Using Surrogates in Covariate-adjusted Response-adaptive Randomized Experiments with Delayed Outcomes

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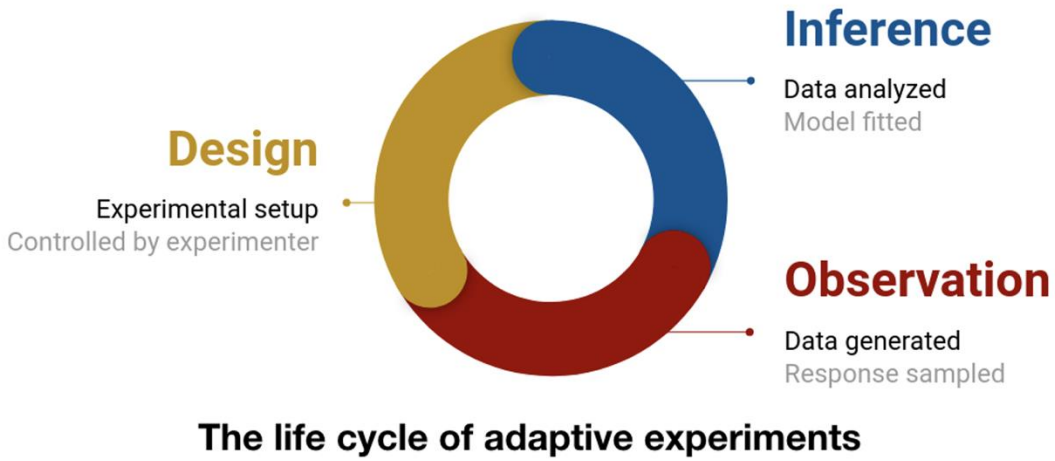
Adaptive experiments with Delay and Surrogates

- **Adaptive experiments:** important randomized experiments in real-world applications
  - Tech world: A/B testing
  - Med or Pharma: Clinical trials

- One big challenge is:
  - primary outcome of interest is usually **delayed** or **censored**
  - only intermediate outcomes (**surrogate**) are observed

