Time-Varying Causal Treatment Effects

JOOLHEALTH

BariFit

Susan A Murphy

VE RI TAS HARVARD

MD2K Center of Excellence for Mobile Sensor Data-to-Knowledge

The Methodology Center advancing methods, improving health

Outline

- Introduction to mobile health
- Causal Treatment Effects (aka Causal Excursions)
- (A wonderfully simple) Estimation Method
- HeartSteps

HeartSteps

Context provided via data from:

Wearable band → activity and sleep quality;

Smartphone sensors → busyness of calendar, location, weather;

Self-report → stress, user burden

In which contexts should the smartphone provide the user with a tailored activity suggestion?

Data from wearable devices that sense and provide treatments

- On each individual: $O_1, A_1, Y_2, \ldots, O_t, A_t, Y_{t+1}, \ldots$

- t: Decision point
- O_t: Observations at t^{th} decision point (high dimensional)
- A_t: Treatment at t^{th} decision point (aka: action)
- Y_{t+1}: Proximal outcome (aka: reward, utility, cost)

Structure of Mobile Health Intervention

1) Decision Points: times, t, at which a treatment might be delivered.
    1) Regular intervals in time (e.g. every minute)
    2) At user demand

<u>Heart Steps</u>: approximately every 2-2.5 hours:
pre-morning commute, mid-day, mid-afternoon, evening commute, after dinner

Structure of Mobile Health Intervention

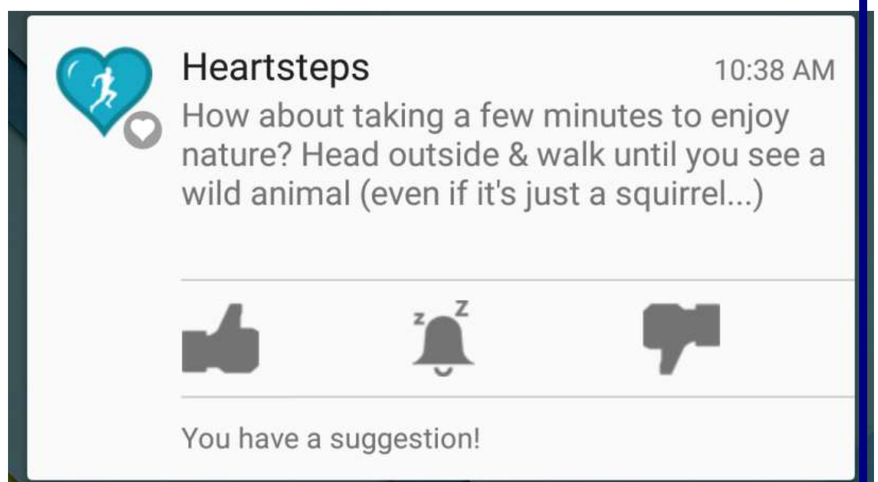
2) Observations O_t
   1) Passively collected (via sensors)
   2) Actively collected (via self-report)

Heart Steps: classifications of activity, location, weather, step count, busyness of calendar, user burden, adherence…….

Structure of Mobile Health Intervention

3) Treatment A_t
   1) Types of treatments/engagement strategies that can be provided at a decision point, t
   2) Whether to provide a treatment

<u>HeartSteps</u>: tailored activity suggestion (yes/no)



Availability

- Treatments, A_t, can only be delivered at a decision point if an individual is *available*.
  - O_t includes I_t=1 if available, I_t=0 if not

- Availability is known pre-decision point, i.e., pretreatment.

- Availability is not the same as adherence!

Structure of Mobile Health Intervention

4) Proximal Outcome Y_{t+1}

Heart Steps: Step count over 30 minutes following decision point, t

Continually Learning Mobile Health Intervention

1) Trial Designs: Are there effects of the actions on the proximal response? *experimental design*

2) Data Analytics for use with trial data: Do effects vary by the user's internal/external context,? Are there delayed effects of the actions? *causal inference*

3) Learning Algorithms for use with trial data: Construct a "warm-start" treatment policy. *batch Reinforcement Learning*

4) Online Algorithms that personalize and continually update the mHealth Intervention. *online Reinforcement Learning*

Micro-Randomized Trial Data

On each of n participants and at each of $t=1,..,T$ decision points:

- O_t observations at decision point t,
  - includes I_t=1 if available, I_t=0 if not
- A_t=1 if treated, A_t=0 if not treated at decision t
  - Randomized, $p_t(H_t) = P[A_t=1 | H_t, I_t=1]$
- Y_{t+1} proximal outcome

$H_t=\{(O_i, A_i, Y_{i+1}), i=1,\ldots,t-1; O_t\}$ denotes data through t

Conceptual Models

Generally data analysts fit a series of increasingly more complex models:

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t$$

and then next,

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t + \beta_1 A_t S_t$$

and so on…

- Y_{t+1} is activity over 30 min. following t
- $A_t = 1$ if activity suggestion and 0 otherwise
- Z_t summaries formed from t and past/present observations
- S_t potential moderator (e.g., current weather is good or not)

Conceptual Models

Generally data analysts fit a series of increasingly more complex models:

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t$$

and then next,

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t + \beta_1 A_t S_t$$

and so on…

$\alpha_1^T Z_t$ is used to reduce the noise variance in Y_{t+1}
(Z_t is sometimes called a vector of control variables)

Causal, Marginal Effects

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t$$

β_0 is the effect, marginal over all observed and all unobserved variables, of the activity suggestion on subsequent activity.

