Maximin-Projection Learning for Optimal Treatment Decision with Heterogeneous Data

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Sources of heterogeneity

- **Data Integration (Meta analysis)**
  - Results combined from different studies to identify similar patterns.
  - Heterogeneity due to different study populations.
  - Heterogeneity due to different study periods.

- **Divide and conquer (Massive data)**
  - Data too large to fit an overall model, a possible solution is divide and conquer.
  - Estimator for each group often differs.
  - Heterogeneity due to large-scale data.
Motivating Example I

Schizophrenia study (Tarrier et al., 2004)

- A multi-center, randomized controlled trial with an 18 month follow-up period.
- To examine the effectiveness of cognitive-behavioral therapy for patients with schizophrenia.
- Treatments: the cognitive-behavioural therapy plus treatment as usual (CBT); supportive counselling plus treatment as usual (SC); and treatment as usual (TAU).
- $Y$: the reduction of PANSS score.
- $X$: PANSS score at baseline; log duration of untreated psychosis.
- Over 400 patients initially enrolled in 11 mental health units in England; 165 patients finish the follow-up study and have completed information for both $X$ and $Y$.
- Data are from three geographical locations (Manchester/Salford, Liverpool and North Nottinghamshire).
Schizophrenia study (Continued)

- We compare CBT \((A = 1)\) vs. CS \((A = 0)\).
- For each group, consider the following model

\[
E(Y_{gj} | X_{gj}, A_{gj}) = h_g(X_{gj}) + A_{gj} \left( \beta_{g0} + \beta_{g1}X_{gj}^{(1)} + \beta_{g2}X_{gj}^{(2)} \right),
\]

and estimate \(\beta_{g0}, \beta_{g1}, \beta_{g2}\) by A-learning.

Table: Estimators of groupwise optimal treatment regime (standard errors in parenthesis)

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\beta_{g0})</td>
<td>−8.51(6.96)</td>
<td>1.42(4.98)</td>
<td>0.47(5.74)</td>
</tr>
<tr>
<td>(\beta_{g1})</td>
<td>−1.53(4.75)</td>
<td>0.05(6.55)</td>
<td>−4.89(5.74)</td>
</tr>
<tr>
<td>(\beta_{g2})</td>
<td>2.65(5.70)</td>
<td>5.41(3.52)</td>
<td>−11.67(4.27)</td>
</tr>
</tbody>
</table>
Health assessment questionnaire (HAQ) progression data

- An observational study to investigate the influence of early disease modifying antirheumatic drug (DMARD) treatment for patients with recent onset inflammatory polyarthritis (Farragher et al., 2010).
- 847 patients enrolled from 1990 to 2000.
- We focused on treatments: methotrexate \((A = 1)\) and sulfasalazine \((A = 0)\).
- \(Y\): reduction in HAQ scores between baseline and 5 years.
- \(X\): age, baseline HAQ score, number of swollen joints and number of tender joints.
- Patients enrolled at different times showing heterogeneity; we considered three groups: 1990 - 1992 \((G = 1)\); 1993 - 1996 \((G = 2)\); 1997 - 2000 \((G = 3)\).
HAQ data (continued)

- We estimate the group-wise optimal treatment regime using A-learning based on the same models as in the previous example.

**Table:** Estimators of groupwise optimal treatment regime (standard errors in paranthesis)

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\hat{\beta}_{g0}$</td>
<td>$-0.39(0.11)$</td>
<td>$-0.09(0.10)$</td>
<td>$0.48(0.33)$</td>
</tr>
<tr>
<td>$\hat{\beta}_{g1}$</td>
<td>$0.26(0.15)$</td>
<td>$0.24(0.11)$</td>
<td>$-0.17(0.14)$</td>
</tr>
<tr>
<td>$\hat{\beta}_{g2}$</td>
<td>$0.09(0.12)$</td>
<td>$0.18(0.13)$</td>
<td>$1.02(0.36)$</td>
</tr>
<tr>
<td>$\hat{\beta}_{g3}$</td>
<td>$0.03(0.12)$</td>
<td>$-0.34(0.15)$</td>
<td>$0.01(0.19)$</td>
</tr>
</tbody>
</table>

- Heterogeneity inside the data
Questions:

- How to effectively combine different treatment regimes?
- How to take into account data heterogeneity?

