Ranking and Selection with Covariates

Simulation for Personalized Decision Making

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Joint work with L. Jeff Hong and Haihui Shen (CityUHK)

Outline

Introduction

Ranking and Selection

- Classical experimental design problem in statistics and simulation
- Select the best from a finite set of alternatives, whose performances are unknown and can only be learned by *expensive* sampling
- E.g., inventory, drug discovery, portfolio selection (`simopt.org`)

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- **Goal:** use minimal samples to identify the best
  1. Frequentist
  2. Bayesian

Frequentist Approaches

- Specify where to take samples and how many samples to achieve certain statistical guarantee
- Dudewicz and Dalal (1975)
- Rinott (1978)
- Kim and Nelson (2001)
- Hong (2006)
- Frazier (2014)
- Fan et al. (2016)
- etc.

Bayesian Approaches

- Given N sampling opportunities, specify where to take samples sequentially to make the most of them
- Chen et al. (2000)
- Chick and Inoue (2001)
- Frazier et al. (2009)
- Chick and Frazier (2012)
- etc.

Covariates

- A.k.a. side information, auxiliary quantities, or contextual variables
- Personalized decision making emerges (big data and advanced IT)
  - personalized medicine
  - customized advertisements
  - robo-advisors
  - smart building

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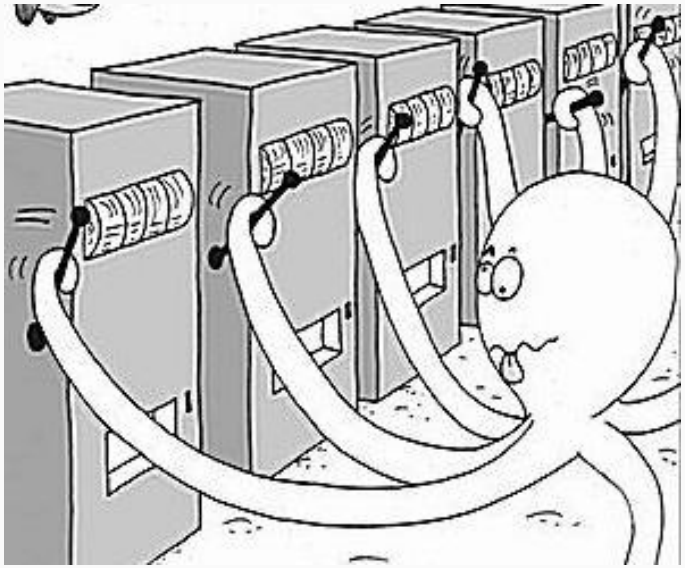
- R&S with covariates is not yet defined
- Our work serves as an attempt to fill in the gap

Related Literature: Multi-armed Bandit Problem

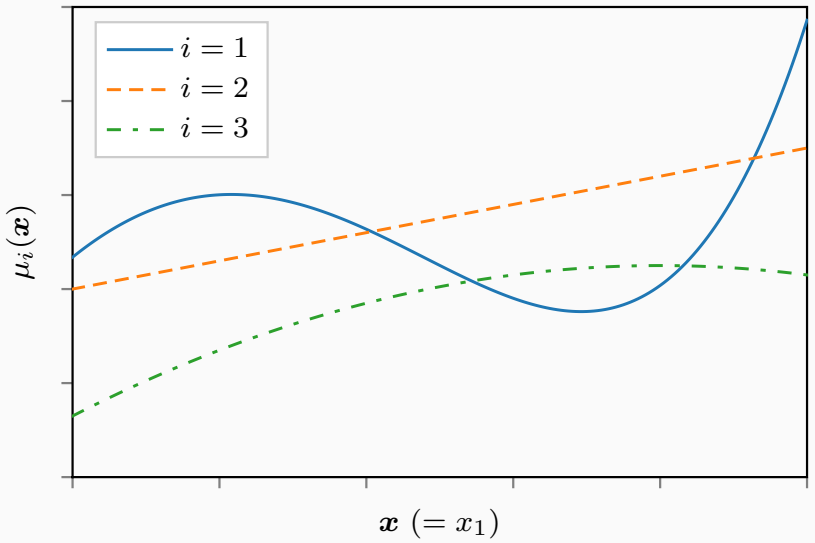


- Classical framework for sequential decision making (Robbins, 1952)
- Minimize “regret”, unlike R&S that identifies the best
- MAB with covariates (contextual bandit)
  - Non-parametric approaches: Rigollet and Zeevi (2010), Perchet and Rigollet (2013), Slivkins (2014), etc.
  - Parametric approaches: Dani et al. (2008), Rusmevichientong and Tsitsiklis (2010), Goldenshluger and Zeevi (2013), etc.

Formulation

Ranking and Selection with Covariates (R&S-C)

- Consider k alternatives with performances $\mu_1(X), \ldots, \mu_k(X)$, where $X = (X_1, \ldots, X_d)^\intercal$ are the covariates



- **Goal:** identify $i^*(x) := \underset{1 \le i \le k}{\arg\max}\{\mu_i(X) | X = x\}$, a decision rule
- The decision rule is computed *offline*, but it can be applied *online* to select the best alternative for the subsequent individuals after observing their covariates

Value of Covariates

- In conventional R&S, the goal is to select the best alternative to be $i^\dagger$, regardless of the realized value of X:

$$i^\dagger := \arg\max_{1 \le i \le k} \{\mathbb{E}[\mu_i(X)]\},$$

  where the expectation is taken with respect to the distribution of X
- By Jensen's inequality,

$$\mathbb{E}[\mu_{i^*(X)}(X)] = \mathbb{E}\left[\max_{1 \le i \le k} \mu_i(X)\right] \ge \max_{1 \le i \le k} \mathbb{E}[\mu_i(X)] = \mathbb{E}[\mu_{i^\dagger}(X)]$$

