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

APS workshop May 29, 2016

Presenters:

Inbal Nahum-Shani, University of Michigan
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Susan Murphy, University of Michigan
Bonnie Spring, Northwestern University

Moderator: Daniel Almirall, University of Michigan

Workshop Goals and Presenters

Just-in-time Adaptive Interventions (JITAIs)

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

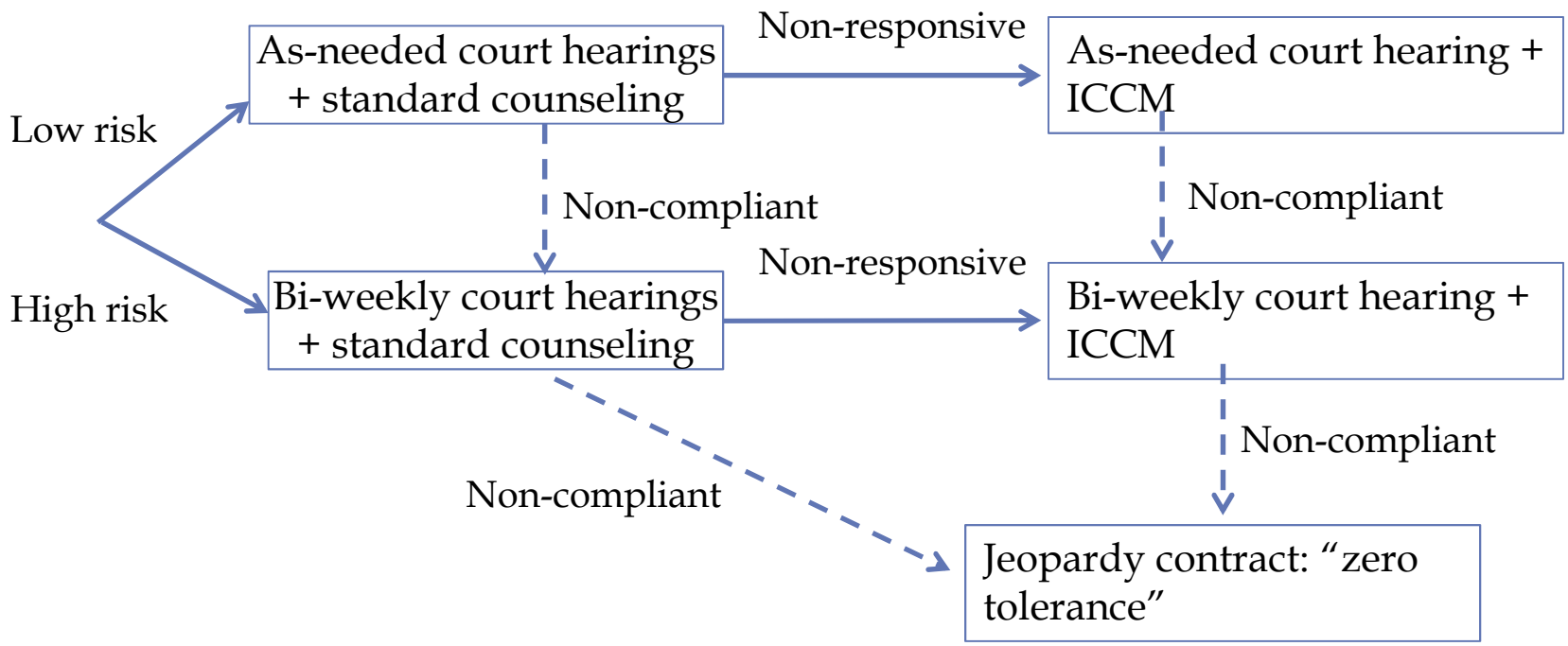
"Suddenly 'Time' and 'Timing' are everywhere"

(Ancona et al., 2001; AMR)

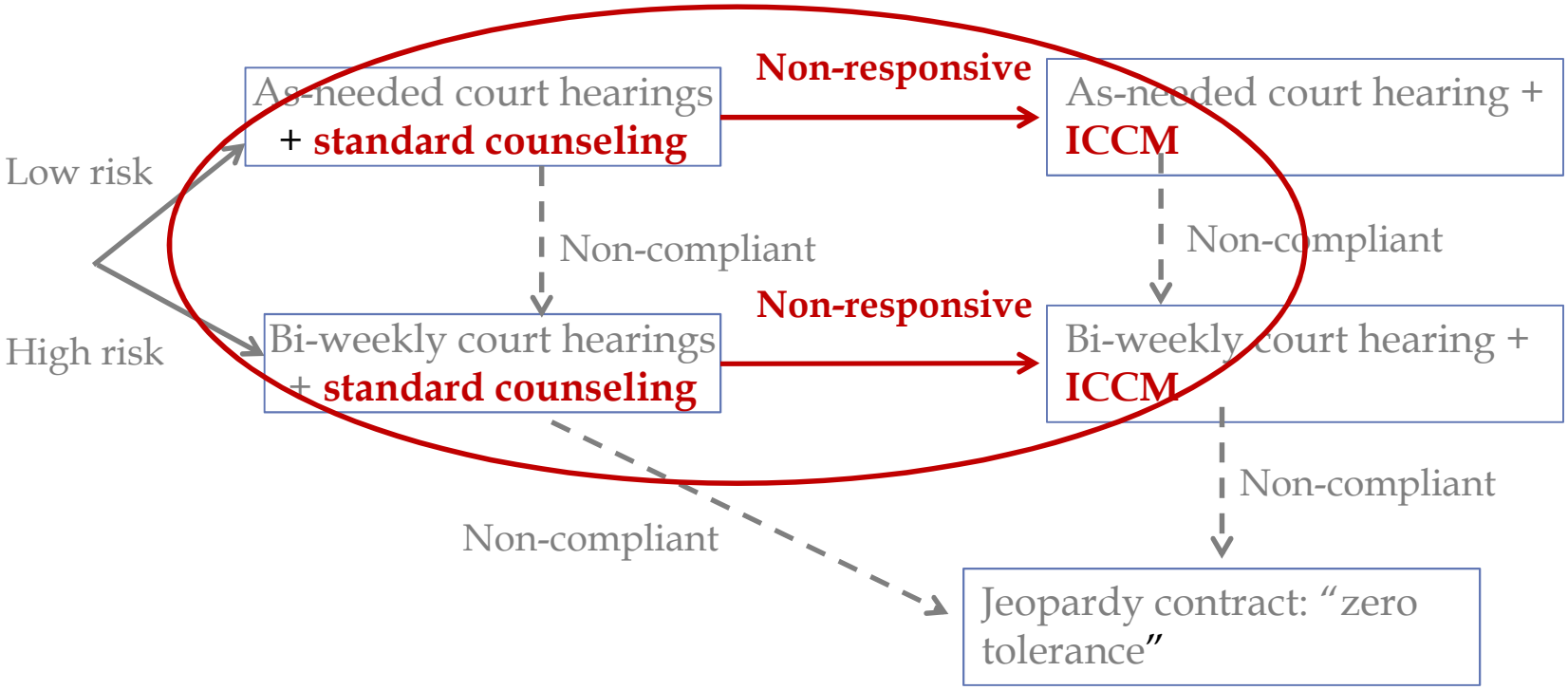
Review of AIs

- 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



Adaptive Drug Court Program



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

If drug-positive urine specimens ≥ 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

2. Intervention options:
Type/Dose

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 ≥ 2

Then, intervention= {Intensify treatment}

Else if drug-positive urine specimens < 2

Then, intervention = {Maintain treatment intensity}

3. Decision rule

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}

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

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}

5. Outcomes:

Distal →Long-term goal of intervention:

Program graduation (14 consecutive weekly negative drug urine specimens)

Proximal→ Short-term goal of decision rules:

Abstinence in the course of intervention (mediator)

