and smoking lapse compared to no intervention?

2. When stressed and not stressed minutes are micro-randomized to no intervention or intervention, will intervention be more effective than no intervention only under stress? no stress? either?

<table>
<thead>
<tr>
<th></th>
<th>No Intervention</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not Stressed</strong></td>
<td>- - -</td>
<td>&gt;&gt;&gt;</td>
</tr>
<tr>
<td><strong>Stressed</strong></td>
<td>- - -</td>
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- **Aim:** Develop a decision rule to guide optimal timing of a stress management intervention prompt to prevent smoking relapse
JITAI Outcomes: How to tell if the intervention is working?

• **Proximal outcome**: short-term goal the intervention is intended to achieve
  - Reduce probability/increase time to a lapse
  - Reduce probability/increase time to next stress episode
  - May be a mediator on the pathway to the distal outcome

• **Distal outcome**: ultimate goal the intervention is intended to achieve
  - Reduced probability/increased time to smoking relapse
  - To be examined when JITAI is tested in an RCT
Dynamic Vulnerability Model: States of Increasing Risk of Adverse Health Outcome *(detected by sensors)*

- **Unstressed**
- **Lapsed**
- **Stressed**
- **Relapsed**

**Figure 1: Dynamic Model of Illness Vulnerability**
### Study Population, Setting, Timeline

<table>
<thead>
<tr>
<th>Day</th>
<th>Smoking Status</th>
<th>Location</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SMOKING</td>
<td>50% lab / 50% field</td>
<td>In-person Treatment</td>
</tr>
<tr>
<td>2</td>
<td>SMOKING</td>
<td>Field</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>TAPERING</td>
<td>50% lab / 50% field</td>
<td>In-person Treatment</td>
</tr>
<tr>
<td>4</td>
<td>QUIT DAY</td>
<td>3 hrs lab + field</td>
<td>In-person Treatment</td>
</tr>
<tr>
<td>5</td>
<td>POST-QUIT</td>
<td>Field</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>POST-QUIT</td>
<td>Field</td>
<td>Phone Coaching</td>
</tr>
<tr>
<td>7</td>
<td>POST-QUIT</td>
<td>Field</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>POST-QUIT</td>
<td>Field</td>
<td>Phone Coaching</td>
</tr>
<tr>
<td>9</td>
<td>POST-QUIT</td>
<td>Field</td>
<td></td>
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<tr>
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<td>POST-QUIT</td>
<td>Field</td>
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<td>Field</td>
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</tr>
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<td>13</td>
<td>POST-QUIT</td>
<td>Field</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>POST-QUIT</td>
<td>Field + 2hrs lab</td>
<td></td>
</tr>
</tbody>
</table>

- Chronic smokers, >6 cigs/day
- Trained on equipment, stress apps and relaxation skills
- Helped to quit smoking
- Monitored 4 days pre- and 10 days post-quit
- Intervention (prompt to perform relaxation exercises begins post-quit)
Assessments

- **Autosense** cheststrap & wristband passively sense respiration, ECG, accelerometry, 6-axis inertial sensing
  - **cStress** classifies every minute as Stress / Not Stress / Unclear, validated against cold pressor, public speaking, PASAT
  - **Puffmarker** detects smoking puffs, validated against CO and EMA

- Random & event contingent EMAs for smoking, mood, context

- $microincentives for sensor wear, rapid responding, session attendance
The Sense2Stop Intervention

- Prompt to perform stress management exercises from one of 3 stress-regulation apps

- Intervention delivery involves:
  - Phone alert prompt to use one of the stress-regulation apps, which opens on phone
  - MS Band vibration
  - Message on MS Band

**The Sense2Stop Intervention**
The Micro-Randomization

• Randomization to intervention or no intervention could happen every minute, BUT no randomization occurs under conditions of “UNAVAILABILITY:”
  1. Can’t provide a stress classification: stress level unclear; physically active; poor data (UNCERTAINTY)
  2. Person driving (SAFETY)
  3. < 60 minutes since last intervention; < 10 minutes since EMA (BURDEN)

• Micro-randomization probabilities set to yield:
  • average of 3 interventions/day across morning, afternoon, evening w/50% under Stress, 50% under No Stress
Summary of Protocol -

- Classify Autosense output every minute as Stress/Not stress/Unclear.
- Micro-randomize “available” minutes to intervention/no intervention.

Band vibration, phone alert prompt to use stress-regulation app.
JITAI Components:

- **Decision points**: a time at which a treatment decision is made
  - Decision points: each minute
  - Treatment decision: whether to deliver stress management intervention or no intervention

- **Intervention options**: possible treatments/actions
  - Either no intervention or pushing a prompt to use a stress management app: Head Space, Mood Surfing, Thought Shakeup
JITAI Components

• **Tailoring variable**: information about the participant that is used to decide which intervention option to provide
  - Stress is our primary candidate tailoring variable
  - Should additional candidate tailoring variables be considered as intervention triggers (e.g., location, craving, cues, overeating)?

• **Decision rule**: should a prompt be provided
  - Only under stress?
  - Only under no-stress?
  - Both? (*not a useful tailoring variable*)
Potential Decision Rule if Stress proves to be a Tailoring Variable

Every minute

IF availability = Yes,

Then,

If passively sensed stress = Yes,

Then IO= prompt stress-regulation

Else if passively sensed stress = No

Then IO=‘do nothing’

Else If availability=No,

Then IO= ‘do nothing’
Questions? ....... Comments?

Thanks!

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Discussion Questions

• Micro-randomized Trial Design (Murphy, et al.)
  • Is there a role for MRTs to enhance engagement in the JITAI itself?

• Sense2stop: Vulnerability to Smoking (Spring, et al.)
  • What is the advantage of using sensor-based assessments for deciding whether to intervene or not versus using EMA-based assessments (prompts for information) or some combination of both?

• HeartSteps: Physical Activity (Klasnja, et al.)
  • How does one decide which JITAI components to randomize as part of the micro-randomized trial versus which components are actually used in the JITAI with no randomization?

• Just-in-time Adaptive Interventions (Nahum-Shani, et al.)
  • What kind of preliminary research is most useful to have conducted prior to considering whether or not to use an MRT to build a JITAI?
The End

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