- The use of covariates guarantees that the selected alternative has a better performance

Probability of Correct Selection (PCS)

- Let $\widehat{i^*}(\boldsymbol{x})$ denote the decision rule derived by a selection procedure
- Indifference zone (IZ): for a prespecified IZ parameter $\delta > 0$,

$$\left\{ \mu_{i^*(\boldsymbol{x})}(\boldsymbol{x}) - \mu_{\widehat{i^*}(\boldsymbol{x})}(\boldsymbol{x}) < \delta \right\}$$

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- Conditional PCS: given $X = x$,

$$\mathrm{PCS}(x) := \mathbb{P}\left(\mu_{i^*(x)}(x) - \mu_{\widehat{i^*}(x)}(x) < \delta \right),$$

  where the probability is taken w.r.t. the distribution of the samples that are used to derive $\widehat{i^*}(x)$
- Unconditional PCS: $\mathrm{PCS}_{\mathrm{E}} := \mathbb{E}\left[\mathrm{PCS}(X)\right]$

- **Goal:** design a selection procedure so that $\mathrm{PCS}_{\mathrm{E}} \geq 95\%$
  - The probability that a random individual from will select her personalized best decision is at least 95%

Linear Model

- Let $Y_i(\boldsymbol{x})$ denote the random performance of alternative i at $\boldsymbol{x}$

Assumption (A1)

For each $i = 1, \cdots, k$, conditionally on $\boldsymbol{X} = \boldsymbol{x}$,

$$\mu_i(\boldsymbol{x}) = \boldsymbol{x}^\intercal \boldsymbol{\beta}_i,$$
$$Y_i(\boldsymbol{x}) = \mu_i(\boldsymbol{x}) + \epsilon_i,$$

where $\boldsymbol{\beta}_i = (\beta_{i1}, \cdots, \beta_{id})^\intercal \in \mathbb{R}^d$ is a vector of unknown parameters, and ϵ_i follows the normal distribution with mean 0 and variance σ_i^2.

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- Set $X_1 \equiv 1$ to include the intercept term
- Use basis functions of the covariates to handle nonlinearity
- Learning $\mu_i(\boldsymbol{x})$ is equivalent to estimating $\boldsymbol{\beta}_i$
  - Use ordinary least squares (OLS) to estimate $\boldsymbol{\beta}_i$

Fixed Design

- Need to decide where to take samples and how many of them
  - Offline computation
  - Samples do not arrive randomly

- Choose and fix m design points $\boldsymbol{x}_1, \cdots, \boldsymbol{x}_m$, with $m \geq d$
  - Eliminate the randomness in choosing design points
  - Simplify the analysis

- Fixed design is suitable if the samples are generated from a simulation model, but may not be suitable for some real experiments
- Placement of the design points is very important

A Statistical Issue

- Many R&S procedures have two stages: Dudewicz and Dalal (1975), Rinott (1978), Chen et al. (1997), Kim and Nelson (2001), Hong (2006)
- The first stage estimates the variances of all alternatives to determine the remaining sample sizes in the second stage

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What is the distribution of the overall sample mean?

Stein (1945)

if $Y_1, Y_2, \ldots$ are i.i.d. normal and N depends on the first-stage samples only through the sample variance, then $\overline{Y}(N)$ is still normal conditionally on the first-stage sample variance

Extended Stein's Lemma

- In R&S-C, the estimate $\widehat{\beta}_i$ plays a role similar to the sample mean in R&S

Lemma

Let $Y = \mathcal{X}\beta + \epsilon$, where $\beta \in \mathbb{R}^d$, $\mathcal{X} \in \mathbb{R}^{m \times d}$, and $\epsilon \sim \mathcal{N}(0, \sigma^2 \mathcal{I})$. Assume that $\mathcal{X}^\intercal \mathcal{X}$ is nonsingular. Let T be a random variable independent of $\sum_{\ell=1}^{n} Y_\ell$ and of $\{Y_\ell : \ell \geq n+1\}$, where $Y_1, Y_2, \ldots$ are independent samples of Y. Suppose that $N \geq n$ is an integer-valued function of T and no other random variables. Let $\widehat{\beta} = N^{-1}(\mathcal{X}^\intercal \mathcal{X})^{-1} \mathcal{X}^\intercal \sum_{\ell=1}^{N} Y_\ell$. Then, for any $x \in \mathbb{R}^d$,

1. $x^\intercal \widehat{\beta} \big| T \sim \mathcal{N}\left(x^\intercal \beta, \frac{\sigma^2}{N} x^\intercal (\mathcal{X}^\intercal \mathcal{X})^{-1} x\right)$;
2. $\dfrac{\sqrt{N}(x^\intercal \widehat{\beta} - x^\intercal \beta)}{\sigma \sqrt{x^\intercal (\mathcal{X}^\intercal \mathcal{X})^{-1} x}}$ *is independent of T and has the standard normal distribution.*

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- Later, T is the OLS estimator of σ^2 based on the first-stage sample
- $(nm - d)T/\sigma^2$ follows the chi-squared distribution and it is independent of $\sum_{\ell=1}^{n} Y_\ell$ and of $\{Y_\ell : \ell \geq n+1\}$