Adaptive Intervention: Elements

Decision Points ← Trigger

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

} **Adaptation process**

Outcomes: Proximal + Distal → **Guide**

Adaptive Intervention: Elements

Minutes | Day | Week | Month | Months



Decision Points ← Trigger

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

} **Adaptation process**

Outcomes: Proximal + Distal → **Guide**

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

In the Drug Court Program

Minutes | Day | Week | Month | Months

Decision Points ← Trigger

Tailoring Variable ← Monitoring

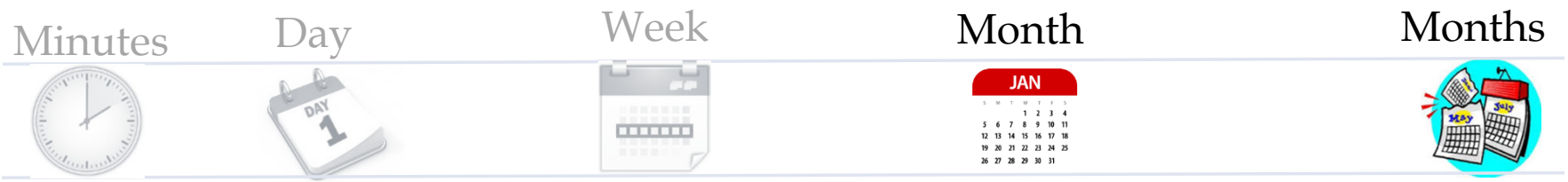
Decision rule → Individualizing

Intervention Options ← Delivering

Outcomes: Proximal + Distal → **Guide**

Monthly Drug-Positive US → (-) → Ongoing Abstinence → (+) → Graduation

In the Drug Court Program



Decision Points ← Trigger

Tailoring Variable ← Monitoring

Decision rule → Individualizing

Intervention Options ← Delivering ← Clinic

Outcomes: Proximal + Distal → Guide

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

In the Drug Court Program

Minutes | Day | Week | Month | Months

Decision Points ← Trigger

Tailoring Variable ← Monitoring

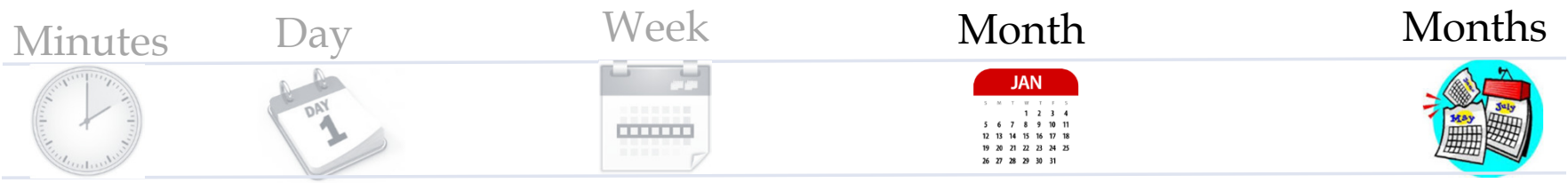
Decision rule → Individualizing ← Intensify only if non-response

Intervention Options ← Delivering ← Clinic

Outcomes: Proximal + Distal **Guide**

Monthly Drug-Positive US

In the Drug Court Program



Every month

Decision Points ← Trigger

Tailoring Variable ← Monitoring

Decision rule → Individualizing ← Intensify only if non-response

Intervention Options ← Delivering ← Clinic

Outcomes: Proximal + Distal **Guide**

Monthly Drug-Positive US

In the Drug Court Program

Every month

Decision Points ← Trigger

Tailoring Variable ← Monitoring ← Every week

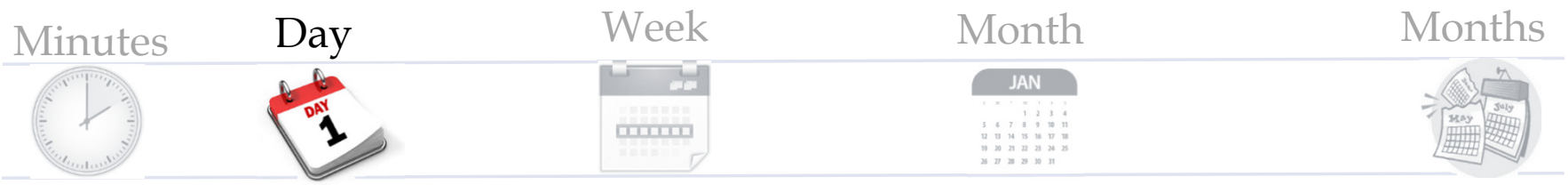
Decision rule → Individualizing ← Intensify only if non-response

Intervention Options ← Delivering ← Clinic

Outcomes: Proximal + Distal **Guide**

Monthly Drug-Positive US

What if Hypothetically…



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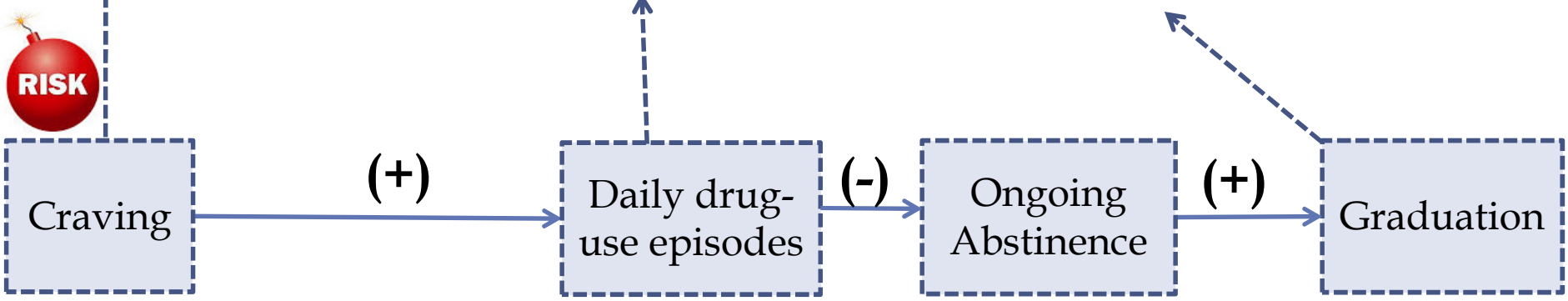
Tailoring Variable ← Monitoring

Decision rule → Individualizing

Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide



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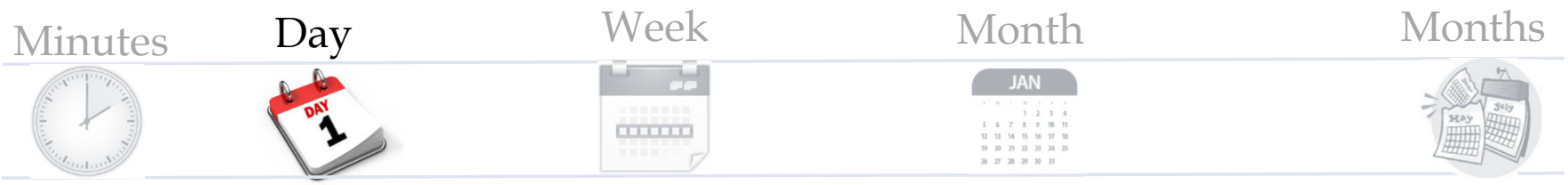


