On Testing Conditional Qualitative Treatment Effects

Chengchun Shi

Department of Statistics North Carolina State University

Joint work with Wenbin Lu and Rui Song

July 30, 2017

Data

- A: Treatment (0 or 1)
- X: Covariates
- Y: Observed outcome (usually the larger the better)

Data

- A: Treatment (0 or 1)
- X: Covariates
- Y: Observed outcome (usually the larger the better)
- $Y^*(a)$: Potential outcome a = 0, 1

Data

- A: Treatment (0 or 1)
- X: Covariates
- Y: Observed outcome (usually the larger the better)
- $Y^*(a)$: Potential outcome a = 0, 1

Objective

Identify the optimal regime d_{opt} to reach the best clinical outcome

Data

- A: Treatment (0 or 1)
- X: Covariates
- Y: Observed outcome (usually the larger the better)
- $Y^*(a)$: Potential outcome a = 0, 1

Objective

Identify the optimal regime d_{opt} to reach the best clinical outcome

• Maximize $EY^*(d) = E[d(X)Y^*(1) + \{1 - d(X)\}Y^*(0)]$

$$d: X \to \{0, 1\}.$$

• Q(x, a) = E[Y|X = x, A = a],

- Q(x, a) = E[Y|X = x, A = a],
- $\tau_0(x) = Q(x,1) Q(x,0)$,

- Q(x, a) = E[Y|X = x, A = a],
- $\tau_0(x) = Q(x,1) Q(x,0)$,
- $V(d) = EY^*(d) = E[d(X)Y^*(1) + \{1 d(X)\}Y^*(0)].$

- Q(x, a) = E[Y|X = x, A = a],
- $\tau_0(x) = Q(x,1) Q(x,0)$,
- $V(d) = EY^*(d) = E[d(X)Y^*(1) + \{1 d(X)\}Y^*(0)].$

Optimal treatment regime

• SUTVA, no unmeasured confounders

- Q(x, a) = E[Y|X = x, A = a],
- $\tau_0(x) = Q(x,1) Q(x,0)$,
- $V(d) = EY^*(d) = E[d(X)Y^*(1) + \{1 d(X)\}Y^*(0)].$

Optimal treatment regime

- SUTVA, no unmeasured confounders
- optimal treatment regime

$$d_{opt}(x) = I(\tau_0(x) \ge 0).$$

• There are two types of clinically "important" variables.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.
 - Prescriptive variables are those involved in $d_{opt}(x)$.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.
 - Prescriptive variables are those involved in $d_{opt}(x)$.
- Predictive variables have interactions with the treatment.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.
 - Prescriptive variables are those involved in $d_{opt}(x)$.
- Predictive variables have interactions with the treatment.
- Prescriptive variables have qualitative interactions with the treatment.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.
 - Prescriptive variables are those involved in $d_{opt}(x)$.
- Predictive variables have interactions with the treatment.
- Prescriptive variables have qualitative interactions with the treatment.
- Prescriptive variables ⊆ predictive variables.

- There are two types of clinically "important" variables.
 - Predictive variables are those involved in $\tau_0(x)$.
 - Prescriptive variables are those involved in $d_{opt}(x)$.
- Predictive variables have interactions with the treatment.
- Prescriptive variables have qualitative interactions with the treatment.
- Prescriptive variables ⊆ predictive variables.
- Predictive variables ⊈ prescriptive variables.

• A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

• A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

• $d_{opt}(x) = I\{\exp(-x_1)x_2 \ge 0\} = I(x_2 \ge 0).$

A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

- $d_{opt}(x) = I\{\exp(-x_1)x_2 \ge 0\} = I(x_2 \ge 0).$
- x_1 and x_2 are the predictive variables.

• A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

- $d_{opt}(x) = I\{\exp(-x_1)x_2 \ge 0\} = I(x_2 \ge 0).$
- x_1 and x_2 are the predictive variables.
- x_2 is the prescriptive variable.

A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

- $d_{opt}(x) = I\{\exp(-x_1)x_2 \ge 0\} = I(x_2 \ge 0).$
- x_1 and x_2 are the predictive variables.
- x_2 is the prescriptive variable.
- x_1 and x_2 have interactions with the treatment.

A tiny example:

$$\tau_0(x) = \exp(-x_1)x_2,$$

for
$$\{x_1, x_2, \dots, x_p\} \in [-1, 1]^p$$
.