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1^T Z_t + \beta_0 A_t + \beta_1 A_t S_t$$

$\beta_0 + \beta_1$ is the effect when the weather is good (S_t=1), marginal over other observed and all unobserved variables, of the activity suggestion on subsequent activity.

Goal

- Develop data analytic methods that are consistent with the scientific understanding of the meaning of the β coefficients
- Challenges:
  - Time-varying treatment (A_t, $t=1,\ldots T$)
  - "Independent" variables: Z_t, S_t, I_t that may be affected by prior treatment
- Robustly facilitate noise reduction via use of controls, Z_t

Outline

- Introduction to mobile health
- Causal Treatment Effects (aka Causal Excursions)
- (A wonderfully simple) Estimation Method
- HeartSteps

Potential Outcomes

- $\bar{A}_t = \{A_1, A_2, \ldots, A_t\}$ (random treatments),

$\bar{a}_t = \{a_1, a_2, \ldots, a_t\}$ (realizations of treatments)

- $Y_{t+1}(\bar{a}_t)$ is a potential proximal response
- $I_t(\bar{a}_{t-1})$ is a potential "available for treatment" indicator
- $H_t(\bar{a}_{t-1})$ is a potential history vector
  - $S_t(\bar{a}_{t-1})$ is a vector of features of history $H_t(\bar{a}_{t-1})$

Marginal & Causal Effect

Excursion effect at decision point *t*:

$$E[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})]$$

Marginal & Causal Effect

Excursion effect at decision point *t*:

$$E\left[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})\right]$$

- Effect is conditional on availability

Marginal & Causal Effect

Excursion effect at decision point t:

$$E[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0\ ) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})]$$

– Effect is conditional on availability; only concerns the subpopulation of individuals available at decision t

Marginal & Causal Effect

Excursion effect at decision point *t*:

$$E[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0\,) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})]$$

– Effect is conditional on availability; only concerns the subpopulation of individuals available at decision *t*

– Effect is marginal over any $Y_u,\ u \le t,\ A_u, u < t$ not in $S_t(\bar{A}_{t-1})$---over all variables not in $S_t(\bar{A}_{t-1})$.

Marginal & Causal Effect

Excursion effect at decision point t:

$$E[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})]$$

- Effect is conditional on availability; only concerns the subpopulation of individuals available at decision t

- Effect is marginal over any $Y_u,\ u \leq t,\ A_u, u < t$ not in $S_t(\bar{A}_{t-1})$---over all variables not in $S_t(\bar{A}_{t-1})$.

Consistency & Micro-Randomized $A_t \rightarrow$

$$E[Y_{t+1}(\bar{A}_{t-1}, 1) - Y_{t+1}(\bar{A}_{t-1}, 0\ ) \mid I_t(\bar{A}_{t-1}) = 1, S_t(\bar{A}_{t-1})]$$

$$=$$

$$E[\ E[Y_{t+1} | A_t = 1, I_t = 1, H_t] - E[Y_{t+1} | A_t = 0, I_t = 1, H_t] |\ I_t = 1, S_t]$$

$$=$$

$$E\left[\frac{A_t Y_{t+1}}{p_t(H_t)} - \frac{(1 - A_t) Y_{t+1}}{\left(1 - p_t(H_t)\right)} \ | I_t = 1, S_t\right]$$

($p_t(H_t)$ is randomization probability)

Marginal Treatment Effect

Treatment Effect Model:

$$E[\ E[Y_{t+1}|A_t = 1, I_t = 1, H_t] - E[Y_{t+1}|A_t = 0, I_t = 1, H_t] |\ I_t = 1, S_t] = {S_t}^T \beta$$

H_t is participant's data up to and at time t
S_t is a vector of data summaries and time, t, $(S_t \subseteq H_t)$
I_t indicator of availability

We aim to conduct inference about β!

Outline

- Introduction to mobile health
- Causal Treatment Effects (aka Causal Excursions)
- (A wonderfully simple) Estimation Method
- HeartSteps

"Centered and Weighted Least Squares Estimation"

- Simple method for complex data
- Enables unbiased inference for a causal, marginal, treatment effect (the β's)
- Inference for treatment effect is not biased by how we use the controls, Z_t, to reduce the noise variance in Y_{t+1}

https://arxiv.org/abs/1601.00237

Estimation

- Select probabilities: $\tilde{p}_t(s) \in (0,1)$
- Form weights: $W_t = \left(\frac{\tilde{p}_t(S_t)}{p_t(H_t)}\right)^{A_t} \left(\frac{1-\tilde{p}_t(S_t)}{1-p_t(H_t)}\right)^{1-A_t}$
- Center treatment actions: $A_t \to \left(A_t - \tilde{p}_t(S_t)\right)$

- Minimize:

$$E_n\left[\sum_{t=1}^{T}\left(Y_{t+1} - Z_t{}^T\alpha - \left(A_t - \tilde{p}_t(S_t)\right)S_t{}^T\beta\right)^2 I_t W_t\right]$$

- E_n is empirical distribution over individuals.