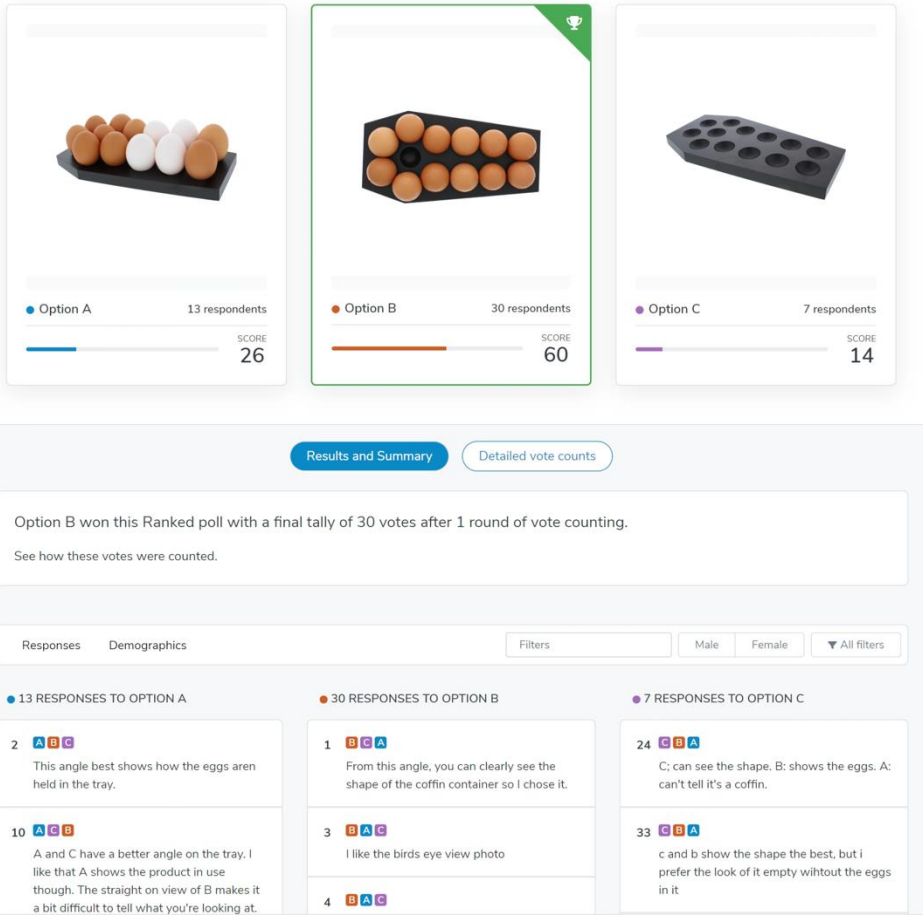


The life cycle of adaptive experiments

Adaptive experiments with Delay and Surrogates

Scenario 1: Advertisement on Amazon

- **Treatment**: different versions of advertisement of an item
- **Goal**: more dollars! (customer purchase)
- **Policy**: adjust Ad traffic every week
- **Delay**: dollars can be delayed
- **Surrogate**: click rate, add to cart, …



Adaptive experiments with Delay and Surrogates

Scenario 2: HIV treatment and cash transfer

- **Treatment**: cash transfer to encourage HIV therapy uptake
- **Goal**: less virus! (HIV viral load)
- **Policy**: adjust Ad traffic every week (dollars can be delayed)
- **Delay**: miss schedule clinical visits
- **Surrogate**: HIV symptom report from phone call check in

Conditional cash transfers can significantly reduce AIDS morbidity and mortality in extremely vulnerable populations and should be considered an essential intervention to achieve AIDS-related sustainable development goals by 2030. Feb 12, 2024

Nature
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Income determines the impact of cash transfers on HIV/AIDS

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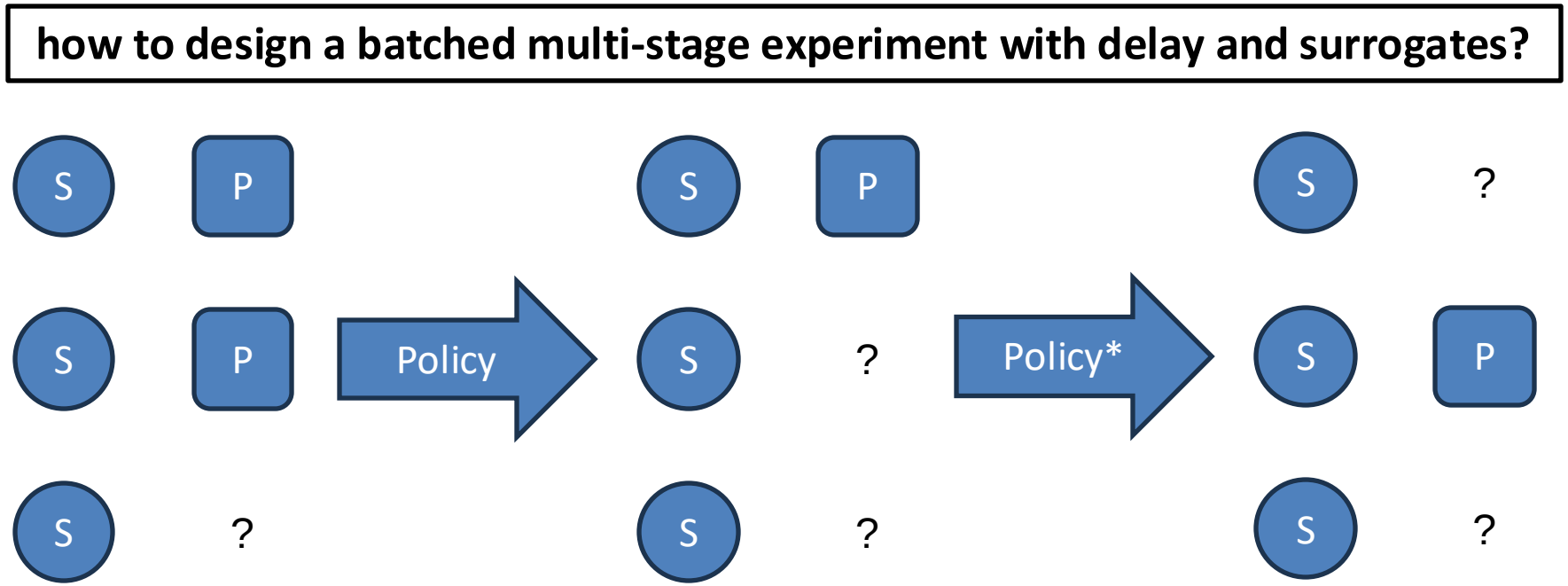
The effects of cash transfer programmes on HIV-related ...

by A Richterman · 2022 · Cited by 22 — By increasing economic well-being, empowerment among women and educational attainment, **cash transfers** may lead to lower-risk sexual behaviours (...

