Isotonic subgroup selection

CCIMI 7th Annual Academic Conference

May 2023

Manuel Müller

University of Cambridge, CCIMI

<□ > <□ > <□ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □



Henry Reeve

Timothy Cannings

Richard Samworth

M., M. M., Reeve, H. W. J., Cannings, T. I. and Samworth, R. J. (2023). Isotonic subgroup selection. arXiv:2305.04852.

Subgroup selection in regression: Identify a subset of the covariate domain on which the regression function satisfies a particular property (e.g. exceeds a threshold).

Subgroup selection in regression: Identify a subset of the covariate domain on which the regression function satisfies a particular property (e.g. exceeds a threshold).

Setting:

Fix $\sigma > 0$. Let $\mathcal{P}_{Mon,d}(\sigma)$ be the family of distributions P on $\mathbb{R}^d \times \mathbb{R}$ such that for $(X, Y) \sim P$,

Subgroup selection in regression: Identify a subset of the covariate domain on which the regression function satisfies a particular property (e.g. exceeds a threshold).

Setting:

Fix $\sigma > 0$. Let $\mathcal{P}_{Mon,d}(\sigma)$ be the family of distributions P on $\mathbb{R}^d \times \mathbb{R}$ such that for $(X, Y) \sim P$,

(i) the regression function $\eta(x) := \mathbb{E}(Y|X = x)$ is increasing^{*} on \mathbb{R}^d .

$$^*x_0 \preccurlyeq x_1 \Longrightarrow \eta(x_0) \le \eta(x_1).$$

Isotonic Subgroup Selection

Subgroup selection in regression: Identify a subset of the covariate domain on which the regression function satisfies a particular property (e.g. exceeds a threshold).

Setting:

Fix $\sigma > 0$. Let $\mathcal{P}_{Mon,d}(\sigma)$ be the family of distributions P on $\mathbb{R}^d \times \mathbb{R}$ such that for $(X, Y) \sim P$,

(i) the regression function $\eta(x) := \mathbb{E}(Y|X = x)$ is increasing^{*} on \mathbb{R}^d .

(ii) $Y - \eta(X) \mid X$ is sub-Gaussian with variance parameter σ^2 .

$$^*x_0 \preccurlyeq x_1 \Longrightarrow \eta(x_0) \le \eta(x_1).$$

Isotonic Subgroup Selection

Notation:

Fix
$$\tau \in \mathbb{R}$$
. Define τ -superlevel set by $\mathcal{X}_{\tau}(\eta) := \{x \in \mathbb{R}^d : \eta(x) \ge \tau\}.$

Notation:

► Fix $\tau \in \mathbb{R}$. Define τ -superlevel set by $\mathcal{X}_{\tau}(\eta) := \{x \in \mathbb{R}^d : \eta(x) \ge \tau\}.$

• μ denotes the marginal distribution of X.

Notation:

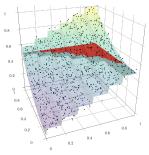
- ► Fix $\tau \in \mathbb{R}$. Define τ -superlevel set by $\mathcal{X}_{\tau}(\eta) := \{x \in \mathbb{R}^d : \eta(x) \ge \tau\}.$
- μ denotes the marginal distribution of *X*.

$$\blacktriangleright \mathcal{D} := ((X_1, Y_1), \dots, (X_n, Y_n)).$$

Notation:

- ► Fix $\tau \in \mathbb{R}$. Define τ -superlevel set by $\mathcal{X}_{\tau}(\eta) := \{x \in \mathbb{R}^d : \eta(x) \ge \tau\}.$
- μ denotes the marginal distribution of *X*.

$$\blacktriangleright \mathcal{D} := ((X_1, Y_1), \dots, (X_n, Y_n)).$$

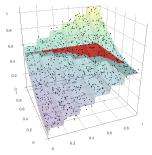


Goal: algorithm that returns a selected set $\hat{A}(\mathcal{D}) \subseteq \mathbb{R}^d$