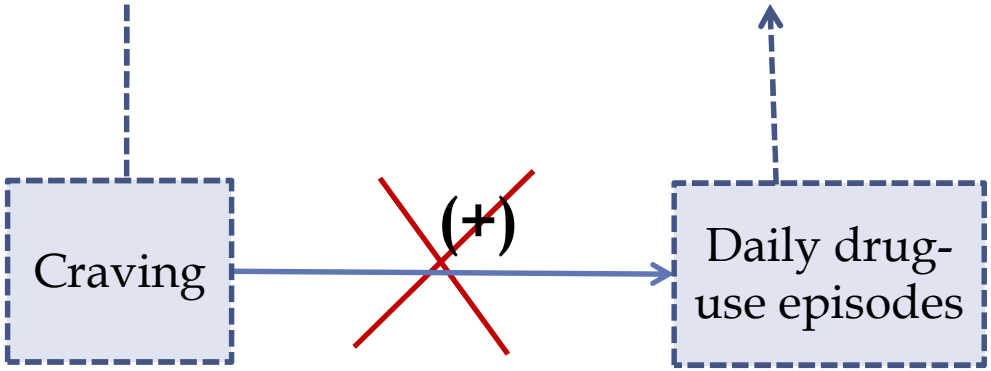
Decision Points ← Trigger

Tailoring Variable ← Monitoring

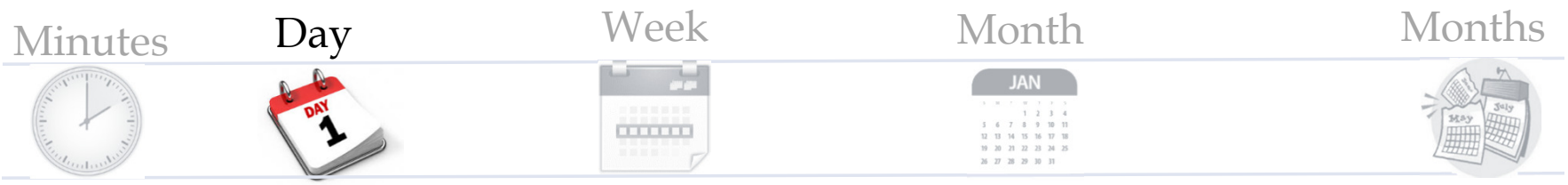
Decision rule → Individualizing

Intervention Options ← Delivering

Outcomes: Proximal + Distal → **Guide**



What if Hypothetically…



Decision Points ← Trigger

Tailoring Variable ← Monitoring

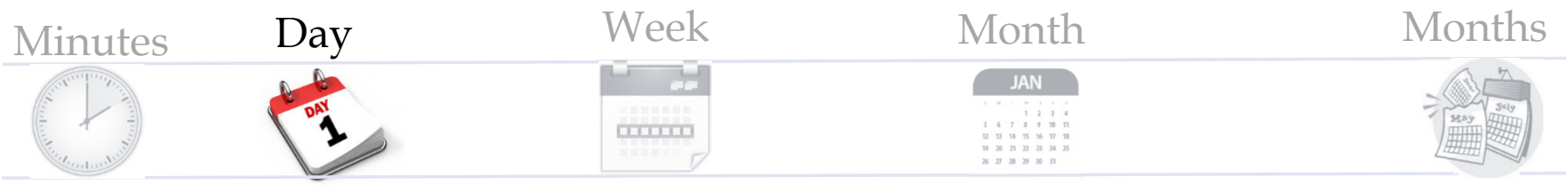
Decision rule → Individualizing

Intervention Options ← Delivering ← As soon as craving occurs, in the natural environment

Outcomes: Proximal + Distal → **Guide**

Craving → Craving-Regulation Intervention → Daily drug-use episodes

What if Hypothetically



Decision Points ← Trigger

Tailoring Variable ← Monitoring

Decision rule → Individualizing ← Prompt only if craving is high

Intervention Options ← Delivering ← As soon as craving occurs, in the natural environment

Outcomes: Proximal + Distal → Guide

Craving

What if Hypothetically…

Every few minutes

Decision Points ← Trigger

Every few minutes

Tailoring Variable ← Monitoring

Decision rule → Individualizing

Based on Craving status

Intervention Options ← Delivering

As soon as craving occurs, in the natural environment

Outcomes: Proximal + Distal → Guide

Craving

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)

  Just in Time Support
- 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 JITAIs
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 ≥ U_0 → Risk for smoking

Then, IO = {Urge surfing }

Else if Urge < U_0

Then, IO = {Nothing}

Else, if response to promote=No → Risk for Waste/Disruption

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 snakes
  - 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}

Opportunity to reinforce resisting food cravings

Distal outcome: Weight loss/management
Proximal outcome: Unhealthy snacking episodes

What's in Common?

Rapidly & Ecologically
- Scientist-specified
- Patient initiated

Decision Points

Trigger

Rapid, Ecological
- Active
- Passive

Tailoring Variable

Decision rule

Intervention Options

Monitoring

Individualizing

Delivering

Outcomes: Proximal + Distal

Guide

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

What's in Common?

Decision Points ← Trigger

Tailoring Variable ← Monitoring

Decision rule → Individualizing

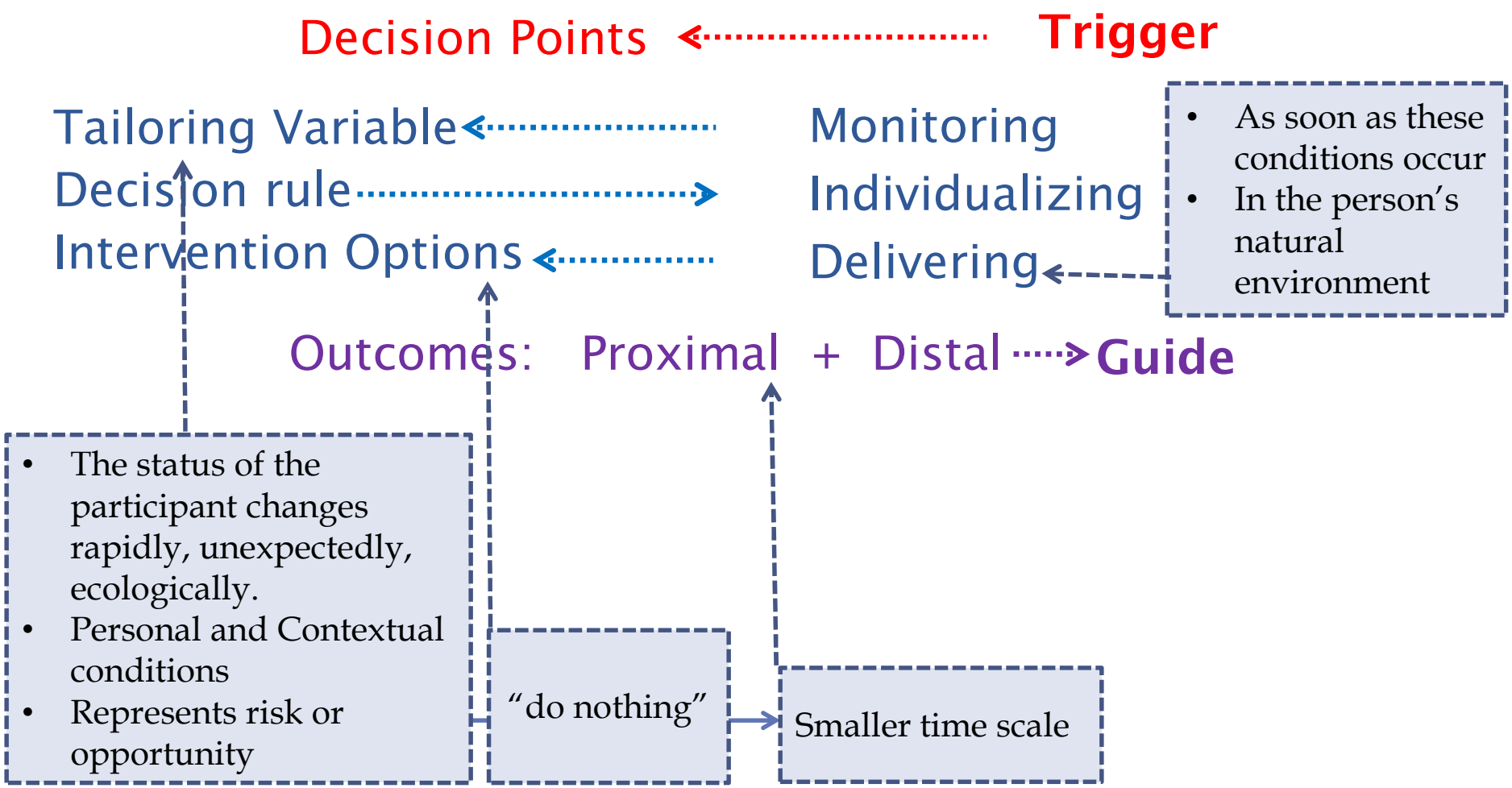
Intervention Options ← Delivering

Outcomes: Proximal + Distal → Guide

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

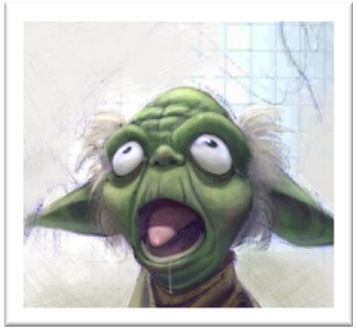
Smaller time scale

What's in Common?



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?

Practice forming your JITAI!