Adaptive experiments with Delay and Surrogates

- The formal question is:



- A trade-off between **long-term goals** vs **short-term decisions**

Adaptive experiments with Delay and Surrogates

- **Experiment structure:**
  - T: stages
  - n_t: number of units in stage t

- **Data structure**: for unit i at stage t
  - X_{it}: covariate information
  - A_{it}: received treatment
  - $(Y_{it}(1), Y_{it}(0), S_{it}(1), S_{it}(0))$: potential outcomes
  - Y_{it}: observed primary outcome
  - S_{it}: observed surrogate outcome
  - D_{it}: delay (0 for no delay, 1 for one stage, …, ∞ for censoring)

Adaptive experiments with Delay and Surrogates

- The goal is

  - to **estimate the average treatment effect (ATE)** at the end of study

$$\tau = \mathbb{E}[Y(1) - Y(0)].$$

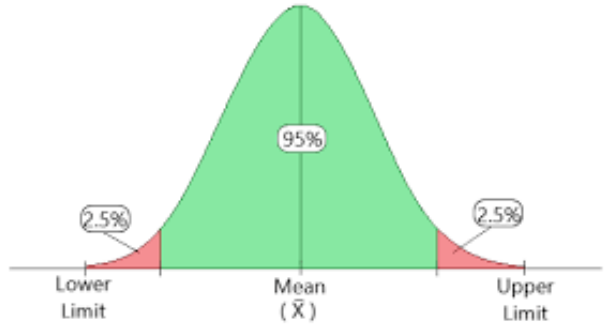
  - to quantify the uncertainty of the estimator given limited sample size (inference)

$$[\hat{\tau} - \delta, \hat{\tau} + \delta]$$

- Adaptive design to achieve optimality

  - **Minimize variance of some estimator!**

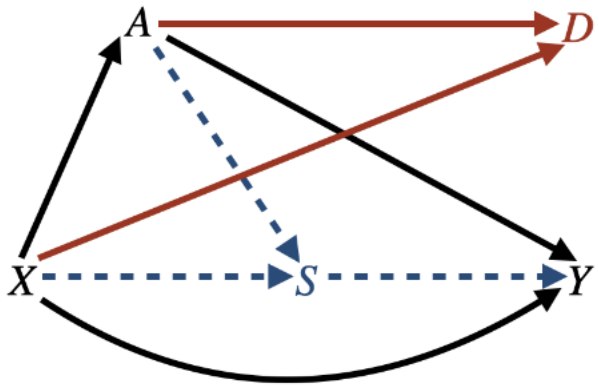
  - Unlike regret minimization in bandit settings



Adaptive experiments with Delay and Surrogates

- Arbitrary delays are very hard problems ☹
  - Delays can be **very heavy tailed**
  - Delays **entangle with surrogates and outcomes**

- Some structural conditions on the delay mechanism:
  - Finite support
  - Explained by covariates (conditionally independent of surrogates and outcome)



High level idea

- What estimator to use?
  - adjust for delay distribution
  - use surrogate for temporary decision
  - small variance

- Best fit: one statistical tool in causal inference
  - **semiparametric bound: minimal variance estimator**

- Two steps for design:
  - **Explore** nuisance parameters
  - **Optimize** traffic

Covariate-based estimation

Surrogate-based estimation

$$\mathbb{V}_{\text{SPEB}} = \mathbb{E}[(\tau(1,X) - \tau(0,X) - \tau)^2] + \mathbb{E}\left[\frac{(\tau(1,X,S) - \tau(1,X))^2}{\sum_{t=1}^{T} r_t e_t(X)} + \frac{(\tau(0,X,S) - \tau(0,X))^2}{\sum_{t=1}^{T} r_t (1 - e_t(X))}\right] + \mathbb{E}\left[\frac{(Y - \tau(1,X,S))^2}{\sum_{t=1}^{T} r_t e_t(X) \rho_1(T-t|X)} + \frac{(Y - \tau(0,X,S))^2}{\sum_{t=1}^{T} r_t (1 - e_t(X)) \rho_0(T-t|X)}\right]$$

Outcome-based estimation

Procedure: Policy Explore Stage

Stage 1 to Stage $D^* + 1$:

- Randomize units. Let God roll the dice!