Selection Procedures

Two-Stage (TS) Procedure

Step 0. Specify the target $\mathrm{PCS}_{\mathrm{E}}$ $1-\alpha$, the IZ parameter $\delta > 0$, the first-stage sample size $n_0 \geq 2$, the number of design points $m \geq d$, and the design matrix $\mathcal{X}$ with a nonsingular $\mathcal{X}^\intercal\mathcal{X}$. Solve the following equation

$$\mathbb{E}\left\{\int_0^\infty \left[\int_0^\infty \Phi\left(\frac{h}{\sqrt{(n_0 m - d)(t^{-1}+s^{-1})\boldsymbol{X}^\intercal(\mathcal{X}^\intercal\mathcal{X})^{-1}\boldsymbol{X}}}\right)\eta(s)\mathrm{d}s\right]^{k-1}\eta(t)\mathrm{d}t\right\} = 1-\alpha$$

for h, where $\Phi(\cdot)$ is the standard normal cdf, $\eta(\cdot)$ is the pdf of the chi-squared distribution with $(n_0 m - d)$ degrees of freedom, and the expectation is taken with respect to the distribution of $\boldsymbol{X}$.

Step 1. For all $i = 1, \cdots, k$, take n_0 batches of observations on $\mathcal{X}$: $\boldsymbol{Y}_{i\ell} = (Y_{i\ell}(\boldsymbol{x}_1), \cdots, Y_{i\ell}(\boldsymbol{x}_m))^\intercal, \ell = 1, \cdots, n_0$. Let

$$\widehat{\boldsymbol{\beta}}_i(n_0) = \frac{1}{n_0}(\mathcal{X}^\intercal\mathcal{X})^{-1}\mathcal{X}^\intercal \sum_{\ell=1}^{n_0} \boldsymbol{Y}_{i\ell},$$

$$S_i^2 = \frac{1}{n_0 m - 1 - d} \sum_{\ell=1}^{n_0} (\boldsymbol{Y}_{i\ell} - \mathcal{X}\widehat{\boldsymbol{\beta}}_i(n_0))^\intercal (\boldsymbol{Y}_{i\ell} - \mathcal{X}\widehat{\boldsymbol{\beta}}_i(n_0)).$$

Furthermore, let $N_i = \max\left\{\left\lceil \frac{h^2 S_i^2}{\delta^2} \right\rceil, n_0\right\}$.

Step 2. For all $i = 1, \cdots, k$, take $N_i - n_0$ batches of observations on $\mathcal{X}$ and denote them as $\boldsymbol{Y}_{i,n_0+1}, \cdots, \boldsymbol{Y}_{iN_i}$. Let $\widehat{\boldsymbol{\beta}}_i = \frac{1}{N_i}(\mathcal{X}^\intercal\mathcal{X})^{-1}\mathcal{X}^\intercal \sum_{\ell=1}^{N_i} \boldsymbol{Y}_{i\ell}$. Then, the selected alternative conditioning on $\boldsymbol{X}$ is given by

$$\widehat{i^*}(\boldsymbol{x}) = \underset{1\le i\le k}{\arg\max}\left\{\boldsymbol{x}^\intercal \widehat{\boldsymbol{\beta}}_i\right\}.$$

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Theorem (Shen, Hong, and Zhang 2018)

Procedure TS ensures that $\text{PCS}_\text{E} \ge 1 - \alpha$ under Assumption A1.

Heteroscedastic Errors

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where $\boldsymbol{\beta}_i = (\beta_{i1}, \cdots, \beta_{id})^\intercal \in \mathbb{R}^d$ is a vector of unknown parameters, and $\epsilon_i(\boldsymbol{x})$ follows the normal distribution with mean 0 and variance $\sigma_i^2(\boldsymbol{x})$.

Procedure TS$^+$

- Has a structure similar to Procedure TS
- Allows different design points to have different sample sizes
- The constant h is computed in a different way

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- If Procedure TS is used in the presence of heteroscedastic errors, it may fail to deliver the desired PCS_E guarantee.
- Procedure TS$^+$ may behave in an overly conservative manner in the presence of homoscedastic error.

Least Favorable Configuration

- The hardest mean configuration of alternatives for a selection procedure
- *Slippage configuration* for R&S: there exists a unique best alternative and all the other alternatives have equal means which differ from the best by exactly the IZ parameter