Minimize

$$E_n\left[\sum_{t=1}^{T}\left(Y_{t+1}-Z_t{}^T\alpha\ -\left(A_t-\tilde{p}_t(S_t)\right)S_t{}^T\beta\right)^2 I_t W_t\right]$$

Good but incorrect intuition:

Weighted least squares with a working independence correlation matrix and a centered treatment indicator, $A_t - \tilde{p}_t(S_t)$ thus using the assumption:

- $E[Y_{t+1}|A_t, I_t = 1, Z_t] = Z_t{}^T\alpha + \left(A_t - \tilde{p}_t(S_t)\right)S_t{}^T\beta$

E_n is expectation with respect to empirical distribution

Minimize

$$E_n\left[\sum_{t=1}^{T}\left(Y_{t+1} - Z_t{}^T\alpha \; - \left(A_t - \tilde{p}_t(S_t)\right)S_t{}^T\beta\right)^2 I_t W_t\right]$$

Good but incorrect intuition:

- $E[Y_{t+1}|A_t, I_t = 1, Z_t] \neq Z_t{}^T\alpha + \left(A_t - \tilde{p}_t(S_t)\right)S_t{}^T\beta$

E_n is expectation with respect to empirical distribution

Minimize

$$E_n\left[\sum_{t=1}^{T}\left(Y_{t+1} - Z_t{}^T\alpha\ - \left(A_t - \tilde{p}_t(S_t)\right)S_t{}^T\beta\right)^2 I_t W_t\right]$$

The Modeling Assumption:

$$E\left[\begin{pmatrix} E[Y_{t+1}|A_t = 1, I_t = 1, H_t] - \\ E[Y_{t+1}|A_t = 0, I_t = 1, H_t] \end{pmatrix} | I_t = 1, S_t\right] = S_t{}^T\beta_0$$

If $\tilde{p}_t$ depends at most on features in S_t, then, under moment conditions, $\hat{\beta}$ is consistent for β_0

Theory

Under moment conditions, $\sqrt{n}\left(\hat{\beta}-\beta_0\right)$ converges to a Normal distribution with mean *0* and var-covar matrix, $\left(\sum_p\right)^{-1}\sum\left(\sum_p\right)^{-1}$

$$\sum_p = \mathrm{E}\left[\sum_{t=1}^{T}\tilde{p}_t(S_t)\left(1-\tilde{p}_t(S_t)\right)I_t S_t {S_t}^T\right]$$

Z_t and S_t are finite dimensional feature vectors.

Gains from Randomization

- Causal inference for a marginal treatment effect
- Inference on treatment effect is robust to working model:

$$E[Y_{t+1} | I_t = 1, H_t] \approx {Z_t}^T \alpha$$

  - $Z_t \subseteq H_t$
  - Contrast to literature on partially linear, single index models and varying coefficient models

Price due to Marginal Estimand

This "LS-like" method can only use a working independence correlation matrix

– Estimating function is biased if off-diagonal elements in working correlation matrix: in general,

$$E\big[\big(Y_{t+1} - {Z_t}^T\alpha - -\big(A_t - \tilde{p}_t(S_t)\big){S_t}^T\beta\big)I_tW_tI_uW_u\sigma_{t,u}Z_u\big] \neq 0$$

if $u \neq t$

Choice of Weights

Choice of $\tilde{p}_t(S_t)$ determines marginalization over time under model misspecification of treatment effect.

Example: $S_t = 1$, $\tilde{p}_t(S_t)$=$\tilde{p}$. Resulting $\hat{\beta}$ is an estimator of