- Behavior & Population?
- Outcomes? -Distal (scientific/clinical goal) & Proximal (guided by mediational theories pinpointing the necessary processes needed to achieve the distal outcome)
- Intervention Options? -Guided by the proximal outcomes
- Tailoring variables? -Guided by theory concerning moderation.
- Decision points? -Guided by the dynamics of the tailoring variable and in-the-moment nature of the effect of the intervention options.
- Decision rules?

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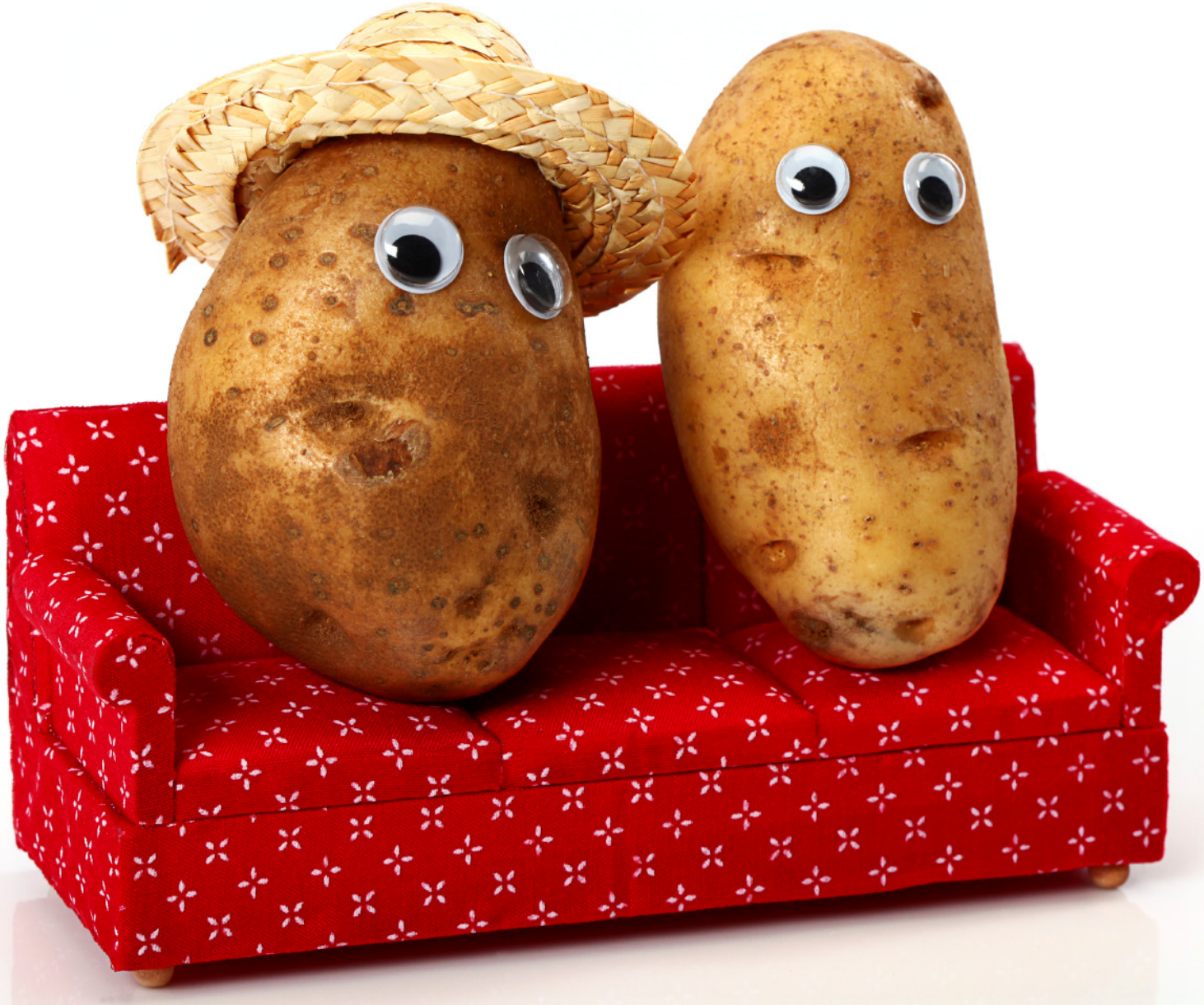
HeartSteps: A JITAI for encouraging regular, opportunistic physical activity

Predrag "Pedja" Klasnja
University of Michigan & Group Health Research Institute



Heartsteps

HeartSteps Goals

- Help individuals increase—and sustain—their physical activity levels
- Increase activity by supporting *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


PUSH
push pull signs.com © RD


PULL
push pull signs.com © RD

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

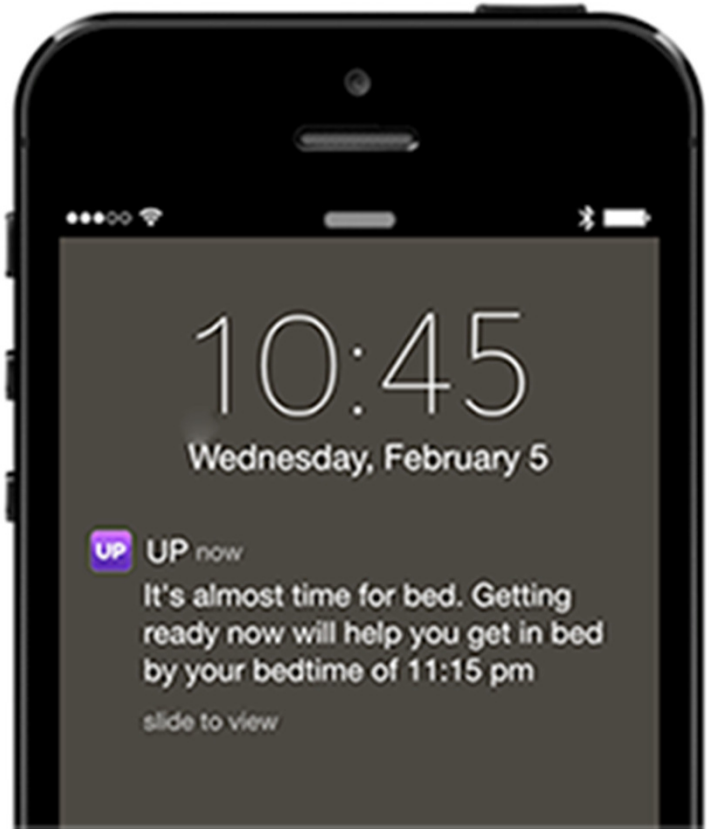
But…

- 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

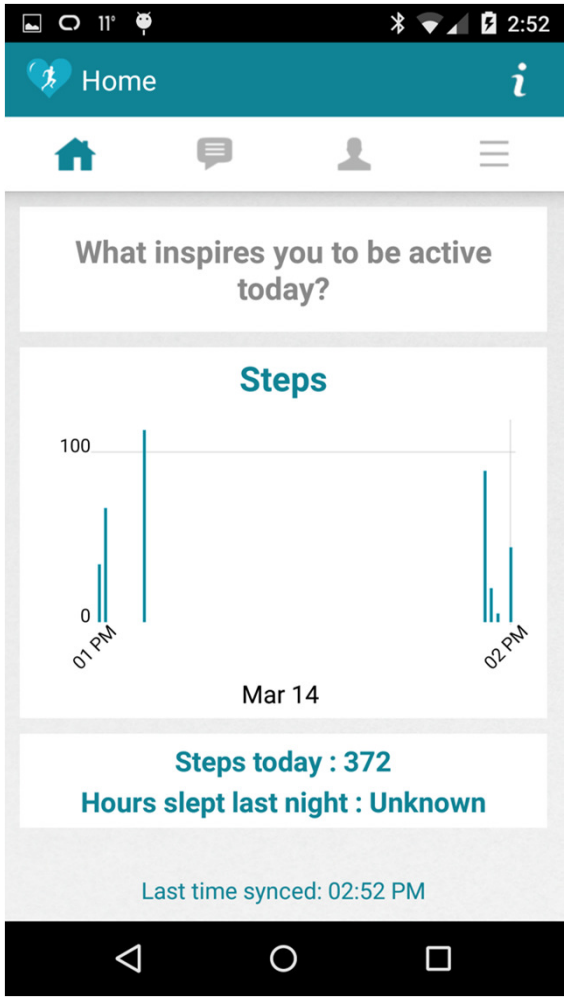
Develop a JITAI that includes the right combination of...