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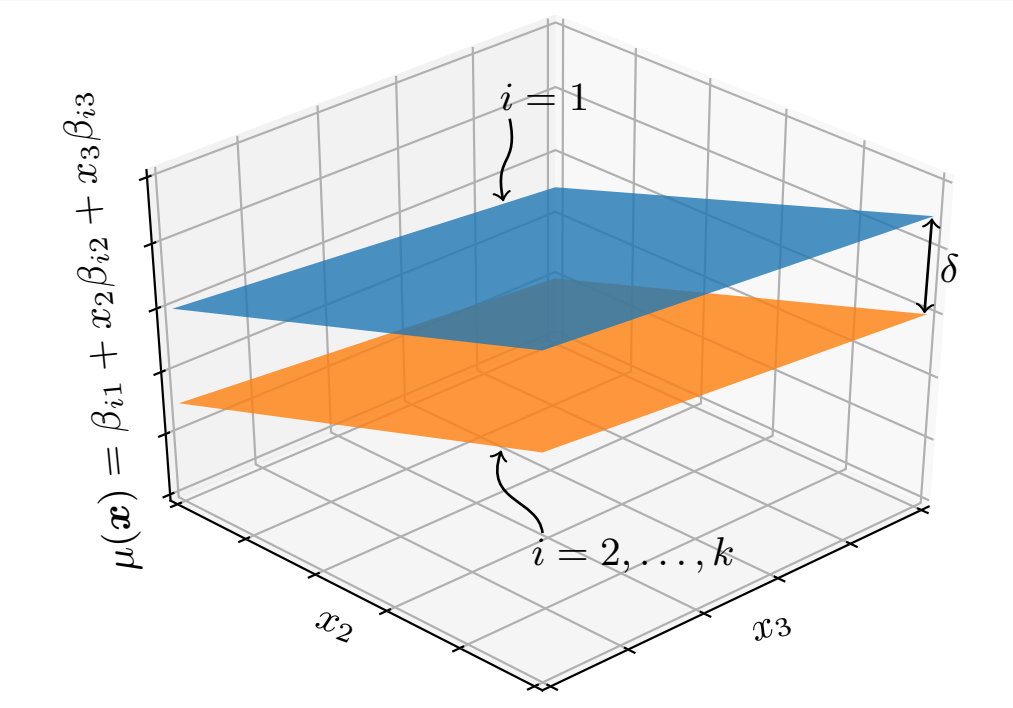
- The hardest mean configuration of alternatives for a selection procedure
- *Slippage configuration* for R&S: there exists a unique best alternative and all the other alternatives have equal means which differ from the best by exactly the IZ parameter
- Generalized slippage configuration (GSC):

$$\mu_1(\boldsymbol{x}) - \mu_i(\boldsymbol{x}) = \delta, \quad \text{for all } \boldsymbol{x} \in \Theta \text{ and for all } i = 2, \ldots, k.$$



Numerical Experiments

Setup

- Covariates $X_1, \cdots, X_d$, are i.i.d. Unif$[0, 1]$
- $m = 2^d$ design points: $\mathcal{X} = \{0, 0.5\} \times \cdots \times \{0, 0.5\}$
- Benchmark case (0):
  - $d = 3$ and $k = 5$
  - Mean configuration: GSC, $\beta_{10} - \delta = \beta_{i0} = 0,\ \beta_{1j} = \beta_{ij} = 1$
  - Homoscedastic errors: $\sigma_i^2(\boldsymbol{x}) \equiv \sigma_i^2$
  - Equal variances among alternatives: $\sigma_1 = \cdots = \sigma_k = 10$
- Comparing cases:
  (1) $k = 2$
  (2) $k = 8$
  (3) Mean configuration: generate components of $\boldsymbol{\beta}_i$ randomly from Unif$[0, 5]$
  (4) Increasing variances: $\sigma_1 = 5$, $\sigma_2 = 7.5$, $\sigma_3 = 10$, $\sigma_4 = 12.5$, $\sigma_5 = 15$
  (5) Decreasing variances
  (6) Heteroscedastic errors: $\sigma_i^2(\boldsymbol{x}) = 100(\boldsymbol{x}^\intercal \boldsymbol{\beta}_i)^2$
  (7) $d = 1$
  (8) $d = 5$
  (9) Covariates have (truncated) multivariate normal distribution

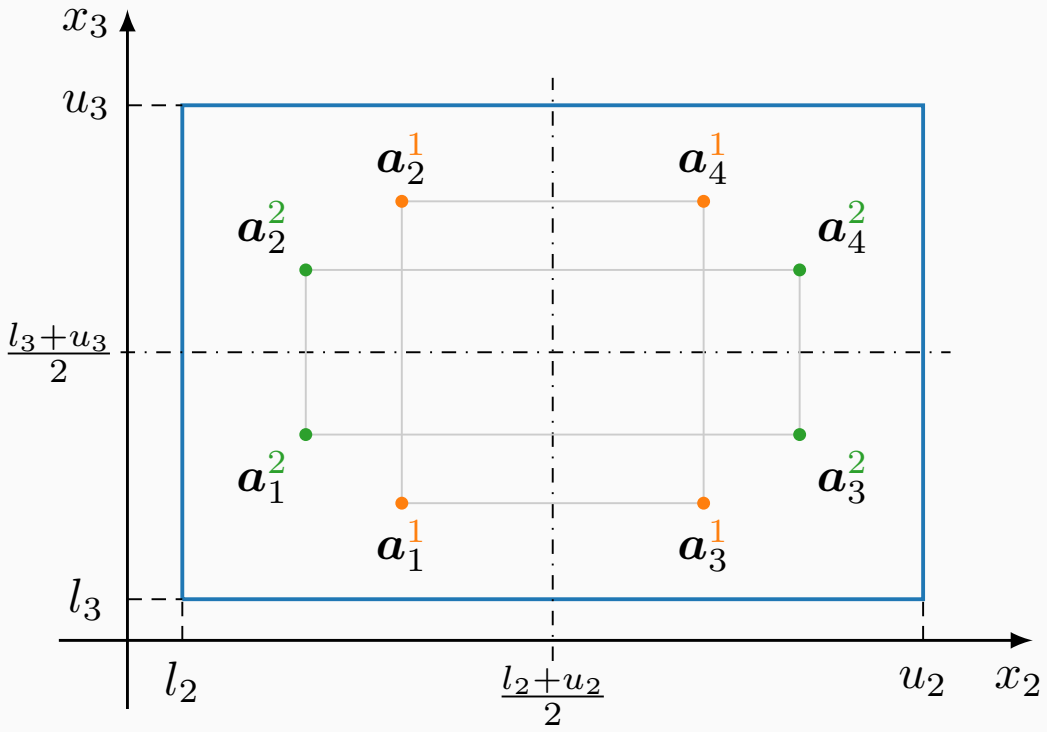
Numerical Results

- PCS_{E} is designed to be 95% (i.e., $\alpha = 0.05$), $\delta = 1, n_0 = 50$
- 10^4 macro-replications are carried out for each procedure
- 10^5 sample of $\boldsymbol{X}$ are used to compute $\widehat{\text{PCS}}_{\text{E}}$ of each procedure