- $d_{opt}(x) = I\{\exp(-x_1)x_2 \ge 0\} = I(x_2 \ge 0).$
- x_1 and x_2 are the predictive variables.
- x_2 is the prescriptive variable.
- x_1 and x_2 have interactions with the treatment.
- x_2 has qualitative interaction with the treatment.

• Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.

- Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.
- Chang et al. (2015) and Hsu (2017) proposed nonparametric tests for testing the qualitative treatment effects.

- Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.
- Chang et al. (2015) and Hsu (2017) proposed nonparametric tests for testing the qualitative treatment effects.
- Here, we focus on the conditional qualitative treatment effects (CQTE).

- Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.
- Chang et al. (2015) and Hsu (2017) proposed nonparametric tests for testing the qualitative treatment effects.
- Here, we focus on the conditional qualitative treatment effects (CQTE).
 - Formalize the notion of CQTE and present equivalent representations of no CQTE.

- Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.
- Chang et al. (2015) and Hsu (2017) proposed nonparametric tests for testing the qualitative treatment effects.
- Here, we focus on the conditional qualitative treatment effects (CQTE).
 - Formalize the notion of CQTE and present equivalent representations of no CQTE.
 - Propose a testing procedure for testing the existence of CQTE.

- Gunter et al. (2011) proposed an *S*-score method for quantifying the magnitude of the qualitative treatment effects.
- Chang et al. (2015) and Hsu (2017) proposed nonparametric tests for testing the qualitative treatment effects.
- Here, we focus on the conditional qualitative treatment effects (CQTE).
 - Formalize the notion of CQTE and present equivalent representations of no CQTE.
 - Propose a testing procedure for testing the existence of CQTE.
 - Develop a variable selection procedure for selecting prescriptive variables in a sequential order.

Conditional qualitative treatment effects (CQTE)

• B and C are two disjoint subsets of $[1, \ldots, p]$.

Conditional qualitative treatment effects (CQTE)

- B and C are two disjoint subsets of $[1, \ldots, p]$.
- X^B and X^C are the subsets of X.

Conditional qualitative treatment effects (CQTE)

- B and C are two disjoint subsets of $[1, \ldots, p]$.
- X^B and X^C are the subsets of X.
- X^C have CQTE given X^B , if there exists some nonempty subsets C_1 , C_2 and B such that
 - (i) $\Pr\left\{(X^B,X^C)\in\mathcal{B}\times\mathcal{C}_1\right\}>0$ and $\Pr\left\{(X^B,X^C)\in\mathcal{B}\times\mathcal{C}_2\right\}>0$.
 - (ii) For any $x_1^C \in C_1$, $x_2^C \in C_2$ and $x^B \in \mathcal{B}$, we have

$$\arg \max_{a} \mathbb{E} \left\{ Y^{*}(a) | X^{B} = x^{B}, X^{C} = x_{1}^{C} \right\}$$

$$\neq \arg \max_{a} \mathbb{E} \left\{ Y^{*}(a) | X^{B} = x^{B}, X^{C} = x_{2}^{C} \right\}.$$

• $B = \emptyset$.

- $B = \emptyset$.
- \bullet CQTE = QTE.

- \bullet $B = \emptyset$.
- CQTE = QTE.
- Let

$$\tau_0^{C}(x^{C}) = E\{\tau_0(X)|X^{C} = x^{c}\}.$$

No CQTE means $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \geq 0, a.s$ or $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \leq 0, a.s.$

- \bullet $B = \emptyset$.
- CQTE = QTE.
- Let

$$\tau_0^{C}(x^{C}) = E\{\tau_0(X)|X^{C} = x^{c}\}.$$

No CQTE means $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \geq 0, a.s$ or $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \leq 0, a.s.$

Conditional qualitative treatment effects

B is not empty.

Unconditional qualitative treatment effects

- \bullet $B = \emptyset$.
- CQTE = QTE.
- Let

$$\tau_0^{C}(x^{C}) = E\{\tau_0(X)|X^{C} = x^{c}\}.$$

No CQTE means $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \geq 0, a.s$ or $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \leq 0, a.s.$

Conditional qualitative treatment effects

- B is not empty.
- Assume X^B have QTE.