Notation:

- ► Fix $\tau \in \mathbb{R}$. Define τ -superlevel set by $\mathcal{X}_{\tau}(\eta) := \{x \in \mathbb{R}^d : \eta(x) \ge \tau\}.$
- μ denotes the marginal distribution of X.

$$\blacktriangleright \mathcal{D} := ((X_1, Y_1), \dots, (X_n, Y_n)).$$



Goal: algorithm that returns a selected set $\hat{A}(\mathcal{D}) \subseteq \mathbb{R}^d$ with:

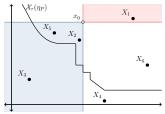
• Type I error control: Fix $\alpha \in (0, 1)$. Require

$$\inf_{P \in \mathcal{P}_{\mathrm{Mon},d}(\sigma)} \mathbb{P}_P\{\hat{A}(\mathcal{D}) \subseteq \mathcal{X}_\tau(\eta)\} \ge 1 - \alpha.$$

Power: Want small expected regret

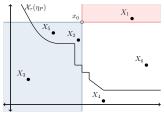
$$\mathbb{E}\big\{\mu\big(\mathcal{X}_{\tau}(\eta)\setminus \hat{A}(\mathcal{D})\big)\big\}.$$

For $x_0 \in \mathbb{R}^d$, define null hypothesis $H_0(x_0) := \{P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau\}.$



- 2. Construct *p*-values \hat{p}_{ℓ} for $H_0(X_{\ell})$, i.e. $\mathbb{P}(\hat{p}_{\ell}(\mathcal{D}) \leq \alpha \mid (X_i)_{i=1}^n) \leq \alpha$ for all $P \in H_0(X_{\ell}), \alpha \in (0, 1), \ell \in \{1, ..., m\};$
- 3. Apply a multiple testing procedure to reject $\mathcal{R}_{\alpha} \subseteq \{1, \ldots, m\}$ with $\mathbb{P}_{P}(\mathcal{R}_{\alpha} \cap \{\ell \in \{1, \ldots, m\} : P \in H_{0}(X_{\ell})\} \neq \emptyset \mid (X_{i})_{i=1}^{m}) \leq \alpha;$
- 4. Output $\hat{A}:=\{x\in \mathbb{R}^d: X_\ell \preccurlyeq x$ for some $\ell\in \mathcal{R}_lpha\}.$

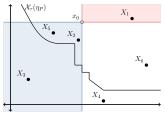
For $x_0 \in \mathbb{R}^d$, define null hypothesis $H_0(x_0) := \{P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau\}.$



High-level strategy:

1. Sub-sample *m* covariate vectors X_1, \ldots, X_m with $m \le n$;

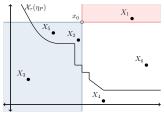
For $x_0 \in \mathbb{R}^d$, define null hypothesis $H_0(x_0) := \{P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau\}.$



High-level strategy:

- 1. Sub-sample *m* covariate vectors X_1, \ldots, X_m with $m \leq n$;
- 2. Construct *p*-values \hat{p}_{ℓ} for $H_0(X_{\ell})$, i.e. $\mathbb{P}(\hat{p}_{\ell}(\mathcal{D}) \leq \alpha \mid (X_i)_{i=1}^n) \leq \alpha$ for all $P \in H_0(X_{\ell}), \alpha \in (0, 1), \ell \in \{1, \dots, m\};$

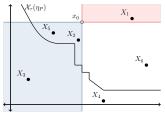
For $x_0 \in \mathbb{R}^d$, define null hypothesis $H_0(x_0) := \{P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau\}.$



High-level strategy:

- 1. Sub-sample *m* covariate vectors X_1, \ldots, X_m with $m \le n$;
- 2. Construct *p*-values \hat{p}_{ℓ} for $H_0(X_{\ell})$, i.e. $\mathbb{P}(\hat{p}_{\ell}(\mathcal{D}) \leq \alpha \mid (X_i)_{i=1}^n) \leq \alpha$ for all $P \in H_0(X_{\ell}), \alpha \in (0, 1), \ell \in \{1, \dots, m\};$
- 3. Apply a multiple testing procedure to reject $\mathcal{R}_{\alpha} \subseteq \{1, ..., m\}$ with $\mathbb{P}_{P}(\mathcal{R}_{\alpha} \cap \{\ell \in \{1, ..., m\} : P \in H_{0}(X_{\ell})\} \neq \emptyset \mid (X_{i})_{i=1}^{m}) \leq \alpha;$

For $x_0 \in \mathbb{R}^d$, define null hypothesis $H_0(x_0) := \{P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau\}.$



High-level strategy:

- 1. Sub-sample *m* covariate vectors X_1, \ldots, X_m with $m \le n$;
- 2. Construct *p*-values \hat{p}_{ℓ} for $H_0(X_{\ell})$, i.e. $\mathbb{P}(\hat{p}_{\ell}(\mathcal{D}) \leq \alpha \mid (X_i)_{i=1}^n) \leq \alpha$ for all $P \in H_0(X_{\ell}), \alpha \in (0, 1), \ell \in \{1, \dots, m\};$
- 3. Apply a multiple testing procedure to reject $\mathcal{R}_{\alpha} \subseteq \{1, \ldots, m\}$ with $\mathbb{P}_{P}(\mathcal{R}_{\alpha} \cap \{\ell \in \{1, \ldots, m\} : P \in H_{0}(X_{\ell})\} \neq \emptyset \mid (X_{i})_{i=1}^{m}) \leq \alpha;$
- 4. Output $\hat{A} := \{ x \in \mathbb{R}^d : X_\ell \preccurlyeq x \text{ for some } \ell \in \mathcal{R}_\alpha \}.$

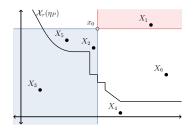
p-value construction

Given $x_0 \in \mathbb{R}^d$, we seek a *p*-value for $H_0(x_0) := \{ P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau \}.$

p-value construction

Given $x_0 \in \mathbb{R}^d$, we seek a *p*-value for $H_0(x_0) := \{ P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau \}.$

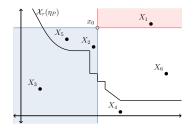
Write $\mathcal{I}(x_0) := \{i \in [n] : X_i \preccurlyeq x_0\}$. Let $X_{(j)}$ be the *j*th nearest neighbor in sup-norm of x_0 among $X_i, i \in \mathcal{I}(x_0)$, and let $Y_{(j)}$ be the corresponding response.



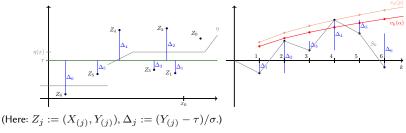
p-value construction

Given $x_0 \in \mathbb{R}^d$, we seek a *p*-value for $H_0(x_0) := \{ P \in \mathcal{P}_{Mon,d}(\sigma) : \eta(x_0) < \tau \}.$

Write $\mathcal{I}(x_0) := \{i \in [n] : X_i \preccurlyeq x_0\}$. Let $X_{(j)}$ be the *j*th nearest neighbor in sup-norm of x_0 among $X_i, i \in \mathcal{I}(x_0)$, and let $Y_{(j)}$ be the corresponding response.



Then, $S_k := \sum_{j=1}^{|\mathcal{I}(x_0)|} (Y_{(j)} - \tau) / \sigma$ is a supermartingale under $P \in H_0(x_0)$. Combination with time-uniform bounds by Howard et al. (2021) gives *p*-values.



Isotonic Subgroup Selection

Combining the presented *p*-value construction with the just illustrated multiple testing procedure defines the proposed procedure $\hat{A}^{\text{ISS}} \equiv \hat{A}^{\text{ISS}}_{\sigma,\tau,\alpha,m}$.