$$\sum_{t=1}^{T} E[I_t]\beta_t \Big/ \sum_{t=1}^{T} E[I_t]$$

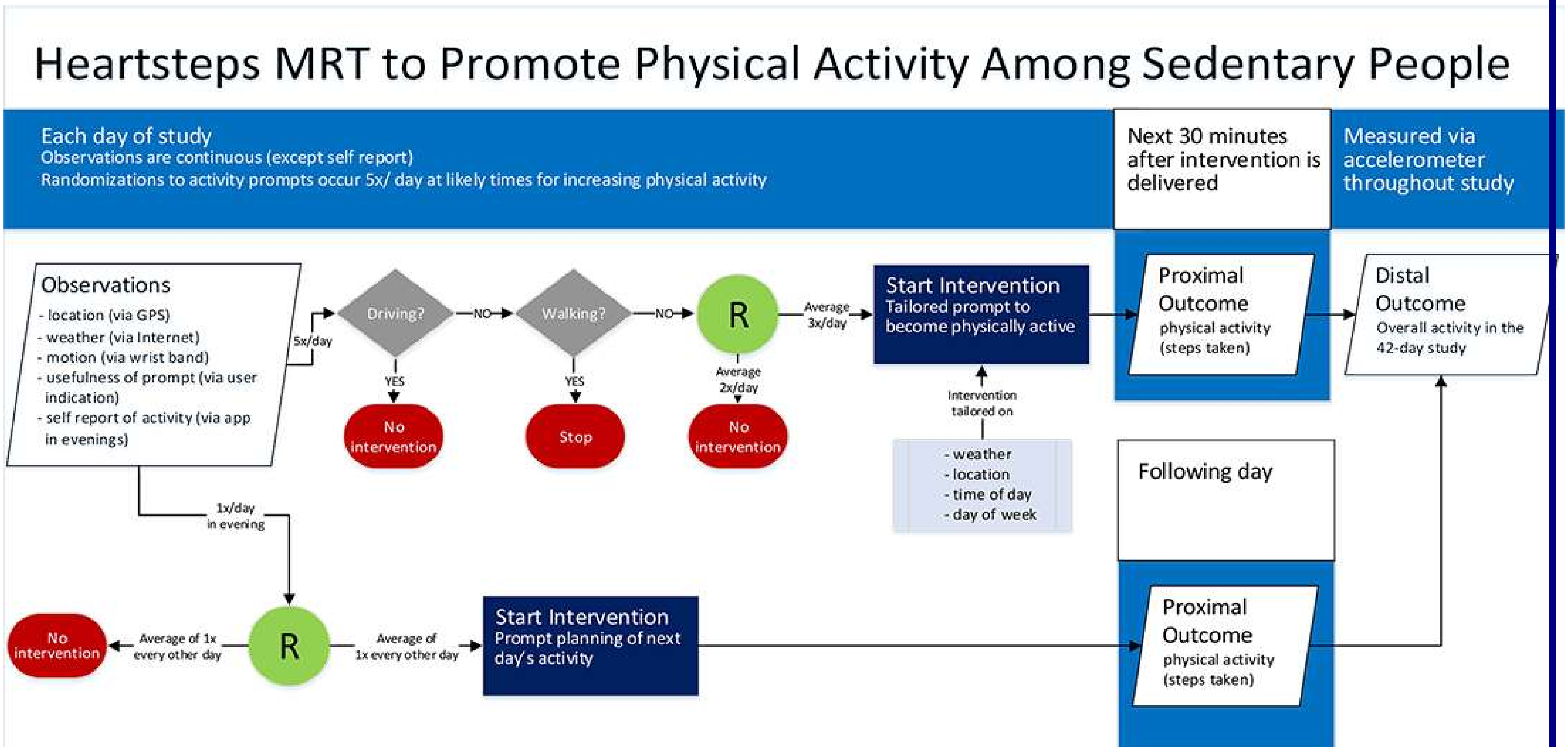
where

$$\beta_t = E[\ E[Y_{t+1}|A_t = 1, I_t = 1, H_t] - E[Y_{t+1}|A_t = 0, I_t = 1, H_t]|\ I_t = 1\ ]$$

Outline

- Introduction to mobile health
- Causal Treatment Effects (aka Causal Excursions)
- (A wonderfully simple) Estimation Method
- HeartSteps

HeartSteps V1



PI: P Klasnja
Location: University of Michigan
Funding: NHLBI/NIA R01HL125440

Heartsteps

On each of $n=37$ participants:

a) Activity suggestion, A_t

- **Provide a suggestion with probability .6**
  - a tailored sedentary-reducing activity suggestion (probability=.3)
  - a tailored walking activity suggestion (probability=.3)
- **Do nothing (probability=.4)**

- 5 times per day * 42 days= 210 decision points

Conceptual Models

$$Y_{t+1} \text{ “}{\sim}\text{” } \alpha_0 + \alpha_1 Z_t + \beta_0 A_t$$

$$Y_{t+1} \text{ “}{\sim}\text{” } \alpha_0 + \alpha_1 Z_t + \alpha_2 d_t + \beta_0 A_t + \beta_1 A_t d_t$$

- $t=1,\ldots T=210$
- Y_{t+1} = log-transformed step count in the 30 minutes *after* the t^{th} decision point,
- $A_t = 1$ if an activity suggestion is delivered at the t^{th} decision point; $A_t = 0$, otherwise,
- Z_t = log-transformed step count in the 30 minutes *prior* to the t^{th} decision point,
- d_t =days in study; takes values in (0,1,….,41)

HeartSteps Analysis

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1 Z_t + \beta_0 A_t \text{, and}$$

$$Y_{t+1} \text{ “}\sim\text{” } \alpha_0 + \alpha_1 Z_t + \alpha_2 d_t + \beta_0 A_t + \beta_1 A_t d_t$$

Causal Effect Term	**Estimate**	**95% CI**	**p-value**
$\beta_0 A_t$ *(effect of an activity suggestion)*	$\hat{\beta}_0$=.13	(-0.01, 0.27)	.06
$\beta_0 A_t + \beta_1 A_t d_t$ *(time trend in effect of an activity suggestion)*	$\hat{\beta}_0$ = .51 $\hat{\beta}_1$ = -.02	(.20, .81) (-.03, -.01)	<.01 <.01

On each of $n=37$ participants:

a) Activity suggestion

- Provide a suggestion with probability .6
  - **a tailored walking activity suggestion (probability=.3)**
  - **a tailored sedentary-reducing activity suggestion (probability=.3)**
- **Do nothing (probability=.4)**