- 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:

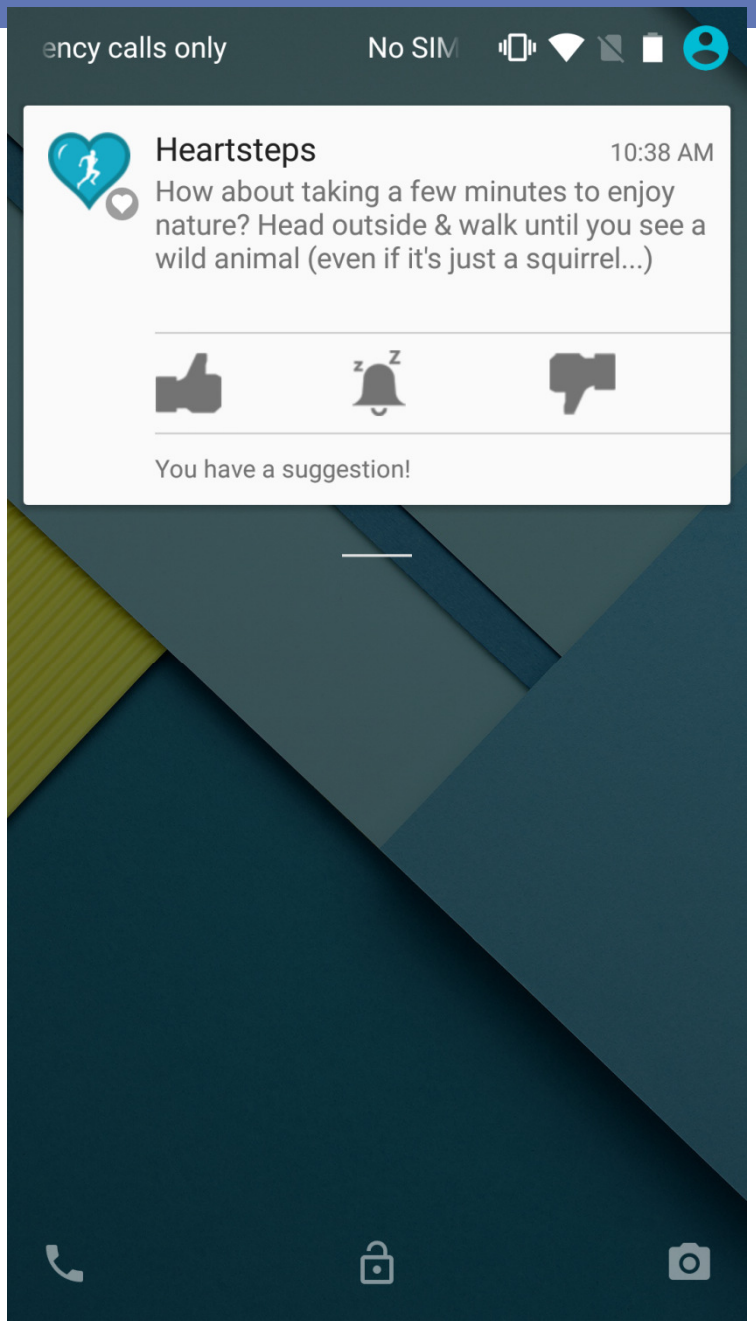
- Feedback on steps
- Daily "what motivates me" message
- Library of previous activity suggestions



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 Suggestions

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

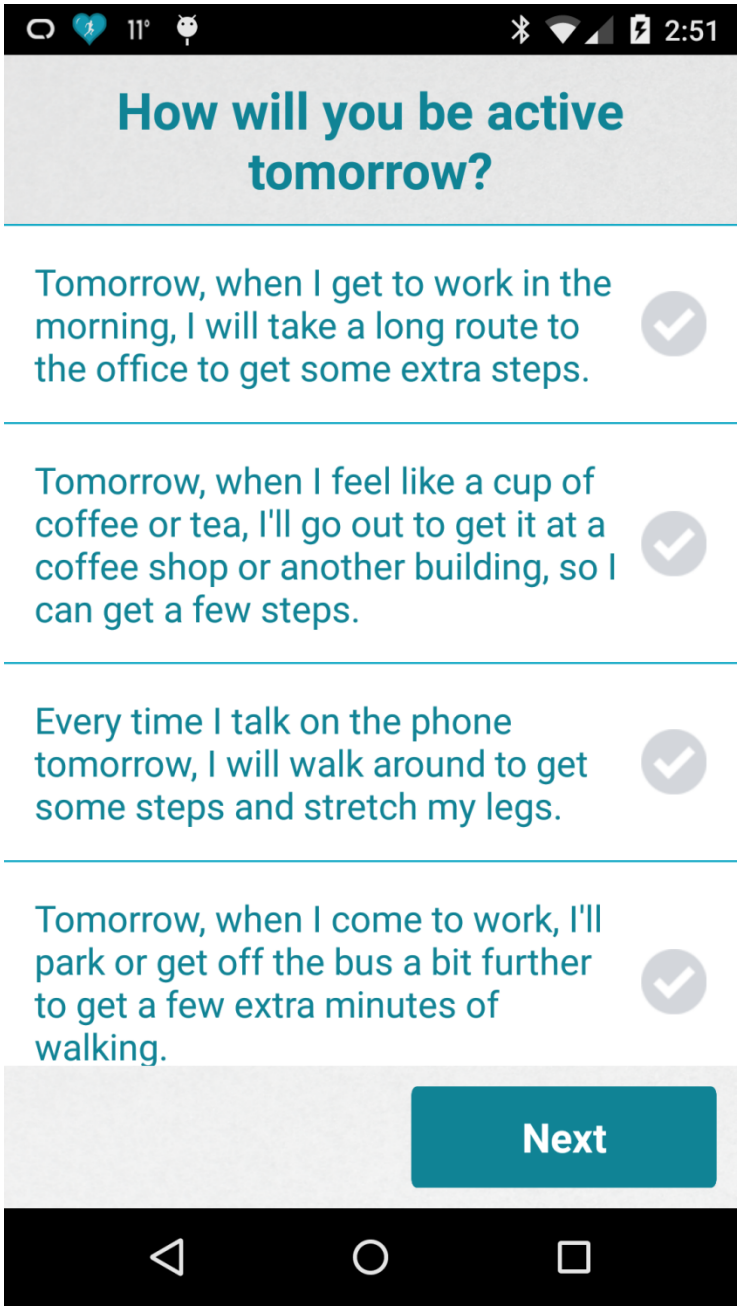
Determine if the suggestions are having direct intended effects (theoretical fidelity)

Ideal outcome

Did the person do suggested activity?