Theorem. For any $n \in \mathbb{N}$, $m \in [n]$, $\alpha \in (0, 1)$, $\sigma > 0$, and $P \in \mathcal{P}_{Mon,d}(\sigma)$, along with $\mathcal{D} \sim P^n$, we have

$$\mathbb{P}_P(\hat{A}_{\sigma,\tau,\alpha,m}^{\mathrm{ISS}}(\mathcal{D}) \subseteq \mathcal{X}_{\tau}(\eta) \mid \mathcal{D}_X) \ge 1 - \alpha.$$

Ideas: martingale test procedures (Duan et al., 2020), time-uniform boundaries on martingales with sub-Gaussian increments (Howard et al., 2021) and the sequential rejection principle (Goeman and Solari, 2010).

Theorem. Let $\sigma, \gamma > 0, \theta > 1$ and $\lambda \in (0, 1)$. There exists $C \ge 1$, depending only on (d, θ) , such that for any $P \in \mathcal{P}_{Mon,d}(\sigma) \cap \mathcal{P}_{\text{Reg},d}(\tau, \theta, \gamma, \lambda), n \in \mathbb{N}$, $m \in [n], \alpha \in (0, 1)$ and $\mathcal{D} \sim P^n$ that^{*a*}

$$\mathbb{E}_{P}\left\{\mu\left(\mathcal{X}_{\tau}(\eta)\setminus\hat{A}^{\mathrm{ISS}}(\mathcal{D})\right)\right\} \leq 1\wedge C\left\{\left(\frac{\sigma^{2}}{n\lambda^{2}}\log_{+}\left(\frac{m\log_{+}n}{\alpha}\right)\right)^{1/(2\gamma+d)} + \left(\frac{\log_{+}m}{m}\right)^{1/d}\right\}.$$

 $a \log_+ x := \log(x \lor e).$

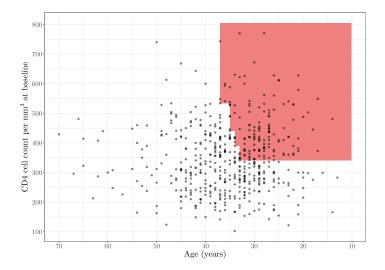
Theorem. Let $\sigma, \gamma > 0, \theta > 1$ and $\lambda \in (0, 1)$. There exists $C \ge 1$, depending only on (d, θ) , such that for any $P \in \mathcal{P}_{Mon,d}(\sigma) \cap \mathcal{P}_{\text{Reg},d}(\tau, \theta, \gamma, \lambda), n \in \mathbb{N}$, $m \in [n], \alpha \in (0, 1)$ and $\mathcal{D} \sim P^n$ that^{*a*}

$$\mathbb{E}_{P}\left\{\mu\left(\mathcal{X}_{\tau}(\eta)\setminus\hat{A}^{\mathrm{ISS}}(\mathcal{D})\right)\right\} \leq 1\wedge C\left\{\left(\frac{\sigma^{2}}{n\lambda^{2}}\log_{+}\left(\frac{m\log_{+}n}{\alpha}\right)\right)^{1/(2\gamma+d)}+\left(\frac{\log_{+}m}{m}\right)^{1/d}\right\}.$$

$$\overline{\log_{+}x:=\log(x\vee e).}$$

Theorem. Our procedure is minimax-optimal up to poly-logarithmic factors among procedures with Type I error control over $\mathcal{P}_{Mon,d}(\sigma) \cap \mathcal{P}_{\text{Reg},d}(\tau,\theta,\gamma,\lambda)$.