Simple solutions:

- Combine the data together and find the optimal treatment regime based on the pooled data (ignore the data heterogeneity!).
- Take average of group-specific optimal treatment regimes (may work bad for some groups).

Our thinking:

- What else can we do with heterogeneous data?
- What is a good criteria for combining treatment regimes?
Model

- \( G \) different population groups:

\[
Y_{gj} = h_g(X_{gj}) + A_{gj} \psi_g(X_{gj}^T \beta_g) + \varepsilon_{gj}
\]

- \( ||\beta_g||_2 = 1, g = 1, \ldots, G, j = 1, \ldots, m \)
- \( h_g \) arbitrary baseline function
- \( \psi_g \) arbitrary monotone increasing function

Objective

Find a decision rule

\[
d : X \rightarrow A = \{0, 1\}
\]

d that works well for patients of all \( G \) groups.
Idea

- Groupwise optimal regime: \( I\{X_0^T\beta_g > \psi_g^{-1}(0)\} \)
- Overall decision: \( I(X_0^T\beta_0 > c_0) \) subject to \( \|\beta_0\|_2 = 1 \)
- Two step strategy:
  - Step 1: Fix \( c_0 \), search some \( \beta_0(c_0) \) achieves some “optimality”
  - Step 2: Optimize over \( c_0 \)

How to define “optimality”

- For each \( \beta \), define the reward function \( R_g(\beta) \) given the decision
  \[ I(X_0^T\beta > c_0). \]

- Maximin effects \( \beta_0 = \text{arg max}_{\beta} \min_{g} R_g(\beta) \)
  - Maximize the minimum reward
  - Minimize the risk of the worst-case scenario
How to choose reward function

Example (Average Percentage of making Correct Decisions (PCD))

Using PCD,

\[ R_g^{(1)}(\beta) = 1 - E|I(X_T g \beta > \psi_g^{-1}(0)) - I(X_T g \beta > c_0)|, \]

The maximin effects \( \beta_0^{(1)} = \arg \max_{\beta : \|\beta\|_2 = 1} \min_g R_g^{(1)}(\beta). \)

Example (Value function)

Using value function,

\[ R_g^{(2)}(\beta) = E\{Y_g^*(d(X_g, \beta))\} - E\{Y_g^*(0)\}, \]

where \( d(X_g, \beta) = I(X_T g \beta > c_0). \)

The maximin effects \( \beta_0^{(2)} = \arg \max_{\beta : \|\beta\|_2 = 1} \min_g R_g^{(2)}(\beta). \)
An intuitive definition for the maximin effects

- Assume $\psi_1^{-1}(0) = \psi_2^{-1}(0) = \cdots = \psi_G^{-1}(0) = \bar{c}$, for each subgroup $g$, the optimal regime becomes

$$I(X_0^T \beta_g > \bar{c}),$$

- Note that $||\beta_g||_2 = 1$, each $\beta_g$ represents the “direction”.
- Intuitively, we can define the maximin effects through “angles”:

$$\beta_0^{(3)} = \arg \min_{||\beta||=1} \max_g \angle(\beta, \beta_g).$$

- More formally, let

$$F(\beta) = \min_g \beta^T \beta_g,$$

and $\beta_0^{(3)}$ is defined as $\arg \max_{||\beta||_2=1} F(\beta)$ (Maximin correlation approach in Avi-Itzhak et al., 1995).
Theorem (Equivalence of $\beta_{0}^{(1)}$ and $\beta_{0}^{(3)}$)