	Procedure TS			Procedure TS$^+$		
Case	h_{Hom}	Sample	$\widehat{\text{PCS}}_{\text{E}}$	h_{Het}	Sample	$\widehat{\text{PCS}}_{\text{E}}$
(0) Benchmark	3.423	46865	0.9610	4.034	65138	0.9801
(1) $k = 2$	2.363	8947	0.9501	2.781	12380	0.9702
(2) $k = 8$	3.822	93542	0.9650	4.510	130200	0.9842
(3) Non-GSC	3.423	46865	0.9987	4.034	65138	0.9994
(4) IV	3.423	52698	0.9618	4.034	73265	0.9807
(5) DV	3.423	52720	0.9614	4.034	73246	0.9806
(6) Het	3.423	58626	0.9232	4.034	81555	0.9846
(7) $d = 1$	4.612	21288	0.9593	4.924	24266	0.9662
(8) $d = 5$	2.141	73428	0.9656	2.710	117630	0.9895
(9) Normal Dist	3.447	47,529	0.9626	4.063	66,061	0.9821

Experimental Design

Optimal Design under the Linearity Assumption



Geometrical Illustration of the Symmetric Design for $d = 3$ and $b = 2$.

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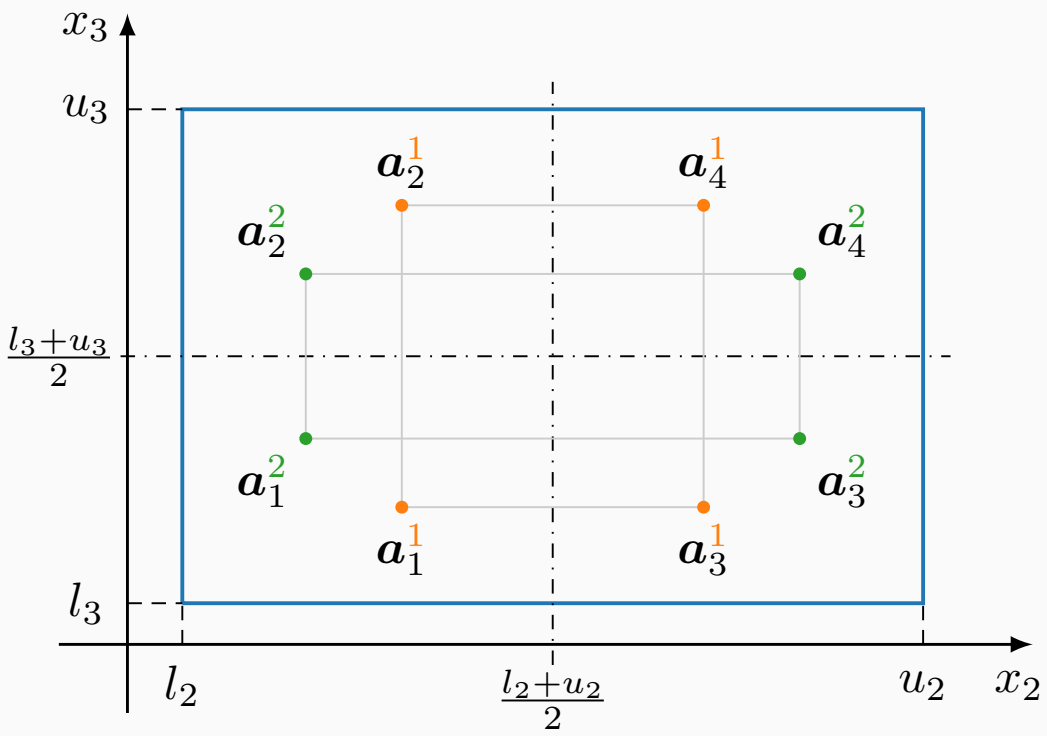
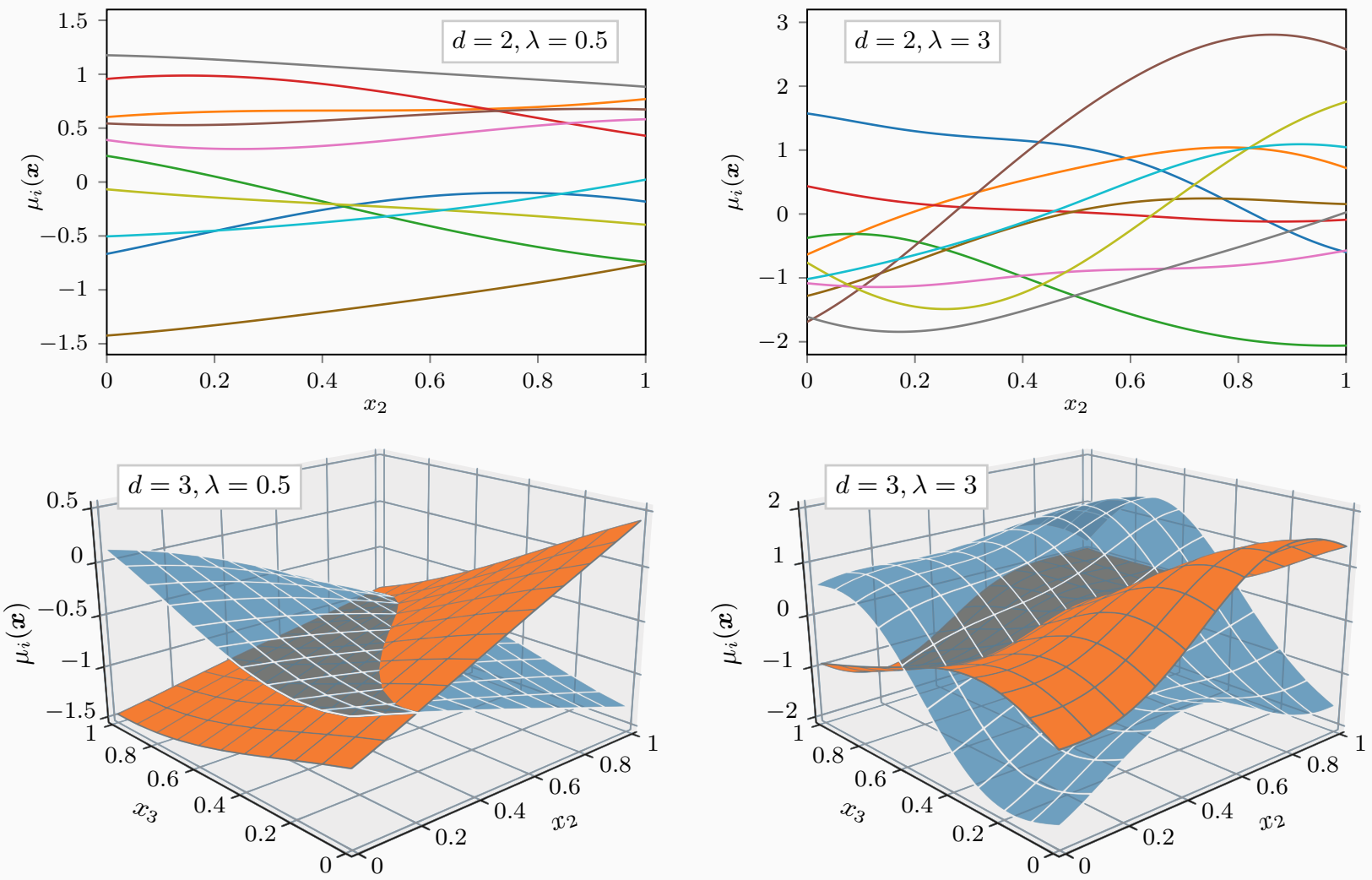


