# Learning Individualized Treatment Rules with Many Treatments: A Supervised Clustering Approach Using Adaptive Fusion

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# Individualized Decision Making

- Example: Personalized Medicine

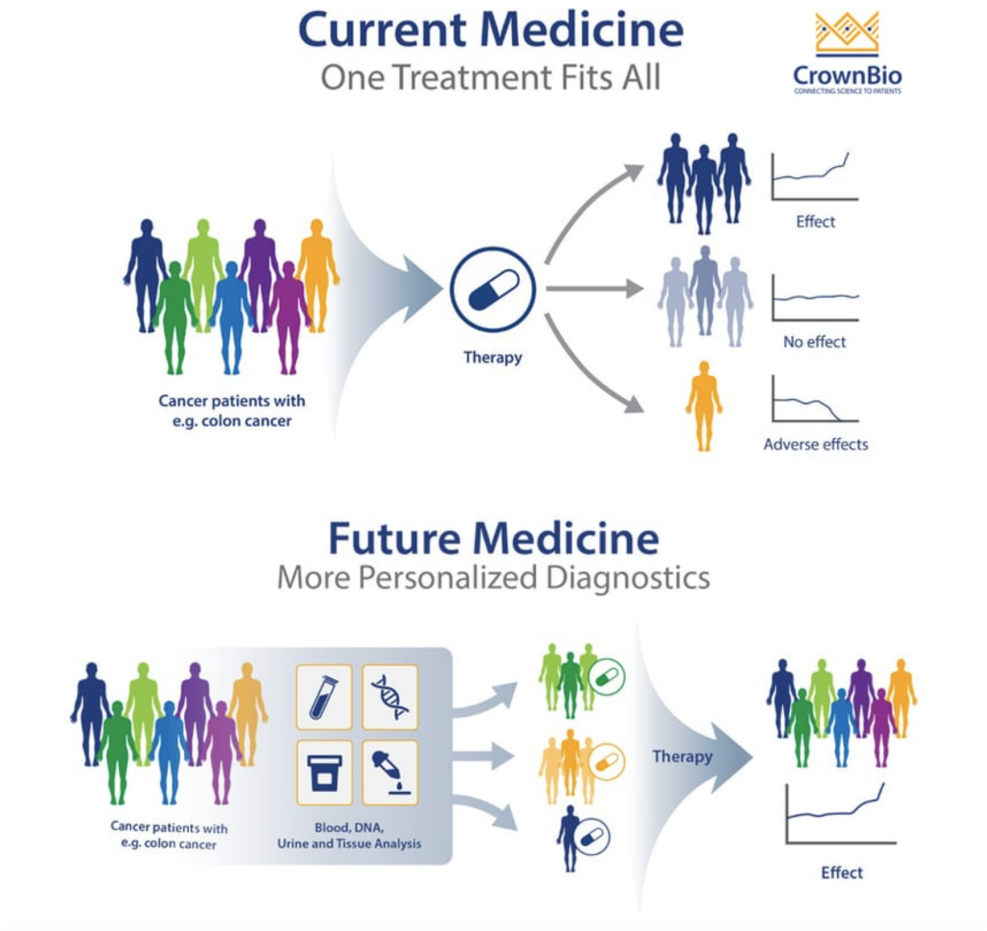


Figure 1: Transition from "one size fits all" to personalized medicine.[1]

[1] https://blog.crownbio.com/pdx-personalized-medicine

# Individualized Decision Making

- Individualized decision making problems:
  - Making personalized decision based on individualized information
  - Goal: find the **best** decision that optimizes a specified criterion
- Focus on precision medicine:
  - *Individualized cancer treatment*: tailoring therapies based on patients' genomic biomarkers to **optimize** future health status
- Data $(Z, A, Y) \in \mathcal{Z} \times \mathcal{A} \times \mathbb{R}$
  1. Features $Z \in \mathcal{Z} \subseteq \mathbb{R}^p$
  2. Assigned treatment $A \in \mathcal{A} = \{1, 2, \ldots, M\}$
  3. Reward $Y \in \mathbb{R}$ (larger the better)
- Individualized Treatment Rule (ITR) $D : \mathcal{Z} \to \mathcal{A}$
- Goal: Learn optimal ITR $D^* \in \mathcal{D}$ that maximizes the value function $\mathcal{V}(D)$

$$D^* \in \arg\max_{D \in \mathcal{D}} \left\{ \mathcal{V}(D) = \mathbb{E}[Y | A = D(X)] \right\}$$

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# Motivations

1. *Many treatments* available but *limited* observations for some specific treatments:
   - Large treatment space:
     - In *Patient-Derived Xenograft*: $|\mathcal{A}| > 20$ [Rashid et al., 2020]
   - Unbalanced structure of treatment assignment:
     - In *Sequenced Treatment Alternatives to Relieve Depression (STAR*D)*: number of patients who received the cognitive therapy *v.s.* venlafaxine is only around 1:3 [Rush et al., 2004]
     - In *Type 2 Diabetes*: observations of baseline treatments such as Metformin and Insulin would dominate others in electronic health record database [Montvida et al., 2018]
   - Classical methods may have *large variability* + *numerical instability*

★ Problem 1: how can we effectively estimate the optimal ITR in this case?