Chosen outcome

Step count in 30 minutes from intervention offering/randomization



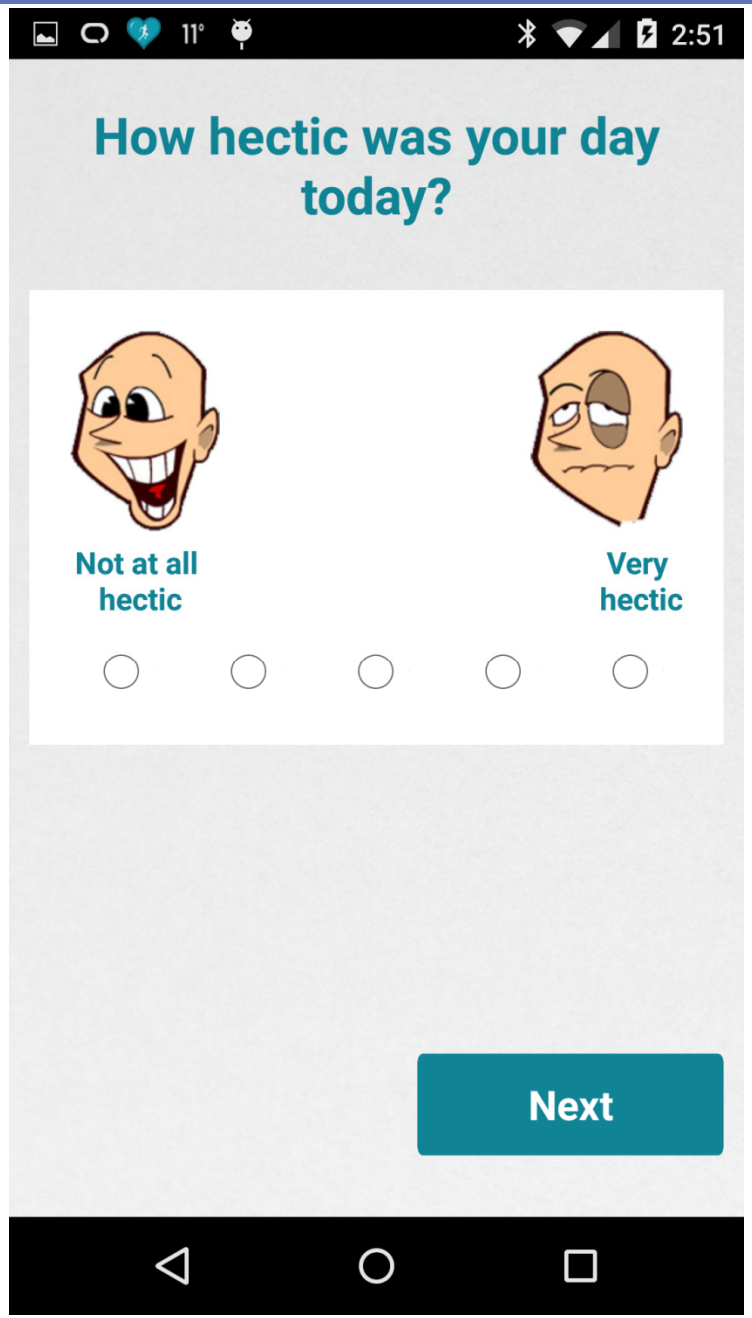
Planning

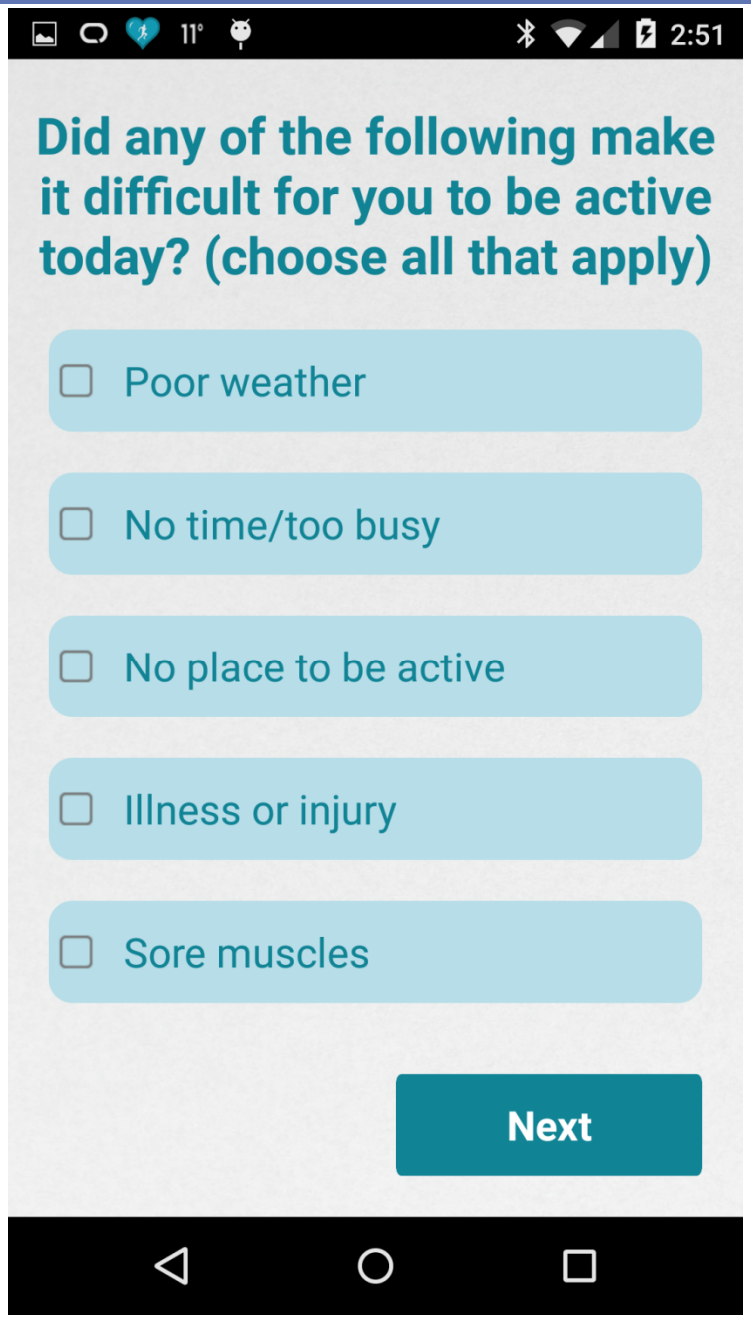
Two types of planning:

- 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


2:51
How hectic was your day today?
Not at all hectic
Very hectic
Next


2:51
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?
- If suggestions have an effect, when should we send 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 change?
- How does context moderate suggestion perceptions?

Pilot Study Methods

- Six-week study with 44 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 proximal effects for each intervention component
- Understand for whom and in what circumstances components have an effect
- Understand how components affect user burden

Augment decision rules in HeartSteps with information (e.g., context, frequency) about when to—and when *not to*—send suggestions

Questions?

Revise your JITAI!

- Behavior & Population?
- Outcomes? -Distal (scientific/clinical goal) & Proximal (guided by mediational theories pinpointing the necessary processes needed to achieve the distal outcome)
- Intervention Options? -Guided by the proximal outcomes
- Tailoring variables? -Guided by theory concerning moderation.
- Decision points? -Guided by the dynamics of the tailoring variable and in-the-moment nature of the effect of the intervention options.
- Decision rules?

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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.

Tailored Activity Suggestion?	Randomization Probability
Yes	$^{2}/_{5}$
No	$^{3}/_{5}$

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

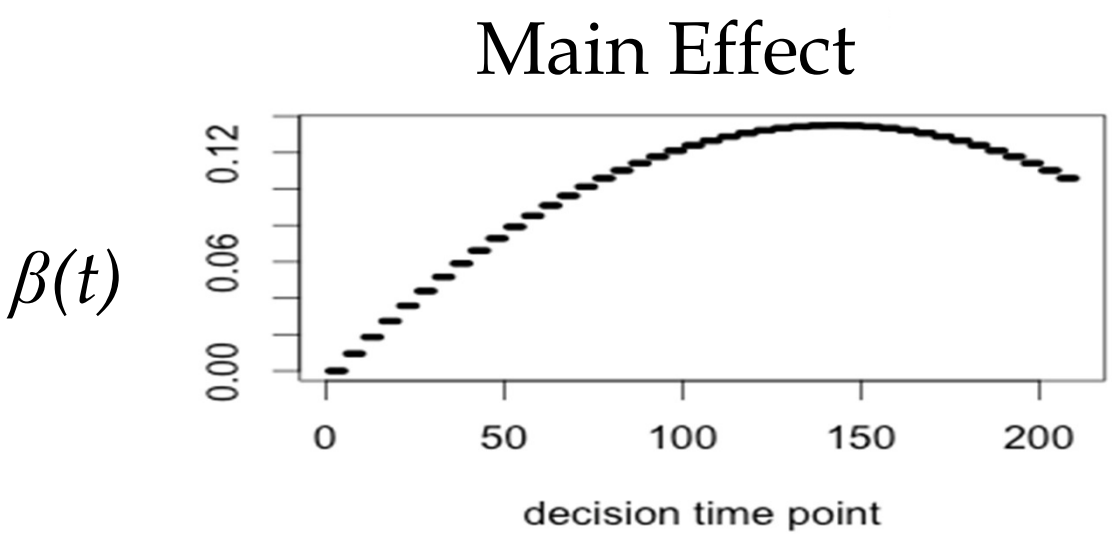
Availability

- 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

Main effect of tailored activity suggestion on proximal step count is likely time-varying –denote by $\beta(t)$, $t=1,\ldots,210$



Sample Size Calculation

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

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

- 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 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 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.

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, α=.05

Standardized Main Effect averaged 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 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?

Beta version of the sample size calculator:
https://pengliao.shinyapps.io/mrt-calculator/

Practice designing a randomized trial!