Geometrical Illustration of the Symmetric Design for $d = 3$ and $b = 2$.

Theorem (Shen, Hong, and Zhang 2018)

Under the linearity assumption, the extreme design minimizes the expected total sample size of Procedure TS among all symmetric designs.

Robustness to the Linearity Assumption



Randomly Generated Surfaces.

Extreme Designs and Minimax Designs for $d = 2, 3$

$d = 2$		$d = 3$	
Extreme Design	Minimax Design	Extreme Design	Minimax Design
$\begin{pmatrix} 1 & 0 \\ 1 & 1 \\ 1 & 0 \\ 1 & 1 \end{pmatrix}$	$\begin{pmatrix} 1 & 1/8 \\ 1 & 3/8 \\ 1 & 5/8 \\ 1 & 7/8 \end{pmatrix}$	$\begin{pmatrix} 1 & 0 & 0 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \\ 1 & 1 & 1 \\ 1 & 0 & 0 \\ 1 & 0 & 1 \\ 1 & 1 & 0 \\ 1 & 1 & 1 \end{pmatrix}$	$\begin{pmatrix} 1 & 0.1557 & 0.2086 \\ 1 & 0.1557 & 0.7914 \\ 1 & 0.8443 & 0.2086 \\ 1 & 0.8443 & 0.7914 \\ 1 & 0.2468 & 0.5000 \\ 1 & 0.7532 & 0.5000 \\ 1 & 0.5000 & 0.1794 \\ 1 & 0.5000 & 0.8206 \end{pmatrix}$