Assume $\psi_{1}^{-1}(0) = \psi_{2}^{-1}(0) = \cdots = \psi_{G}^{-1}(0) = \bar{c}$, $X_{ij}$ i.i.d spherically distributed, then for any $c_{0}$,

$$
\beta_{0}^{(3)} = \arg \max_{\|\beta\|_2=1} \min_{g} R_{g}^{(1)}(\beta).
$$

Theorem (Equivalence of $\beta_{0}^{(2)}$ and $\beta_{0}^{(3)}$)

Assume $\psi_{1} = \psi_{2} = \cdots = \psi_{G} = \psi$, $X_{ij}$ i.i.d spherically distributed, then for any $c_{0}$,

$$
\beta_{0}^{(3)} = \arg \max_{\|\beta\|_2=1} \min_{g} R_{g}^{(2)}(\beta).
$$

Only need to focus on the third definition.
Refinement

- $\beta_0^{(3)} = \arg \max_{||\beta||_2=1} F(\beta)$
- $\beta_0^{(3)}$ always exists: the maximin effect is well defined
- May not be unique when $F_0 \equiv \max_{||\beta||_2=1} F(\beta) < 0$
- The optimization problem

$$\arg \max_{||\beta||_2=1} F(\beta),$$

is a quasi-concave problem (difficult to solve globally).

- Consider $\beta_0^{(4)} = \arg \max_{||\beta||_2 \leq 1} F(\beta)$,
- Solving $\beta_0^{(4)}$ is a tractable concave programming (Seung-Jean et al., 2008).
- $\beta_0^{(4)}$ always exists, and is unique when $F_0 \neq 0$. 
Graphical characterization

- When $F_0 > 0$, $\beta_0^{(4)} = \beta_0^{(3)}$.
- When $F_0 < 0$, $\beta_0^{(4)} = 0$.

**Figure:** Illustration of maximin effects $\beta_0^{(4)}$ (green star), $\beta_0^{(3)}$ (red circle), and subgroup parameters (orange square)
Proposed Maximin-Projection Learning

Estimating procedure

- Assume estimators $\hat{\beta}_1, \ldots, \hat{\beta}_G$ are available with $\|\hat{\beta}_g\|_2 = 1$ for any $g$.
- Concave optimization problem

$$\hat{\beta}_0 = \arg \max_{\beta: \|\beta\|_2 \leq 1} \min_{g=1, \ldots, G} \beta^T \hat{\beta}_g.$$ 

- Equivalent to quadratic constraint linear programming (QCLP):

  maximize \quad t \in \mathbb{R}

  subject to \quad \beta^T \hat{\beta}_g \geq t, \ g = 1, \ldots, G

  \quad \beta^T \beta \leq 1,

- Obtain $\hat{c}_0$ by maximizing the estimated value function:

$$\hat{c}_0 = \arg \max_c \frac{1}{mG} \sum_i \sum_j Y_{ij} I(X_{ij}^T \hat{\beta}_0 > c) \frac{A_i \hat{\pi}_i + (1 - A_i)(1 - \hat{\pi}_i)}{A_i \hat{\pi}_i + (1 - A_i)(1 - \hat{\pi}_i)}$$
Theorem (Consistency)

Define $\hat{B} = (\hat{\beta}_1, \ldots, \hat{\beta}_G)$. Assume that $F_0 \neq 0$, $G \geq 2$, vectors in $B_{l_0}$ are linearly independent, each $\hat{\beta}_g$ is consistent with $||\hat{\beta}_g||_2 = 1$. Then with probability going to 1, the estimated maximin effects $\hat{\beta}_0$ is equal to

$$\begin{cases} [e^T (\hat{B}_{l_0}^T \hat{B}_{l_0})^{-1} e]^{-1/2} \hat{B}_{l_0} (\hat{B}_{l_0}^T \hat{B}_{l_0})^{-1} e & \text{if } F_0 > 0, \\ 0 & \text{if } F_0 < 0. \end{cases}$$

If $F_0 > 0$, then

$$||\hat{\beta}_0 - \beta_0||_2 = \sup_{g \in l_0} O(||\hat{\beta}_g - \beta_g||_2).$$
Theorem (Asymptotic normality)