Unconditional qualitative treatment effects

- \bullet $B = \emptyset$.
- CQTE = QTE.
- Let

$$\tau_0^{C}(x^{C}) = E\{\tau_0(X)|X^{C} = x^{c}\}.$$

No CQTE means $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \geq 0, a.s$ or $\tau_0^{\mathcal{C}}(X^{\mathcal{C}}) \leq 0, a.s.$

Conditional qualitative treatment effects

- B is not empty.
- Assume X^B have QTE.
- CQTE measures whether X^C are "important" in decision making given X^B .

• For any $D \subseteq [1, ..., p]$, define

$$au_0^D(x^D) = \mathsf{E}\{\tau_0(X)|X^D = x^D\},\ d_{opt}^D(x) = I(\tau_0^D(x^D) > 0).$$

9 / 20

• For any $D \subseteq [1, ..., p]$, define

$$\tau_0^D(x^D) = E\{\tau_0(X)|X^D = x^D\},
d_{opt}^D(x) = I(\tau_0^D(x^D) > 0).$$

• Let $W = B \cup C$. Define

$$\begin{split} \mathsf{ER}^{W,B} &= \left\{ \begin{array}{l} 0, \ \ \text{if} \ \ \tau_0^W(X) = 0, a.s. \\ \frac{\mathsf{E}[|d_{opt}^W(X) - d_{opt}^B(X)|I\{\tau_0^W(X^W) \neq 0\}]}{\mathsf{Pr}\{\tau_0^W(X^W) \neq 0\}}, \ \ \text{otherwise}, \\ \mathsf{VD}^{W,B} &= V(d_{opt}^W) - V(d_{opt}^B) \\ &= \ \mathsf{E}\left(\tau_0^W(X^W)[I\{\tau_0^W(X^W) \geq 0\} - I\{\tau_0^B(X^B) \geq 0\}]\right). \end{array} \right. \end{split}$$

Chengchun Shi (NCSU)

CQTE

July 30, 2017

Under certain conditions, the followings are equivalent:

(i) X^c doesn't have CQTE given X^B .

- (i) X^c doesn't have CQTE given X^B .
- (ii) $VD^{W,B} = 0$.

- (i) X^c doesn't have CQTE given X^B .
- (ii) $VD^{W,B} = 0$.
- (iii) $ER^{W,B} = 0$.

- (i) X^c doesn't have CQTE given X^B .
- (ii) $VD^{W,B} = 0$.
- (iii) $ER^{W,B} = 0$.
- (iv) For any x^W such that $\tau_0^W(x^W) \neq 0$, $d_{opt}^W(x) = d_{opt}^B(x)$.

- (i) X^c doesn't have CQTE given X^B .
- (ii) $VD^{W,B} = 0$.
- (iii) $ER^{W,B} = 0$.
- (iv) For any x^W such that $\tau_0^W(x^W) \neq 0$, $d_{opt}^W(x) = d_{opt}^B(x)$.
- (v) For any fixed x^B , $\tau_0^W(x^B, x^C) \ge 0$ for any x^C or $\tau_0^W(x^B, x^C) \le 0$ for any x^C .

 $\bullet \ \tau_0(x_1,x_2)=x_1x_2^2.$

11 / 20

- $\tau_0(x_1, x_2) = x_1 x_2^2$.
- No CQTE.

- $\tau_0(x_1, x_2) = x_1 x_2^2$.
- No CQTE.
- $\tau_0(x_1, x_2) = x_1 \max(x_2, 0)$.

- $\tau_0(x_1, x_2) = x_1 x_2^2$.
- No CQTE.
- $\tau_0(x_1, x_2) = x_1 \max(x_2, 0)$.
- No CQTE.

- $\tau_0(x_1, x_2) = x_1 x_2^2$.
- No CQTE.
- $\tau_0(x_1, x_2) = x_1 \max(x_2, 0)$.
- No CQTE.
- $\bullet \ \tau_0(x_1,x_2)=x_1(x_2-2).$

- $\tau_0(x_1, x_2) = x_1 x_2^2$.
- No CQTE.
- $\tau_0(x_1, x_2) = x_1 \max(x_2, 0)$.
- No CQTE.
- $\tau_0(x_1,x_2)=x_1(x_2-2)$.
- No CQTE.

• Hypothesis testing:

$$H_0: X^C$$
 doens't have CQTE given X^B ,

versus

$$H_1: X^C$$
 has CQTE given X^B .

Hypothesis testing:

$$H_0: X^C$$
 doens't have CQTE given X^B ,

versus

$$H_1: X^C$$
 has CQTE given X^B .