- What kind of randomized trial fits your scientific questions? (micro-randomized trial?)
- Which intervention options do you want to (micro-) randomize?
- How long should your study last?
- How many decision points are there per day?
- On average, how many intervention options do you want per day?
- What will determine availability in your study?
- What level of availability might you expect?
- What should your randomization probabilities be?
- What might the time-varying main effect look like?

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

APS workshop May 29, 2016

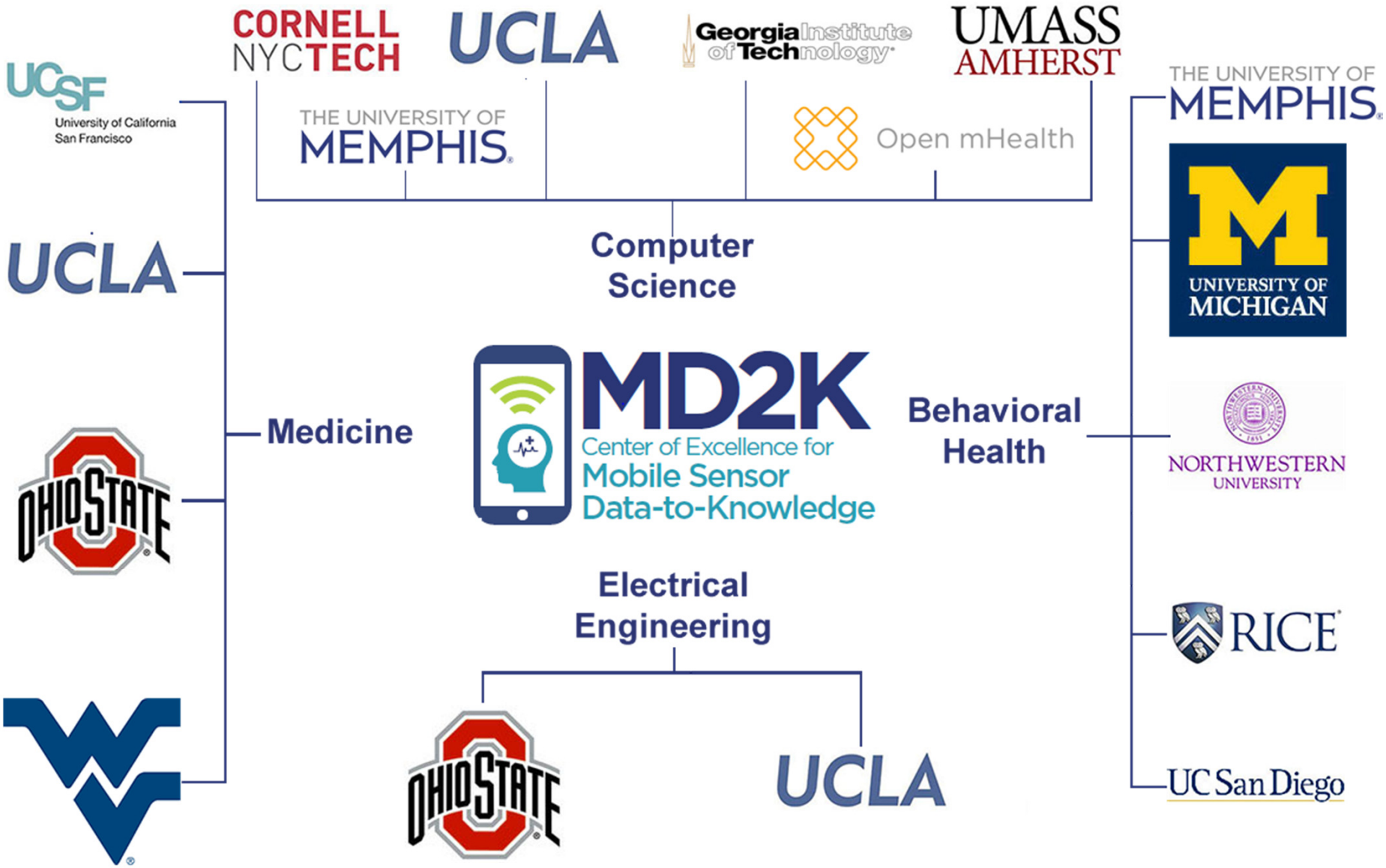
Sense2stop: A JITAI for Addressing States of Vulnerability to Smoking Relapse

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?

Northwestern Medicine®

Bonnie Spring

Kevin Moran

Gwen Ledford

David Conroy

UNIVERSITY OF MICHIGAN

Inbal (Billie) Nahum-Shani

Susan Murphy

UMD DULUTH

Mustafa Al'Absi

RICE

Dave Wetter

THE UNIVERSITY OF MEMPHIS

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?

	No Intervention	Intervention
Not Stressed	**- - -**	**>>>**
Stressed	**- - -**	**>>>**

.

- **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*)