Assume $F_0 > 0$ and

$$\sqrt{m}(\hat{\beta}_g - \beta_g) = \frac{1}{\sqrt{m}} \sum_{i=1}^{m} \psi_{ig} + o_p(1).$$

Under suitable conditions, $\sqrt{m}(\hat{\beta}_0 - \beta_0)$ is asymptotically normally distributed with mean 0 and covariance matrix

$$\frac{1}{||t_0||^2} \sum_{g \in I_0} \left( v_g^T t_0 N(B_{I_0}) - N(t_0)v_g t_0^T \right) \Sigma_g \left( v_g^T t_0 N(B_{I_0}) - N(t_0)v_g t_0^T \right)^T,$$

where $\Sigma_g = E(\psi_{ig} \psi_{ig}^T)$, $v_g = B_{I_0}(B_{I_0}^T B_{I_0})^{-1} e_g$, $t_0 = B_{I_0}(B_{I_0}^T B_{I_0})^{-1} e$, $N(\Phi) = I - \Phi(\Phi^T \Phi)^+ \Phi^T$. 
Overall value function

For each threshold $c$, we define the overall value function under the regime $I(x^T \beta_0 > c)$ as

$$V(\beta_0, c) = \frac{1}{G} \sum_{g=1}^{G} \mathbb{E}\{ h_g(X_{g0}) + \psi(X_{g0}^T \beta_0)I(X_{g0}^T \beta_0 > c) \},$$

and let $c_0 = \arg \max_c V(\beta_0, c)$.

Theorem

*Under certain regularity conditions, we have*

$$\hat{c}_0 - c_0 = O_p(m^{-1/3}).$$

*Moreover, $\sqrt{m}\{ \hat{V}_m(\hat{\beta}_0, \hat{c}_0) - V(\beta_0, c_0) \}$ is asymptotically normal with mean 0 and variance $\nu_0^2$.***
Simulation settings

- Four groups of patients, each generated according to

\[ Y_{gj} = h(X_{gj}) + 2A_{gj}X_{gj}^T\beta_g + \varepsilon_{gj}, \]

\[ X_{gj} \sim_{i.i.d} N(0, I_2) \text{ and } \varepsilon_{gj} \sim_{i.i.d} N(0, 0.25). \]

- Two baseline models for \( h \): linear and nonlinear.

- Two propensity score models: constant and probit.

- For each setting: subgroup estimator obtained using A-learning based on a linear model for \( h \) and logistic model for \( \pi \):

  1. S1: \( \pi \) correct, \( h \) correct,
  2. S2: \( \pi \) correct, \( h \) wrong,
  3. S3: \( \pi \) wrong, \( h \) correct,
  4. S4: \( \pi \) wrong, \( h \) wrong.
Simulation settings (continued)

- Two scenarios for the subgroup parameters (representing different degrees of heterogeneity):
  - (I) (large heterogeneity) \( \beta_1 = (1, 0), \beta_2 = (\cos(10^\circ), \sin(10^\circ)), \beta_3 = (\cos(70^\circ), \sin(70^\circ)), \beta_4 = (0, 1); \)
  - (II) (small heterogeneity) \( \beta_1 = (\cos(30^\circ), \sin(30^\circ)), \beta_2 = (\cos(45^\circ), \sin(45^\circ)), \beta_3 = (\cos(54^\circ), \sin(54^\circ)), \beta_4 = (\cos(60^\circ), \sin(60^\circ)); \)

- The maximin effects parameter \( \beta_0 = (\cos(45^\circ), \sin(45^\circ)) \) for both scenarios.
## Results for estimated maximin regimes

**Table**: Bias, standard deviation (in parenthesis) of $\hat{\beta}_0$ and coverage probability for confidence intervals of $\beta_0$.