  - treatment allocation: $\hat{e}_1 = 1/2$

- Collect some units in both treatment and control arms

- Estimate the nuisance terms:
  - Covariate-based part
  - Surrogate-based part
  - Outcome-based part
  - Delay mechanism

Procedure: Policy Optimization Stage

Stage $D^* + 2$ to Stage T:

- Estimate optimal policy: minimize penalized sample variance estimator

$$\min_{e\in[\delta,1-\delta]^T} \left\{ \frac{1}{\sum_{s=1}^{D^*+1} n_s} \sum_{s=1}^{D^*+1} \sum_{i=1}^{n_s} \left\{ \frac{(Y_{is} - \widehat{\tau}^{(t)}(1, X_{is}, S_{is}))^2}{\sum_{t=1}^{T} r_t e_t \cdot \widehat{\rho}_1^{(t)}(T-t|X_{it})} + \frac{(Y_{is} - \widehat{\tau}^{(t)}(0, X_{is}, S_{is}))^2}{\sum_{t=1}^{T} r_t (1-e_t) \cdot \widehat{\rho}_0^{(t)}(T-t|X_{it})} \right.\right. \tag{2}$$
$$\left.\left. + \frac{(\widehat{\tau}^{(t)}(1, X_{is}, S_{is}) - \widehat{\tau}^{(t)}(1, X_{is}))^2}{\sum_{t=1}^{T} r_t e_t} + \frac{\left(\widehat{\tau}^{(t)}(0, X_{is}, S_{is}) - \widehat{\tau}^{(t)}(0, X_{is})\right)^2}{\sum_{t=1}^{T} r_t (1-e_t)} + \lambda_N \|\boldsymbol{e}\|_2^2 \right\} \right\}.$$

- Randomize units with the corrected score to approach optimal score:

$$\widehat{e}_l = \frac{\sum_{s=1}^{T-D^*} n_s \cdot \widetilde{e}_s - \sum_{s=1}^{D^*+1} n_s \cdot \widehat{e}_s}{\sum_{s=D^*+2}^{T-D^*} n_s}, \text{ for } l = D^*+2, \ldots, T-D^*.$$

- At end of stage T, estimate and infer the ATE

Procedure: Inference Stage

Stage $D^* + 2$ to Stage T:

- Estimate optimal policy: minimize penalized sample variance estimator

$$\min_{e\in[\delta,1-\delta]^T} \left\{ \frac{1}{\sum_{s=1}^{D^*+1} n_s} \sum_{s=1}^{D^*+1} \sum_{i=1}^{n_s} \left\{ \frac{(Y_{is} - \widehat{\tau}^{(t)}(1, X_{is}, S_{is}))^2}{\sum_{t=1}^{T} r_t e_t \cdot \widehat{\rho}_1^{(t)}(T-t|X_{it})} + \frac{(Y_{is} - \widehat{\tau}^{(t)}(0, X_{is}, S_{is}))^2}{\sum_{t=1}^{T} r_t (1-e_t) \cdot \widehat{\rho}_0^{(t)}(T-t|X_{it})} \right.\right. \tag{2}$$
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- Collect more units in both treatment and control arms

Theoretical guarantee

Claim 1: Proposed design strategy converges to the optimal design.

Theorem 3 (Convergence of the proposed design strategy). *Let $n_t = r_t N$ with $r_t > 0$, $\sum_t r_t = 1$. Assume the bounded conditional moments hold as in Theorem 2. Assume sufficient enrollment at the first $(T - D^*)$ (non-delayed) stages:*

$$\sum_{t=1}^{T-D^*} r_t \geq \frac{1}{1-\delta} \cdot \frac{\max\left\{\sqrt{\sigma_0^2/\rho_{0,\infty} + \overline{\sigma}_0^2}, \sqrt{\sigma_1^2/\rho_{1,\infty} + \overline{\sigma}_1^2}\right\}}{\sqrt{\sigma_1^2/\rho_{1,\infty} + \overline{\sigma}_1^2} + \sqrt{\sigma_0^2/\rho_{0,\infty} + \overline{\sigma}_0^2}}. \tag{4}$$

Set $\lambda_N = C\sqrt{\log N/N}$. When $N \to \infty$, we have

(a) $\widetilde{\boldsymbol{e}} - \boldsymbol{e}^* = o_p(1)$, *where* $\boldsymbol{e}^* = \lim_{\lambda \to 0} \boldsymbol{e}^*(\lambda)$, *and*

$$\boldsymbol{e}^*(\lambda) = \underset{\boldsymbol{e} \in [\delta, 1-\delta]^T}{\arg\min}\ \mathcal{L}(\boldsymbol{e}) + \lambda \|\boldsymbol{e}\|_2^2.$$

Theoretical guarantee

Claim 2: The final estimator is asymptotically normal and achieves minimal variance.