- 5 times per day * 42 days= 210 decision points

HeartSteps Analysis

$$Y_{t+1} \text{ ``}\sim\text{''} \alpha_0 + \alpha_1 Z_t + \beta_0 A_{1t} + \beta_1 A_{2t}$$

- $A_{1t} = 1$ if walking activity suggestion is delivered at the t^{th} decision point; $A_{1t} = 0$, otherwise,
- $A_{2t} = 1$ if sedentary-reducing activity suggestion is delivered at the t^{th} decision point; $A_{2t} = 0$, otherwise,

Causal Effect	Estimate	95% CI	p-value
$\beta_0 A_{1t} + \beta_1 A_{2t}$	$\hat{\beta}_0 = .21$ $\hat{\beta}_1 > 0$	(.04, .39) ns	.02 ns

Initial Conclusions

- The data indicates that there is a causal effect of the activity suggestion on step count in the succeeding 30 minutes.
  - This effect is primarily due to the walking activity suggestions.
  - This effect deteriorates with time
  - The walking activity suggestion initially increases step count over succeeding 30 minutes by approximately 271 steps but by day 20 this increase is only approximately 65 steps.

Discussion

Problematic Analyses

- GLM & GEE analyses
- Random effects models & analyses
- Machine Learning Generalizations:
  - Partially linear, single index models & analysis
  - Varying coefficient models & analysis

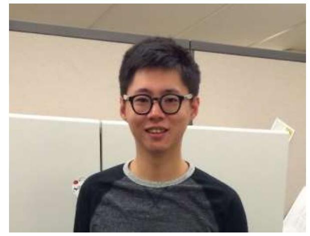
--These analyses do not take advantage of the micro-randomization. Can accidentally eliminate the advantages of randomization for estimating causal effects--

Discussion

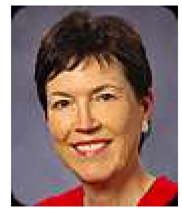
- Randomization enhances:
  - Causal inference based on minimal structural assumptions

- Challenge:
  - How to include random effects which reflect scientific understanding (“person-specific” effects) yet not destroy causal inference?

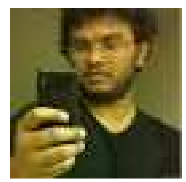
Collaborators!





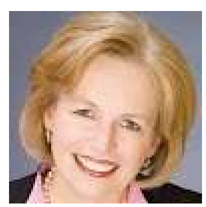




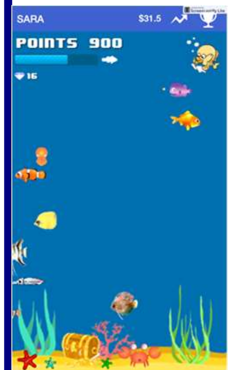






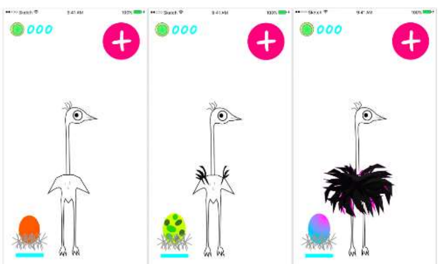

SARA
Substance
Abuse
Research
Assistant

Optimizing mHealth Engagement



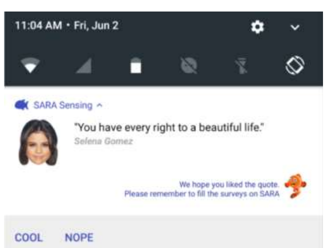
Pull: When you open the app, should the interface provide engagement rewards via a growing aquarium?

- Should the suggested user interface differ by baseline user characteristics?