<table>
<thead>
<tr>
<th>Sce</th>
<th>$\hat{\beta}_0^1$</th>
<th>$\hat{\beta}_0^2$</th>
<th>CP for $\hat{\beta}_0^1$</th>
<th>CP for $\hat{\beta}_0^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sce I</td>
<td>S1 $-0.018(0.037)$</td>
<td>$-0.028(0.051)$</td>
<td>95.0%</td>
<td>97.4%</td>
</tr>
<tr>
<td></td>
<td>S2 $-0.015(0.045)$</td>
<td>$-0.025(0.053)$</td>
<td>98.6%</td>
<td>95.0%</td>
</tr>
<tr>
<td></td>
<td>S3 $-0.016(0.048)$</td>
<td>$-0.024(0.055)$</td>
<td>96.6%</td>
<td>97.2%</td>
</tr>
<tr>
<td></td>
<td>S4 $-0.010(0.061)$</td>
<td>$-0.020(0.069)$</td>
<td>98.2%</td>
<td>97.0%</td>
</tr>
<tr>
<td>Sce II</td>
<td>S1 $3.6 \times 10^{-4}(0.018)$</td>
<td>$-0.001(0.018)$</td>
<td>96.0%</td>
<td>95.0%</td>
</tr>
<tr>
<td></td>
<td>S2 $-0.006(0.033)$</td>
<td>0.003(0.031)</td>
<td>96.8%</td>
<td>96.8%</td>
</tr>
<tr>
<td></td>
<td>S3 $-0.008(0.045)$</td>
<td>0.002(0.042)</td>
<td>96.6%</td>
<td>97.4%</td>
</tr>
<tr>
<td></td>
<td>S4 $-0.012(0.064)$</td>
<td>0.004(0.063)</td>
<td>96.6%</td>
<td>97.8%</td>
</tr>
</tbody>
</table>
Results for estimated value functions

**Table:** Bias, standard deviation of $\hat{V}_m(\hat{\beta}_0, \hat{c}_0)$ and coverage probability for confidence intervals of $V(\beta_0, c_0)$

<table>
<thead>
<tr>
<th>Sce I</th>
<th>Bias</th>
<th>SD</th>
<th>CI</th>
<th>Sce II</th>
<th>Bias</th>
<th>SD</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>0.017</td>
<td>0.083</td>
<td>93.6%</td>
<td>S1</td>
<td>0.007</td>
<td>0.099</td>
<td>95.4%</td>
</tr>
<tr>
<td>S2</td>
<td>0.018</td>
<td>0.074</td>
<td>93.6%</td>
<td>S2</td>
<td>0.005</td>
<td>0.075</td>
<td>95.2%</td>
</tr>
<tr>
<td>S3</td>
<td>0.018</td>
<td>0.134</td>
<td>95.4%</td>
<td>S3</td>
<td>0.011</td>
<td>0.101</td>
<td>95.2%</td>
</tr>
<tr>
<td>S4</td>
<td>0.027</td>
<td>0.137</td>
<td>96.8%</td>
<td>S4</td>
<td>0.003</td>
<td>0.115</td>
<td>95.2%</td>
</tr>
</tbody>
</table>
Comparisons with simple methods

- **Methods to compare:**
  - “maximin treatment regime” \( d(x) = I(x^T \hat{\beta} > \hat{c}_0) \)
  - “pooled treatment regime” \( d(x) = I(x^T \tilde{\beta} > \tilde{c}_0) \)
  - “simple average treatment regime” \( d(x) = I(x^T \bar{\beta} > \bar{c}) \)