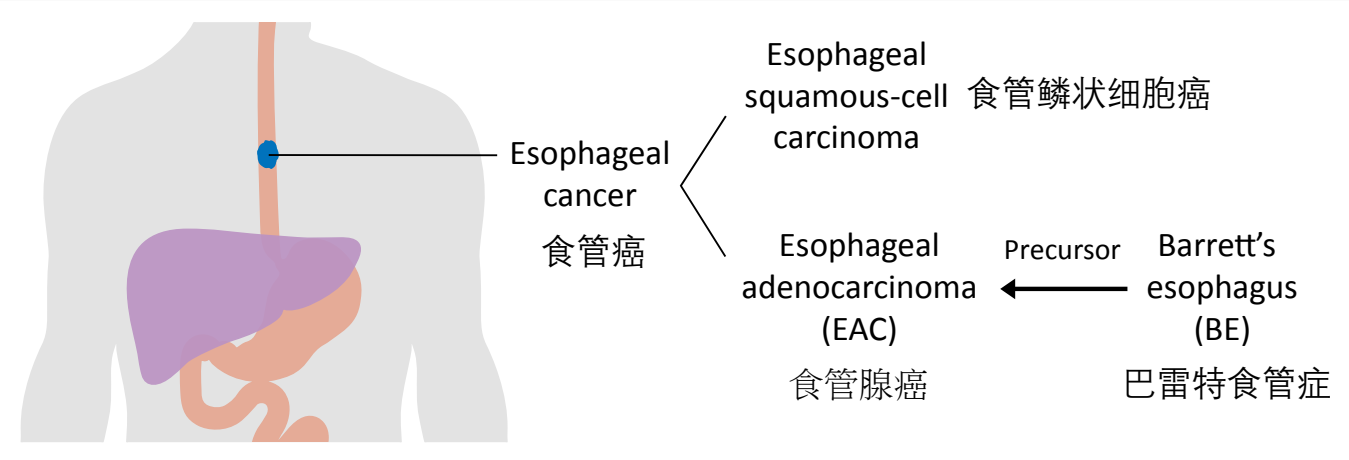
Results over 100 Problems

Case	Extreme Design			Minimax Design		
	S.S.	$\widehat{\text{PCS}}_{\text{E}}$	Regret	S.S	$\widehat{\text{PCS}}_{\text{E}}$	Regret
$d = 2, \lambda = 0.5$	1,730 (2)	0.9931 (0.0118)	0.009 (0.010)	2,869 (5)	0.9975 (0.0045)	0.005 (0.005)
$d = 2, \lambda = 3$	1,730 (2)	0.8555 (0.1399)	0.100 (0.108)	2,941 (50)	0.9801 (0.0292)	0.013 (0.016)
$d = 3, \lambda = 0.5$	2,282 (70)	0.9528 (0.0586)	0.024 (0.027)	4,659 (16)	0.9876 (0.0118)	0.008 (0.007)
$d = 3, \lambda = 3$	2,425 (121)	0.7358 (0.1306)	0.204 (0.139)	4,904 (96)	0.9133 (0.0502)	0.047 (0.030)

Personalized Cancer Treatment

Background

- Esophageal cancer is the 4th and 7th leading cancer among males in China and U.S., respectively.



- EAC is one sub-type of esophageal cancer, and its incidence has increased by 500% over the past 40 years (Bollschweiler et al., 2001; Hur et al., 2013).
- BE is a precursor to EAC, and its management is important and attracts many attentions.

Treatment Regimens

- Consider 3 treatment regimens (i.e., alternatives) for BE; all regimens include standard endoscopic surveillance:
  (1) No drug
  (2) Aspirin chemoprevention
  (3) Statin chemoprevention

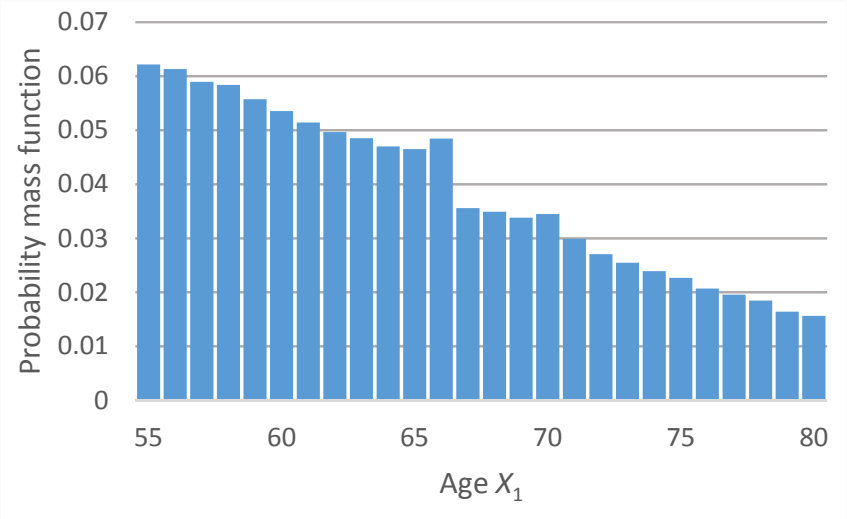
- Consider some individual characteristics (i.e., covariates):
  X_1 Age
  X_2 Risk (i.e., the annual progression rate of BE to EAC)
  X_3 Effect of aspirin (i.e., progression reduction effect)
  X_4 Effect of statin

- The best decision of treatment regimen for BE is patient-specific

Distribution of Covariates

- Assume $X_1, \cdots, X_4$ are independent

Covariates	Distributions	Support	Mean
X_1	Discrete (Figure below)	$\{55, \cdots, 80\}$	64.56
X_2	Unif $(0, 0.1)$	$[0, 0.1]$	0.05
X_3	Triangular $(0, 0.59, 1)$	$[0, 1]$	0.53
X_4	Triangular $(0, 0.62, 1)$	$[0, 1]$	0.54

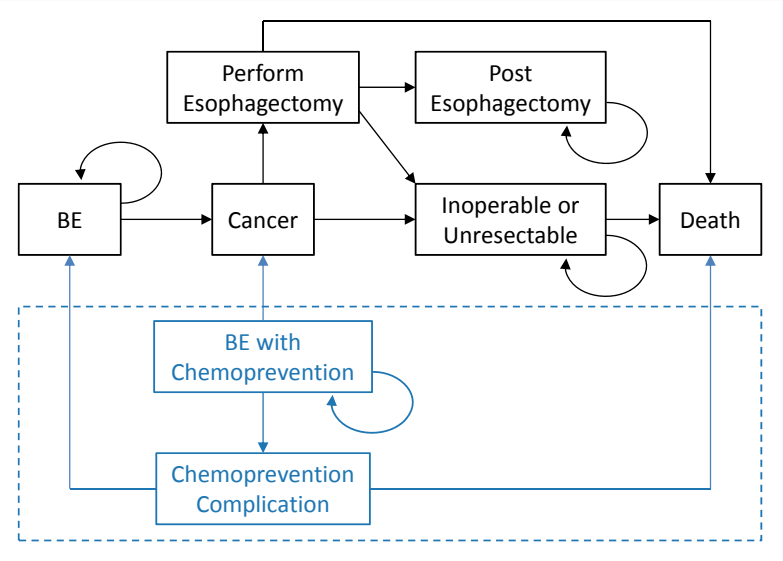


Probability mass function of X_1 (truncated).