• Such hypothesis assesses the incremental value of X^C in optimal treatment decision making conditional on X^B .

Hypothesis testing:

$$H_0: X^C$$
 doens't have CQTE given X^B ,

versus

$$H_1: X^C$$
 has CQTE given X^B .

- Such hypothesis assesses the incremental value of X^C in optimal treatment decision making conditional on X^B .
- If H_0 holds, estimate $d_{opt}^B(x)$.

Hypothesis testing:

$$H_0: X^C$$
 doens't have CQTE given X^B ,

versus

$$H_1: X^C$$
 has CQTE given X^B .

- Such hypothesis assesses the incremental value of X^C in optimal treatment decision making conditional on X^B .
- If H_0 holds, estimate $d_{opt}^B(x)$.
- Otherwise, estimate $d_{opt}^W(x)$.

• Let f^W be the probability density function of X^W .

- Let f^W be the probability density function of X^W .
- Estimate $\tau_0^W(x^W)f^W(x^W)$ by

$$\tau_n^W(x^W) = \frac{1}{n} \sum_{i=1}^n \left(\frac{A_i}{\pi_i} - \frac{1 - A_i}{1 - \pi_i} \right) Y_i K_{hW}^W(x^W - X_i^W),$$

for some multivariate kernel function $k_{h^W}^W$ with the bandwidth h^W .

Chengchun Shi (NCSU)

Testing procedure

$$S_{n}^{W,B} = \int_{x^{W} \in \Omega^{W}} \tau_{n}^{W}(x^{W}) \{d_{n}^{W}(x^{W}) - d_{n}^{B}(x^{B})\} I(x^{W} \notin \hat{E}) d\nu(x^{W}),$$

where

$$\hat{E} = \left\{ x^W : \left| \frac{\tau_n^W(x^W)}{\hat{f}^W(x^W)} \right| \le \eta_n, \left| \frac{\tau_n^B(x^B)}{\hat{f}^B(x^B)} \right| \le \eta_n \right\},\,$$

for some sequence $\eta_n \to 0$. Here, \hat{f}^W and \hat{f}^B are the kernel density estimators of f^W and f^B , respectively.

Testing procedure (Cont'd)

Let

$$\hat{F} = \{x^W : |\tau_n^W(x^W)/\hat{f}^W(x^W)| \le \eta_n, |\tau_n^B(x^B)/\hat{f}^B(x^B)| > \eta_n\}.$$

The test statistic is defined by

$$T_n^{W,B} = \begin{cases} \frac{\{\sqrt{n}S_n^{W,B} - \hat{a}_n(\hat{F})\}/\hat{\sigma}_n(\hat{F}), & \text{if } \nu(\hat{F}) \neq 0, \\ \{\sqrt{n}S_n^{W,B} - \hat{a}_n(\Omega^W)\}/\hat{\sigma}_n(\Omega^W), & \text{otherwise.} \end{cases}$$

We reject the null when $T_n^{W,B} > z_{\infty}$.

Chengchun Shi (NCSU)

Under certain conditions, when H_0 is true, we have

$$\lim Pr(T_n^{W,B} > z_\alpha) \le \alpha,$$

for $0 < \alpha \le 0.5$.

Under certain conditions, when H_0 is true, we have

$$\lim Pr(T_n^{W,B} > z_\alpha) \le \alpha,$$

for 0 <
$$\alpha \le$$
 0.5. If $\Pr\{\tau_0^W(X^W) = 0\} = 0$, we have

$$\lim Pr(T_n^{W,B}>z_\alpha)=0.$$

Under certain conditions, when H_0 is true, we have

$$\lim Pr(T_n^{W,B}>z_\alpha)\leq \alpha,$$

for
$$0 < \alpha \le 0.5$$
. If $Pr\{\tau_0^W(X^W) = 0\} = 0$, we have

$$\lim Pr(T_n^{W,B}>z_\alpha)=0.$$

When H_1 is true, we have

$$\lim Pr(T_n^{W,B} > z_\alpha) \to 1.$$

Chengchun Shi (NCSU)

Under certain conditions, when H_0 is true, we have

$$\lim Pr(T_n^{W,B} > z_\alpha) \le \alpha,$$

for
$$0 < \alpha \le 0.5$$
. If $Pr\{\tau_0^W(X^W) = 0\} = 0$, we have

$$\lim Pr(T_n^{W,B}>z_\alpha)=0.$$

When H_1 is true, we have

$$\lim Pr(T_n^{W,B} > z_\alpha) \to 1.$$

Theorem (Informal statement)

Under certain conditions, $T_n^{W,B}$ has non-negligible powers against some nonstandard $n^{-1/2}$ local alternatives.