- **Evaluation:**
  - obtain the estimated regime based on three groups and apply it to the remaining group;
  - compute PCD (using the estimated group-specific regime as the truth) and estimated value function (using A-learning) of the estimated regime for each group.
<table>
<thead>
<tr>
<th>Testing group</th>
<th>First group</th>
<th>Second group</th>
<th>Third group</th>
<th>Fourth group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pooled</td>
<td>maximin</td>
<td>average</td>
<td></td>
</tr>
<tr>
<td>S1</td>
<td>67.8%(1.42)</td>
<td>71.7%(1.50)</td>
<td>74.9%(1.55)</td>
<td>67.4%(1.41)</td>
</tr>
<tr>
<td></td>
<td>74.9%(1.56)</td>
<td>79.8%(1.64)</td>
<td>77.0%(1.55)</td>
<td>74.3%(1.55)</td>
</tr>
<tr>
<td></td>
<td>78.1%(1.61)</td>
<td>85.0%(1.71)</td>
<td>84.5%(1.71)</td>
<td>80.0%(1.60)</td>
</tr>
<tr>
<td></td>
<td>64.3%(1.35)</td>
<td>68.9%(1.45)</td>
<td>68.8%(1.44)</td>
<td>63.9%(1.34)</td>
</tr>
<tr>
<td>S2</td>
<td>67.8%(1.42)</td>
<td>72.0%(1.51)</td>
<td>74.8%(1.56)</td>
<td>67.5%(1.42)</td>
</tr>
<tr>
<td></td>
<td>74.9%(1.56)</td>
<td>79.8%(1.64)</td>
<td>77.0%(1.59)</td>
<td>73.8%(1.54)</td>
</tr>
<tr>
<td></td>
<td>78.3%(1.62)</td>
<td>84.5%(1.71)</td>
<td>80.0%(1.60)</td>
<td>77.0%(1.59)</td>
</tr>
<tr>
<td></td>
<td>64.2%(1.34)</td>
<td>68.8%(1.44)</td>
<td>63.8%(1.34)</td>
<td></td>
</tr>
<tr>
<td>S3</td>
<td>68.0%(1.43)</td>
<td>71.3%(1.49)</td>
<td>74.9%(1.56)</td>
<td>67.3%(1.41)</td>
</tr>
<tr>
<td></td>
<td>74.9%(1.56)</td>
<td>79.0%(1.62)</td>
<td>76.0%(1.57)</td>
<td>73.4%(1.53)</td>
</tr>
<tr>
<td></td>
<td>78.1%(1.61)</td>
<td>83.8%(1.69)</td>
<td>63.6%(1.33)</td>
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</tr>
<tr>
<td></td>
<td>63.9%(1.34)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S4</td>
<td>68.0%(1.42)</td>
<td>71.3%(1.49)</td>
<td>74.8%(1.55)</td>
<td>67.1%(1.40)</td>
</tr>
<tr>
<td></td>
<td>74.8%(1.55)</td>
<td>79.0%(1.63)</td>
<td>76.2%(1.58)</td>
<td>73.2%(1.53)</td>
</tr>
<tr>
<td></td>
<td>78.0%(1.61)</td>
<td>83.7%(1.69)</td>
<td>63.9%(1.34)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>64.1%(1.34)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Table: PCD and value function (in parenthesis) for the second scenario under estimated “maximin treatment regime”, “pooled treatment regime” and “simple average treatment regime”