Source: U.S. 2013 population data, U.S. Census Bureau.

Simulation Model

- A Markov simulation model was developed by Hur et al. (2004) and Choi et al. (2014) to study the effectiveness of aspirin and statin chemoprevention against EAC.



- A male with BE goes through various health state until death
- The person in each state can die from age-related all-cause mortality
- The time length between state transition is one month
- Detailed structure inside dotted box depends on drug
- Parameters are well calibrated

- Output $Y_i(\boldsymbol{X})$: Quality-adjusted life years (QALYs) after the starting age under treatment regimen i conditioning on $\boldsymbol{X}$.

Advantage of Personalized Medicine: Correct Selection

- Selection of treatment regimen: $\text{PCS}_{\text{E}} = 95\%$, $\delta = 0.2$, $n_0 = 100$
  - (i) In traditional way, the best treatment is the one that works the best on average for the entire population and it is selected via R&S ($i^\dagger \equiv 3$)
  - (ii) Perform personalized medicine through R&S-C with Procedure TS^+

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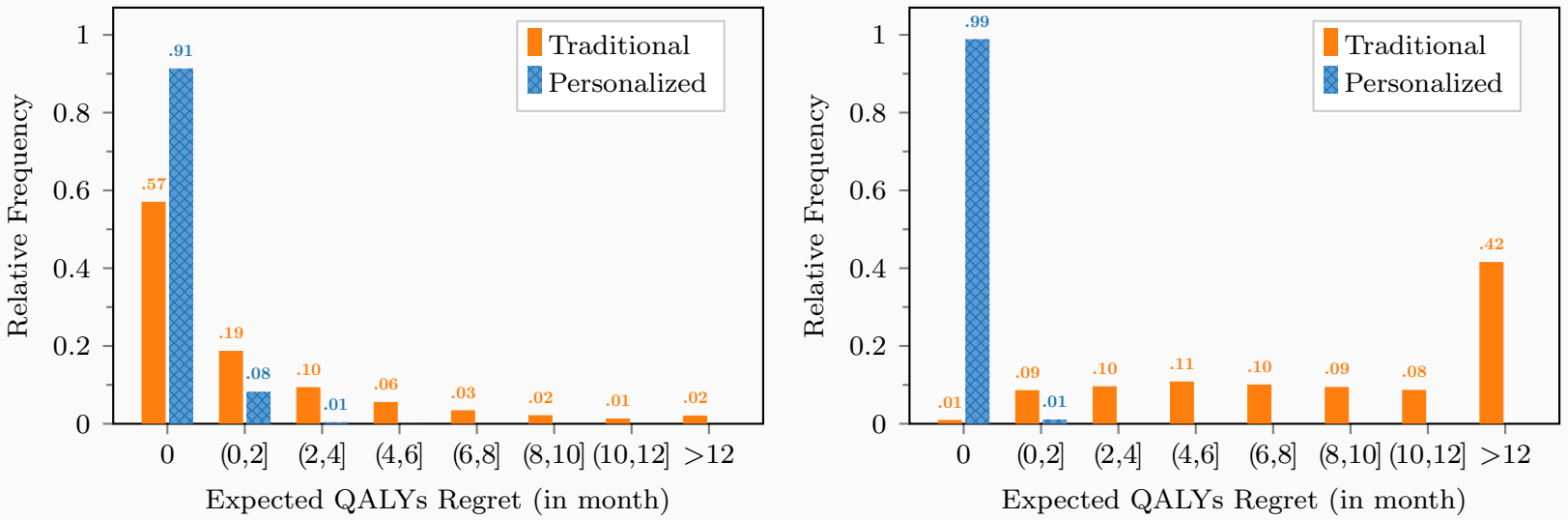
- "True" surfaces of expected QALYs $\mathbb{E}[Y_{i\ell}(\boldsymbol{x})]$ for $\boldsymbol{x} \in \Theta$ and $i = 1, 2, 3$, are obtained through extensive simulation
- 300 macro replications are carried out for Procedure TS$^+$
- 10^5 sample of $\boldsymbol{X}$ are used for evaluation
- Result comparison:
  (i) Traditional way: $\widehat{\mathrm{PCS}_{\mathrm{E}}} = 78.0\%$
  (ii) Personalized way: $\widehat{\mathrm{PCS}_{\mathrm{E}}} = 99.7\%$

Advantage of Personalized Medicine: Expected QALYs

- *"Regret"*: difference in expected QALYs between the true optimal treatment and the treatment selected by an approach
  - Traditional: $\mu_{i^*(X)}(X) - \mu_{i\dagger}(X)$
  - Personalized medicine: $\mu_{i^*(X)}(X) - \mu_{\widehat{i^*(X)}}(X)$



Left: The *entire population*. Right: A *specific group* with $X = (X_1, X_2, 0.9, 0.2)^\intercal$.

Conclusions

Conclusions

- Personalized decisions lead us to consider *ranking and selection with covariates*.

- We use a linear model to capture the relationship between the response and the covariates. It is the simplest yet most useful parametric model in practice.

- There are many directions that R&S-C may be studied, e.g., non-parametric models, Bayesian formulations, sequential procedures.

Thanks!

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