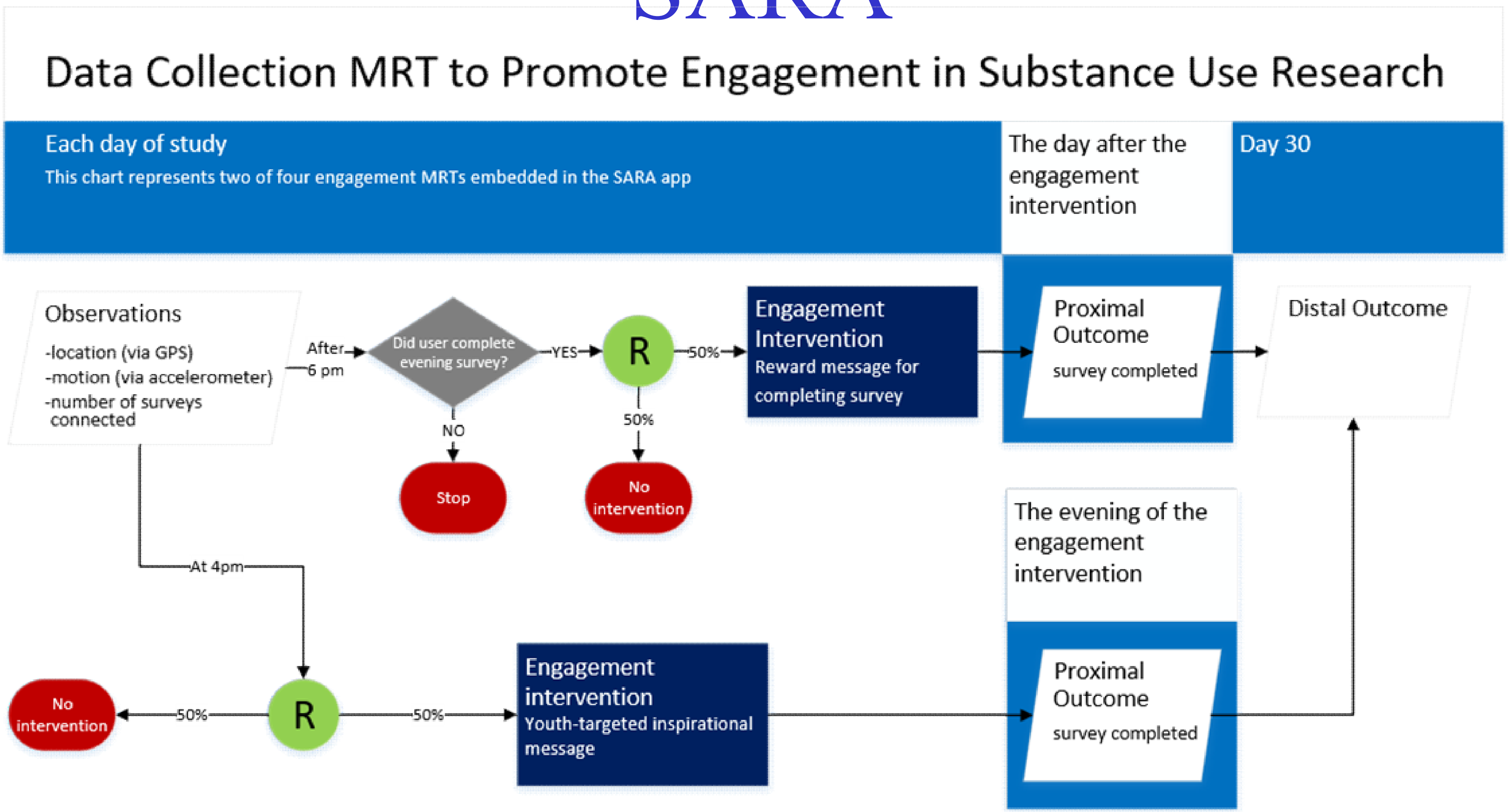


Push: Should the app notify the user to provide an inspirational message?

- Should these messages appear when the user is more or less engaged?