Simulation models:

$$Y = 1 - \frac{X_1 - X_2}{2} + A\phi_1(X_1)\phi_2(X_2) + e,$$

Table: Simulation results.

		VD = 0		VD = 4%		VD = 8%		VD = 12%	
		lpha level		lpha level		lpha level		lpha level	
	n	0.05	0.1	0.05	0.1	0.05	0.1	0.05	0.1
Scenario 1	300	4.3%	6.0%	24.0%	34.0%	58.7%	68.1%	82.2%	87.5%
	600	1.5%	3.3%	36.7%	45.5%	75.8%	83.3%	95.7%	97.3%
Scenario 2	300	7.0%	11.1%	23.8%	32.7%	60.5%	69.3%	88.2%	92.3%
	600	5.5%	10.0%	31.0%	41.8%	83.0%	90.5%	98.3%	99.5%
Scenario 3	300	3.8%	6.5%	37.3%	48.5%	76.3%	79.7%	92.7%	94.7%
	600	2.7%	6.7%	52.5%	61.8%	99.2%	100%	99.8%	99.8%
Scenario 4	300	6.2%	9.8%	39.8%	47.7%	79.2%	87.3%	94.8%	96.7%
	600	5.2%	8.8%	59.3%	68.2%	96.8%	98.3%	99.5%	99.5%
Scenario 5	300	5.2%	9.7%	29.3%	40.5%	68.0%	76.3%	94.0%	96.8%
	600	5.3%	9.5%	36.7%	45.5%	75.8%	83.3%	95.7%	97.3%

• Set $B = \emptyset$. In Step 1, for each variable i, define the set $W_i = \{i\}$ and calculate the p-value p_i for each test statistic $T^{W_i,B}$. Stop if $\min_i p_i > \alpha$. Include the variable that gives the smallest p-value in the set B, i.e,

$$B \leftarrow \{\arg\min_{i} p_{i}\}.$$

③ Set $B = \emptyset$. In Step 1, for each variable i, define the set $W_i = \{i\}$ and calculate the p-value p_i for each test statistic $T^{W_i,B}$. Stop if $\min_i p_i > \alpha$. Include the variable that gives the smallest p-value in the set B, i.e,

$$B \leftarrow \{\arg\min_{i} p_{i}\}.$$

② In Step 2, for each variable $i \notin B$, define $W_i = B \cup \{i\}$ and calculate the p-value p_i for each test statistic $T^{W_i,B}$. Stop if $\min_i p_i > \alpha$. Include the variable that gives the smallest p-value,

$$B \leftarrow B \cup \{ \arg \min_{i} p_i \}.$$

① Set $B = \emptyset$. In Step 1, for each variable i, define the set $W_i = \{i\}$ and calculate the p-value p_i for each test statistic $T^{W_i,B}$. Stop if $\min_i p_i > \alpha$. Include the variable that gives the smallest p-value in the set B, i.e,

$$B \leftarrow \{\arg\min_{i} p_i\}.$$

② In Step 2, for each variable $i \notin B$, define $W_i = B \cup \{i\}$ and calculate the p-value p_i for each test statistic $T^{W_i,B}$. Stop if $\min_i p_i > \alpha$. Include the variable that gives the smallest p-value,

$$B \leftarrow B \cup \{\arg\min_{i} p_{i}\}.$$

3 Continue the second step until it stops. Output *B*.

• Introduce the notion of CQTE and present several equivalent representations of No CQTE.

- Introduce the notion of CQTE and present several equivalent representations of No CQTE.
- Propose a testing procedure for testing No CQTE.

- Introduce the notion of CQTE and present several equivalent representations of No CQTE.
- Propose a testing procedure for testing No CQTE.
- Develop a procedure for selecting prescriptive variables in sequential order.

- Introduce the notion of CQTE and present several equivalent representations of No CQTE.
- Propose a testing procedure for testing No CQTE.
- Develop a procedure for selecting prescriptive variables in sequential order.
- Extend the testing procedure to a high-dimensional setting.

Thank you!