Theorem 2 (Asymptotic normality). *Assume the delays are conditionally independent of the surrogate and potential outcomes, given covariates and historical data. Assume the following conditions hold:*

1. *Bounded conditional moments:* $\max\{m_4(0,s,x), m_4(1,s,x)\} \leq M_4$, *where*

$$m_4(a,s,x) = \mathbb{E}\left\{|Y(a)|^4 \mid S(a) = s, X = x\right\}, a = 0, 1.$$

2. *Convergent scores: there exists a set of propensity scores* $\mathfrak{e}$, *such that*

$$\max_{t\in[T],x\in\mathcal{X}} |\widehat{e}_t(x) - \mathfrak{e}_t(x)| = o_p(1). \tag{3}$$

Let $n_t = r_t N$ *with* $r_t > 0$, $\sum_t r_t = 1$. *Then when* $N \to \infty$, *we have*

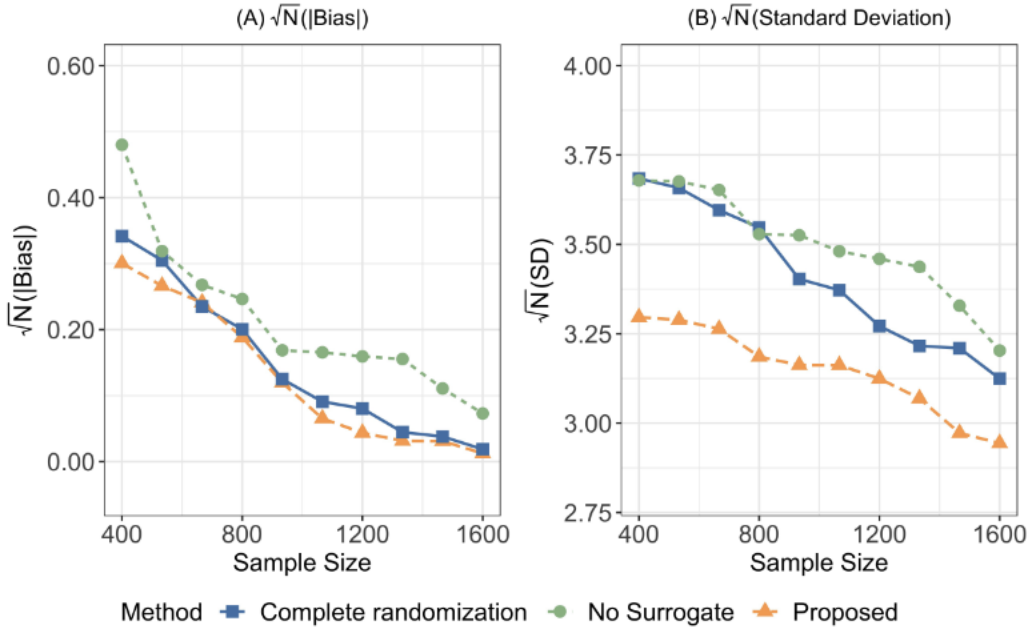
$$\sqrt{N}(\widehat{\tau} - \tau) \to \mathcal{N}(0, \mathbb{V}(\mathfrak{e})).$$

Moreover, the variance estimator satisfies

$$\widehat{\mathbb{V}}(\mathfrak{e}) - \mathbb{V}(\mathfrak{e}) = O_p(\frac{1}{\sqrt{N}}).$$

Synthetic case study: HIV trial

- HIV and cash transfer example
- A randomized experiment in Tanzania
- We generate synthetic data from the experiment (details in paper)
- Compare three design strategies:
    - Complete randomization
    - Do not use surrogates
    - Proposed design
- **Using surrogates and optimization improve estimation inference greatly!**



Thank you!

Questions?