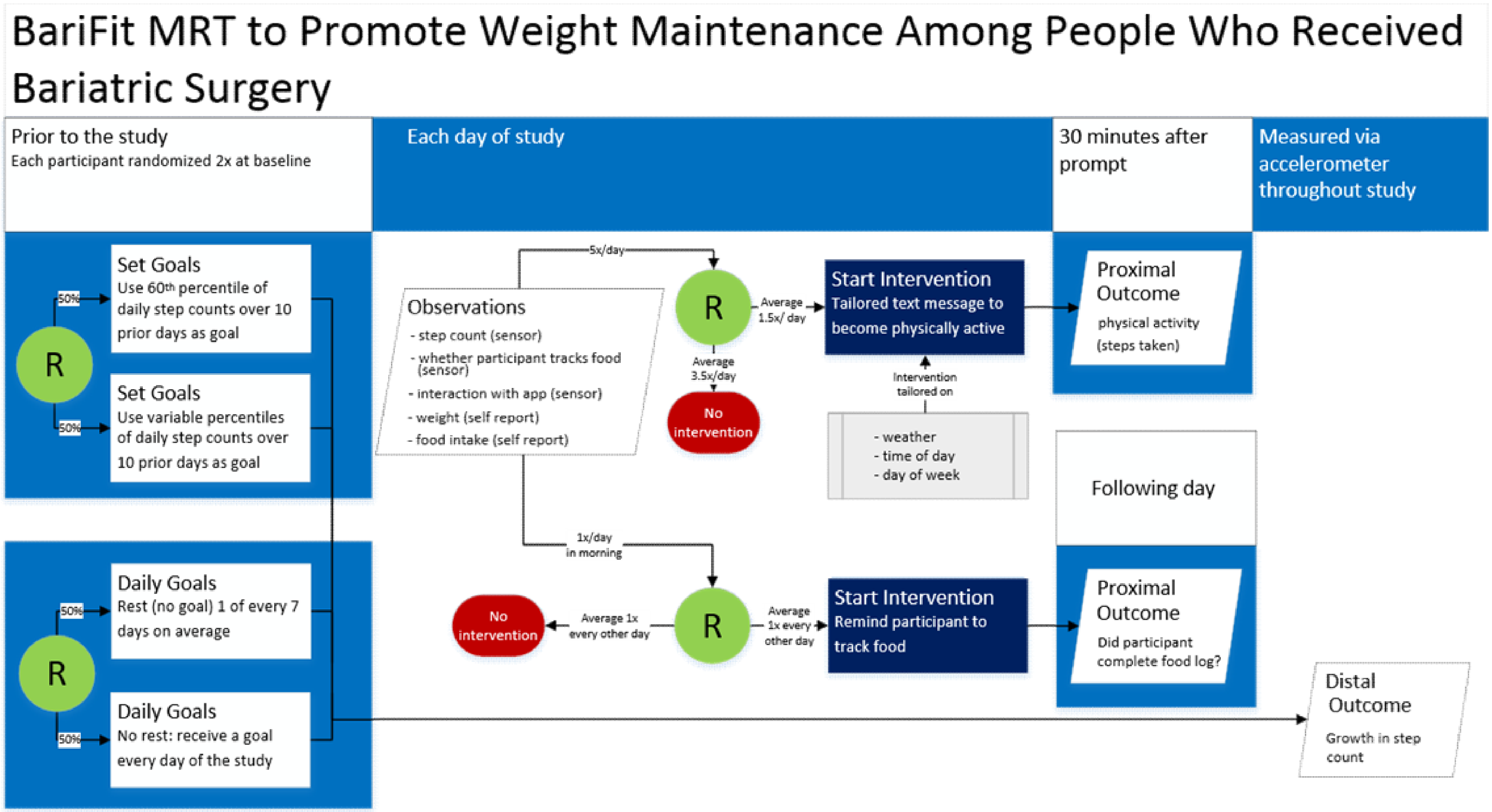


SARA



PIs: M Walton, S Murphy, and M Rabbi Shuvo
Location: University of Michigan
Funding: Michigan Institute for Data Science (PI S. Murphy), University of Michigan Injury Center (PI M. Walton)