<table>
<thead>
<tr>
<th>Testing group</th>
<th>First group</th>
<th>Second group</th>
<th>Third group</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 pooled</td>
<td>87.2%(1.73)</td>
<td>98.0%(1.80)</td>
<td>95.0%(1.79)</td>
<td>90.5%(1.76)</td>
</tr>
<tr>
<td>S1 maximin</td>
<td>87.0%(1.73)</td>
<td>96.7%(1.79)</td>
<td>94.0%(1.78)</td>
<td>89.4%(1.75)</td>
</tr>
<tr>
<td>S1 average</td>
<td>86.9%(1.73)</td>
<td>96.2%(1.79)</td>
<td>94.2%(1.78)</td>
<td>89.8%(1.76)</td>
</tr>
<tr>
<td>S2 pooled</td>
<td>87.2%(1.73)</td>
<td>97.7%(1.80)</td>
<td>94.8%(1.79)</td>
<td>90.4%(1.76)</td>
</tr>
<tr>
<td>S2 maximin</td>
<td>86.9%(1.73)</td>
<td>96.3%(1.79)</td>
<td>93.8%(1.78)</td>
<td>89.3%(1.75)</td>
</tr>
<tr>
<td>S2 average</td>
<td>86.7%(1.73)</td>
<td>96.1%(1.79)</td>
<td>93.8%(1.78)</td>
<td>89.9%(1.76)</td>
</tr>
<tr>
<td>S3 pooled</td>
<td>87.1%(1.73)</td>
<td>97.5%(1.79)</td>
<td>95.1%(1.79)</td>
<td>90.7%(1.76)</td>
</tr>
<tr>
<td>S3 maximin</td>
<td>86.7%(1.73)</td>
<td>95.6%(1.79)</td>
<td>93.4%(1.78)</td>
<td>89.4%(1.75)</td>
</tr>
<tr>
<td>S3 average</td>
<td>86.5%(1.72)</td>
<td>95.4%(1.79)</td>
<td>93.5%(1.78)</td>
<td>89.5%(1.75)</td>
</tr>
<tr>
<td>S4 pooled</td>
<td>87.0%(1.73)</td>
<td>96.6%(1.79)</td>
<td>90.4%(1.78)</td>
<td>90.5%(1.76)</td>
</tr>
<tr>
<td>S4 maximin</td>
<td>85.8%(1.71)</td>
<td>94.4%(1.78)</td>
<td>92.3%(1.77)</td>
<td>88.9%(1.75)</td>
</tr>
<tr>
<td>S4 average</td>
<td>85.9%(1.72)</td>
<td>94.1%(1.78)</td>
<td>92.9%(1.77)</td>
<td>89.0%(1.74)</td>
</tr>
</tbody>
</table>
### Schizophrenia study

**Table:** Maximin and pooled treatment regimes, and the estimated value functions under these regimes

<table>
<thead>
<tr>
<th>Testing group</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maximin</td>
<td>pooled</td>
<td>maximin</td>
</tr>
<tr>
<td>$\hat{\beta}_{g0}$</td>
<td>$-1.00$</td>
<td>$-0.92$</td>
<td>$1.00$</td>
</tr>
<tr>
<td>$\hat{\beta}_{g1}$</td>
<td>$-0.98$</td>
<td>$-0.21$</td>
<td>$-1.00$</td>
</tr>
<tr>
<td>$\hat{\beta}_{g2}$</td>
<td>$0.20$</td>
<td>$-0.14$</td>
<td>$-0.06$</td>
</tr>
<tr>
<td>$\hat{E}Y^*_g(d)$</td>
<td>$24.99$</td>
<td>$23.73$</td>
<td>$30.11$</td>
</tr>
</tbody>
</table>
## HAQ data

**Table:** Maximin and pooled treatment regimes, and the estimated value functions under these regimes

<table>
<thead>
<tr>
<th>Testing group</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maximin</td>
<td>pooled</td>
<td>maximin</td>
</tr>
<tr>
<td>$\hat{\beta}_{g0}$</td>
<td>1.625</td>
<td>0.023</td>
<td>2.900</td>
</tr>
<tr>
<td>$\hat{\beta}_{g1}$</td>
<td>0.838</td>
<td>0.204</td>
<td>0.513</td>
</tr>
<tr>
<td>$\hat{\beta}_{g2}$</td>
<td>0.406</td>
<td>$-0.264$</td>
<td>0.855</td>
</tr>
<tr>
<td>$\hat{\beta}_{g3}$</td>
<td>$-0.365$</td>
<td>$-0.104$</td>
<td>0.077</td>
</tr>
<tr>
<td>$\hat{E}Y^*_g(d)$</td>
<td>0.092</td>
<td>$-0.001$</td>
<td>$-0.037$</td>
</tr>
</tbody>
</table>
Future work

- Is it possible to extend the idea of maximin treatment decision under more general model setting?
- What if the covariates are not spherically distributed?
- Is it possible to extend the idea of maximin treatment decision to multiple stages?
Acknowledgement

- Support: NIH NCI grants RO1CA140632 and PO1CA142538;
- Collaborators: Chengchun Shi, Rui Song and Bo Fu.

Thank you!