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# Motivations

2. Treatments in large treatment space may work *similarly* for patients:
   - *STAR*D* study: treatment options are combined into two class (one involves Selective Serotonin Reuptake Inhibitors (SSRI) + another one not) because treatments within same class have similar treatment effects [Liu et al., 2018, Pan and Zhao, 2021]
   - Few existing methods deal with *clustering treatments*

★ Problem 2: how can we cluster the treatments with similar treatment effects together?

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- Supervised clustering
  - Cluster the relationship $Y \sim Z \times A$ with *fusion penalty*:

$$\min_{\boldsymbol{\zeta}} \left\{ \mathbb{E}_n \Big[ \underbrace{\mathcal{L}\big(Y, \overbrace{\textstyle\sum_{a\in\mathcal{A}} \mathbb{I}[A=a] T(Z, \boldsymbol{\zeta}_a)}^{\bigstar \text{ Heterogeneous treatment effects}}\big)}_{\text{Loss}} \Big] + \underbrace{\textstyle\sum_{1\le l<t\le M} p_{\lambda_n}\left(\|\boldsymbol{\zeta}_l - \boldsymbol{\zeta}_t\|_1\right)}_{\text{Fusion penalty}} \right\},$$

    where $\boldsymbol{\zeta}_a$'s are treatment-specific coefficients
  - Convex minimization problem with *loss + fusion penalty* balanced by $\lambda_n$
  - Interpretation: maximize goodness of fit, while minimize heterogeneity among treatments simultaneously

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# Main Contributions

- Clustering process can be visualized by a *dendrogram plot*:

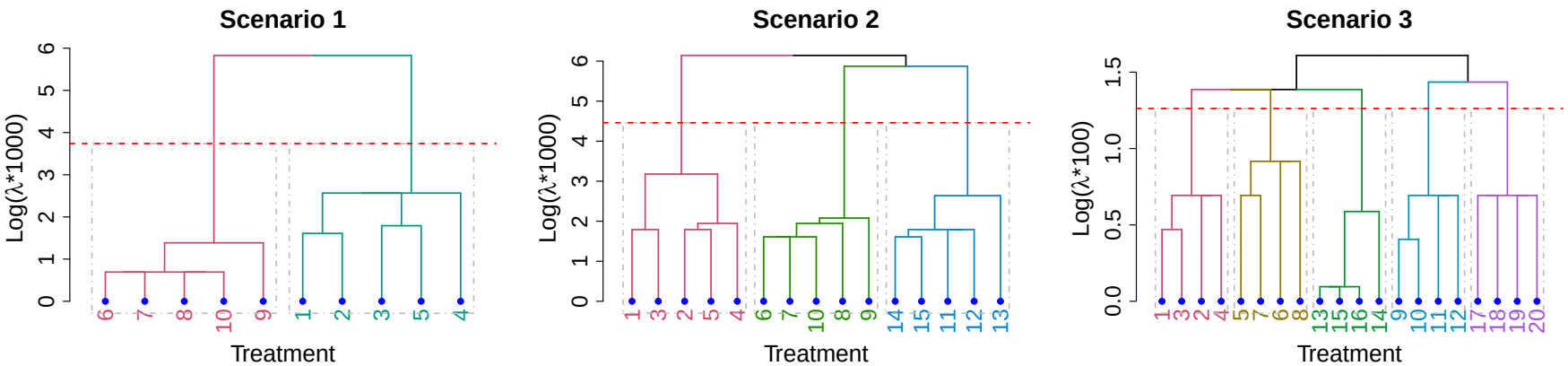


Figure 2: Solution path of estimated treatment group structure as $\lambda_n$ increases. The true treatment group memberships are demonstrated with different colors. The red dotted horizontal lines show the best tuned $\lambda_n$ using cross-validation.

- $\lambda_n = 0$: no penalty is imposed, hence no clustering pattern
- $\lambda_n \uparrow$: fusion penalty encourages similar treatments to merge together
- $\lambda_n$ large enough: all treatments will be merged together

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# Main Contributions

We also

- Solved fusion problem with adaptive proximal gradient algorithm effectively
- Proposed a novel *group-lasso* based method to select important variables
- Provided theoretical guarantee for estimating treatment group structure
- Conducted both simulation studies and real data analysis on cancer treatment to illustrate the superior performance of our method

☺ **Thanks for your listening!**

☼ **Welcome to join our poster session if you have more questions.**

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