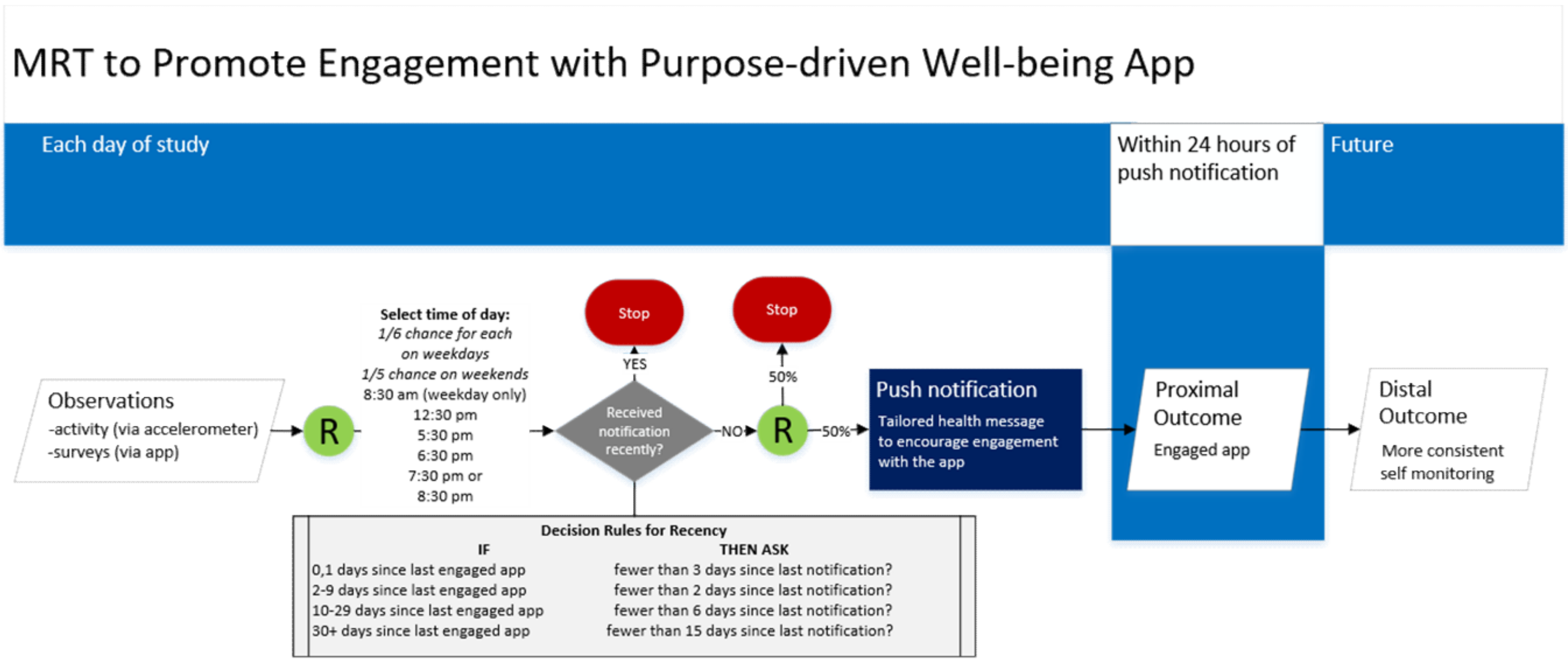
BariFit



PI: P Klasnja

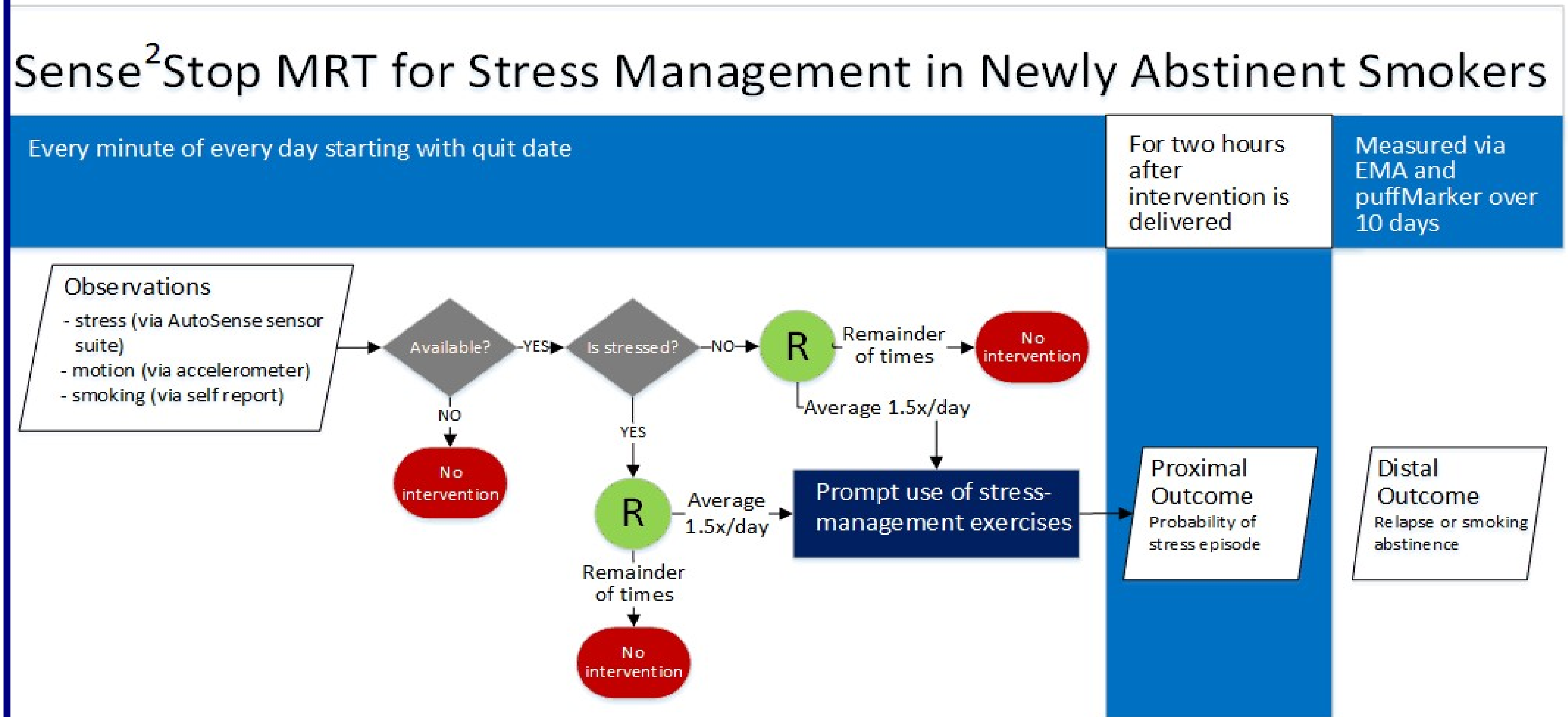
Location & Funding: Kaiser Permanente

Engagement with JOOL



PI: Victor Strecher, PhD, MPH, CEO of JOOL Health
Location & Funding: Ann Arbor, MI
URL: https://www.joolhealth.com

Sense^{2}Stop



PI: S Kumar
Location: Northwestern University, B. Spring, (P.I.)
Funding: NIBIB through funds provided by the trans-NIH Big Data to Knowledge initiative U54EB020404

Experiment to Continually Improve

- "Iterative nature of experimentation" (RA Fisher & G. Box)
- "At Google, experimentation is practically a mantra; we evaluate almost every change that potentially affects what our users' experience." (4 Google scientists)
- "Online experiments are widely used to compare specific design alternatives, but they can also be used to produce generalizable knowledge and inform strategic decision making. Doing so often requires sophisticated experimental designs, iterative refinement, and careful logging and analysis." (3 Facebook scientists)

Minimize

$$E_n\left[\sum_{t=1}^{T}\left(Y_{t+1} - {Z_t}^T\alpha - \left(A_t - \tilde{p}_t(S_t)\right){S_t}^T\beta\right)^2 I_t W_t\right]$$

- Resulting $\hat{\beta}$ is an estimator of

$$\left(E\sum_{t=1}^{T}\tilde{p}_t(S_t)\left(1-\tilde{p}_t(S_t)\right)I_t S_t {S_t}^T\right)^{-1} E\left[\sum_{t=1}^{T}S_t\tilde{p}_t(S_t)\left(1-\tilde{p}_t(S_t)\right)I_t\beta_t(S_t)\right]$$