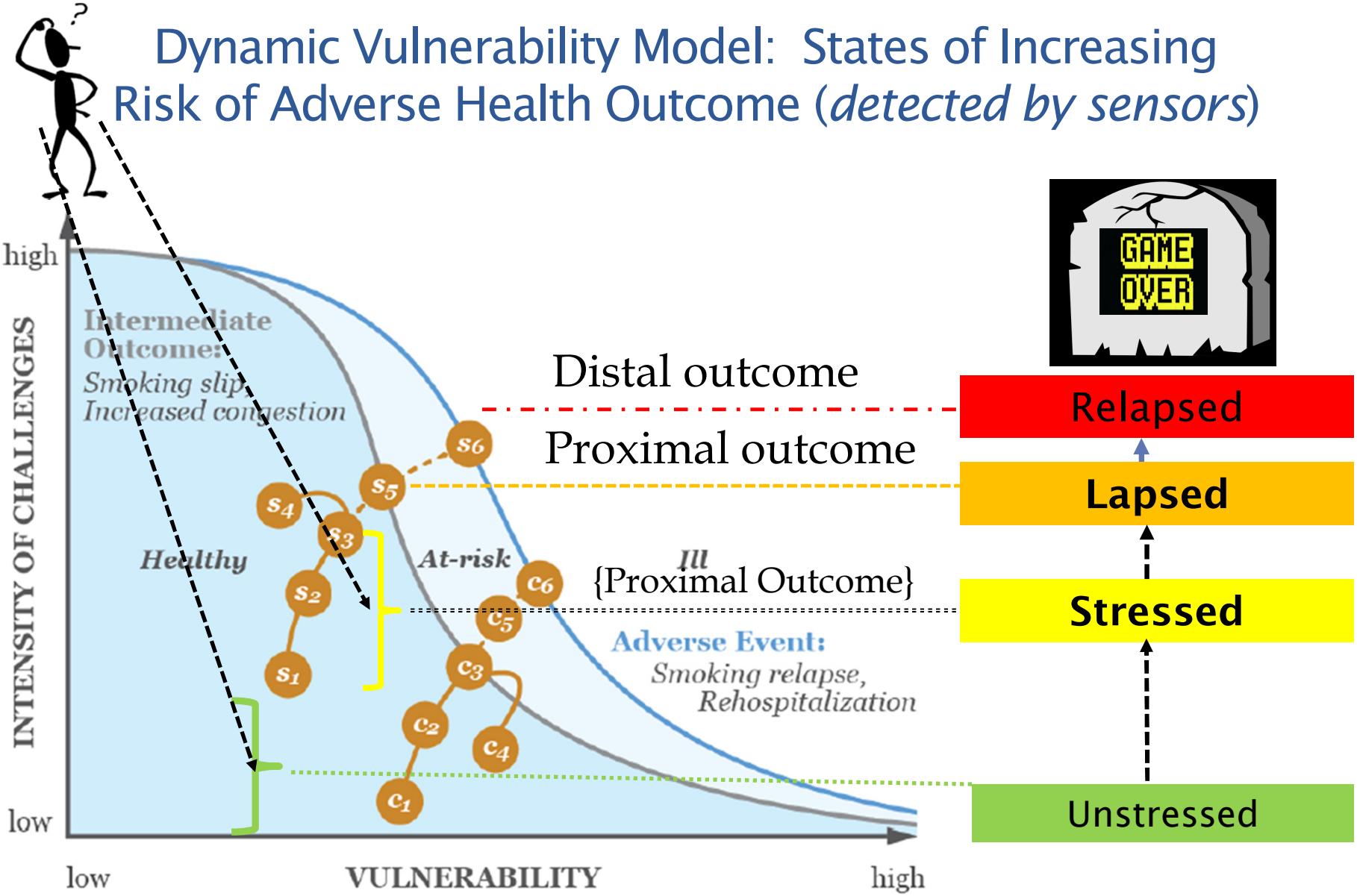


Figure 1: Dynamic Model of Illness Vulnerability

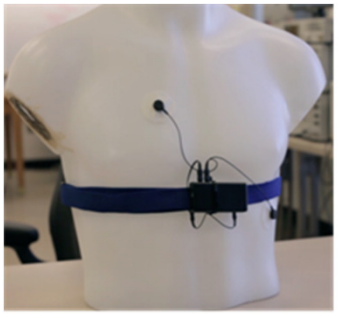
Study Population, Setting, Timeline

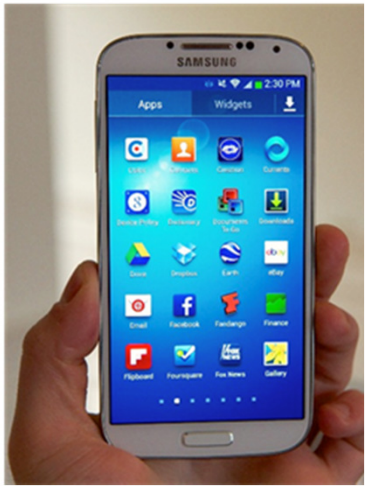
	Day	Smoking Status	Location	Treatment
Observational	1	SMOKING	50% lab / 50% field	In-person Treatment
	2	SMOKING	Field	
	3	TAPERING	50% lab / 50% field	In-person Treatment
Intervention Trial	**4**	**QUIT DAY**	**3 hrs lab + field**	**In-person Treatment**
	5	POST-QUIT	Field	
	6	POST-QUIT	Field	Phone Coaching
	7	POST-QUIT	Field	
	8	POST-QUIT	Field	Phone Coaching
	9	POST-QUIT	Field	
	10	POST-QUIT	Field	
	11	POST-QUIT	Field	
	12	POST-QUIT	Field	
	13	POST-QUIT	Field	
	14	POST-QUIT	Field + 2hrs lab	

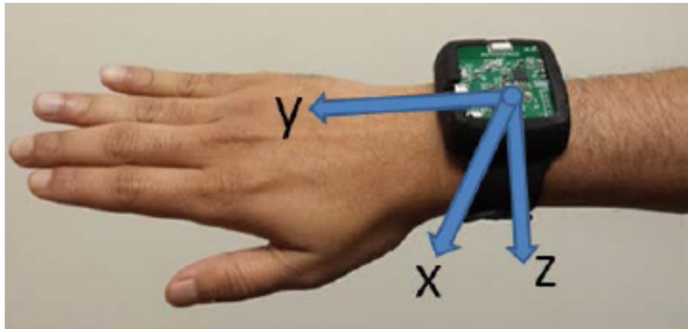
- Chronic smokers, >6 cigs/day
- Trained on equipment, stress apps and relaxation skills
- Helped to quit smoking
- Monitored 4 days pre- and 10 days post-quit
- Intervention (prompt to perform relaxation exercises begins post-quit)

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



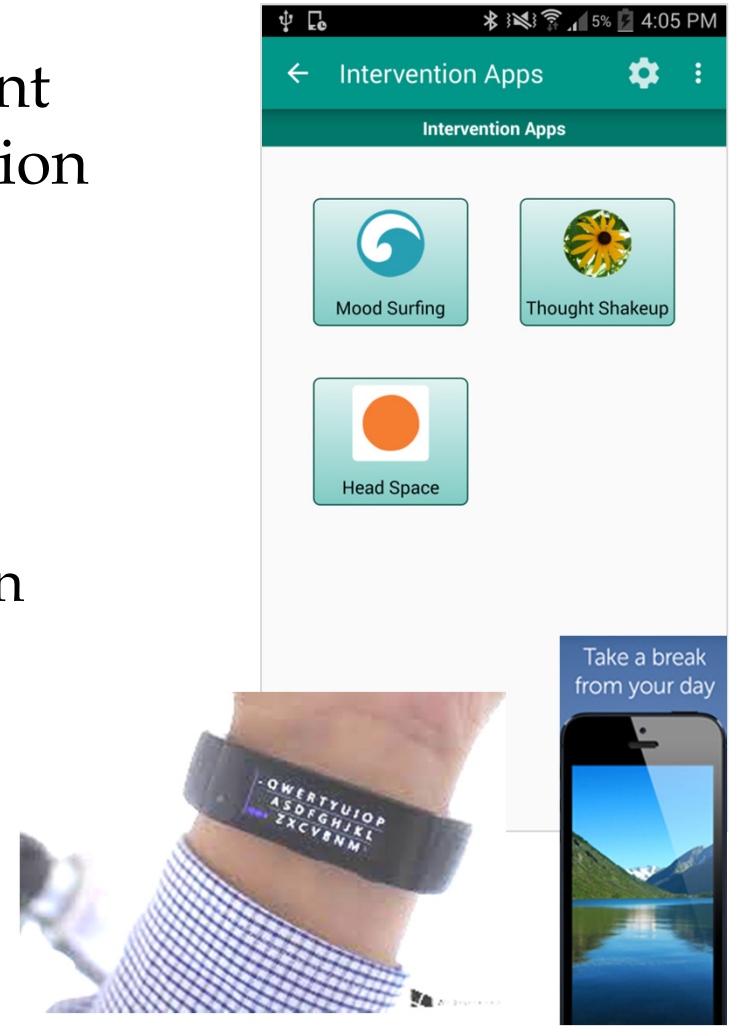




The Sense2Stop Intervention

- 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



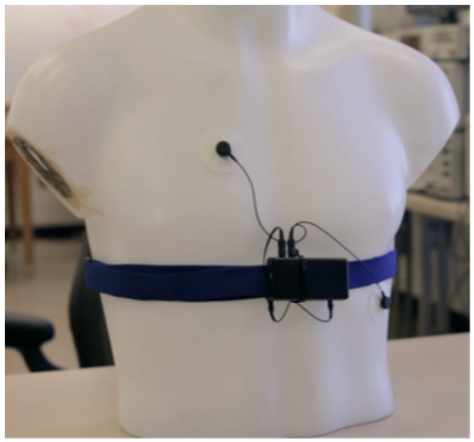
The Micro-Randomization

- 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: s**hould 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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Revise your JITAI and your randomized trial!

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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Sneak Preview by Pedja!

Primary Analyses

$$Y_{t+1} \sim a_0 + a_1 Z_t + \beta_0 (A_t - 0.6)$$

$$Y_{t+1} \sim a_0 + a_1 d(t) + a_2 Z_t + \beta_0 (A_t - 0.6) + \beta_1 d(t)(A_t - 0.6)$$

- A_t: Indicator if suggestion delivered at occasion t
- Y_{t+1}: Log transform of 30-min step count post occasion t
- Z_t: Log transform of 30-min step count prior to occasion t
- $d(t)$: Day in the study for occasion t

Marginal Model Results

$$Y_{t+1} \sim a_0 + a_1 Z_t + \beta_0 (A_t - 0.6)$$

	Estimate	95% LCL	95% UCL	SE	p-value
α_0	1.695	1.461	1.930	0.120	0.000
α_1	0.414	0.356	0.472	0.029	0.000
β_0	0.142	0.013	0.271	0.066	0.030

$\beta_0 \sim 40$ extra steps when a suggestion is delivered vs. not

Time-Trend Model Initial Results

$$Y_{t+1} \sim a_0 + a_1 d(t) + a_2 Z_t + \beta_0 (A_t - 0.6) + \beta_1 d(t)(A_t - 0.6)$$

	Estimate	95% LCL	95% UCL	SE	p-value
α_0	1.694	1.438	1.950	0.131	0.000
α_1	0.000	-0.011	0.012	0.006	0.961
α_2	0.412	0.356	0.469	0.029	0.000
β_0	0.500	0.221	0.778	0.142	0.000
β_1	-0.018	-0.029	-0.006	0.006	0.002

Initially, delivering a suggestion vs. not adds ~ 150 steps but effect gets smaller over time.