AIDS Clinical Trials Group Study 175 (Hammer et al., 1996)



▶ We addressed the problem of subgroup selection in isotonic regression.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

Extensions and further results (see full paper for details):

Variation tailored to bounded responses and classification.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

- Variation tailored to bounded responses and classification.
- Variation tailored to isotonic quantile regression.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

- Variation tailored to bounded responses and classification.
- Variation tailored to isotonic quantile regression.
- Use in heterogeneous treatment effects in randomised controlled trials.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

- Variation tailored to bounded responses and classification.
- Variation tailored to isotonic quantile regression.
- Use in heterogeneous treatment effects in randomised controlled trials.
- Further applications and simulations.

- ▶ We addressed the problem of subgroup selection in isotonic regression.
- We propose a computationally-feasible algorithm controlling Type I error.
- We show minimax-optimality up to poly-logarithmic factors of our method.

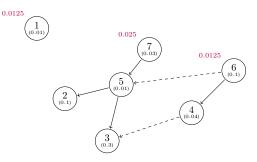
- Variation tailored to bounded responses and classification.
- Variation tailored to isotonic quantile regression.
- Use in heterogeneous treatment effects in randomised controlled trials.
- Further applications and simulations.

- Duan, B., Ramdas, A., Balakrishnan, S., and Wasserman, L. (2020). Interactive martingale tests for the global null. *Electronic Journal of Statistics*, 14(2):4489–4551.
- Goeman, J. J. and Solari, A. (2010). The sequential rejection principle of familywise error control. *The Annals of Statistics*, 38(6):3782-3810.
- Hammer, S. M., Katzenstein, D. A., Hughes, M. D., Gundacker, H., Schooley, R. T., Haubrich, R. H., Henry, W. K., Lederman, M. M., Phair, J. P., Niu, M., et al. (1996). A trial comparing nucleoside monotherapy with combination therapy in HIV-infected adults with CD4 cell counts from 200 to 500 per cubic millimeter. *New England Journal of Medicine*, 335(15):1081–1090.
- Howard, S. R., Ramdas, A., McAuliffe, J., and Sekhon, J. (2021). Time-uniform, nonparametric, nonasymptotic confidence sequences. *The Annals of Statistics*, 49:1055–1080.
- Meijer, R. J. and Goeman, J. J. (2015). A multiple testing method for hypotheses structured in a directed acyclic graph. *Biometrical Journal*, 57(1):123–143.

Key idea: logical relationships of hypotheses $H_0(x_i)$, $i \in [m]$, induce DAG with vertex set [m]. Careful α -budget allocation and sequential rejections are then performed.

Key idea: logical relationships of hypotheses $H_0(x_i)$, $i \in [m]$, induce DAG with vertex set [m]. Careful α -budget allocation and sequential rejections are then performed.

Example: In the first iteration, no hypothesis has been rejected yet and only root nodes are assigned positive α -budget.

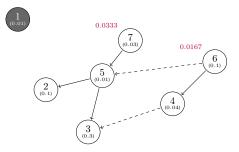


Here, nodes 1, 6 and 7 are current rejection candidates, and 1 will be rejected, as $p_1 = 0.01 \le 0.0125$.

Isotonic Subgroup Selection

Key idea: logical relationships of hypotheses $H_0(x_i)$, $i \in [m]$, induce DAG with vertex set [m]. Careful α -budget allocation and sequential rejections are then performed.

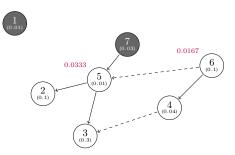
Example: After rejection of node 1 in the first step, we reallocate the α -budget.



Here, node 7 will be rejected.

Key idea: logical relationships of hypotheses $H_0(x_i)$, $i \in [m]$, induce DAG with vertex set [m]. Careful α -budget allocation and sequential rejections are then performed.

Example: Now that node 7 has been rejected, its child 5 receives α -budget sufficiently large for it to be rejected.

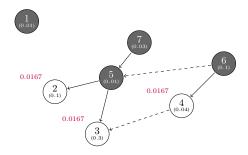


Although p_6 is quite large, 6 is an ancestor of 5 in the induced DAG and will hence also be rejected.

Isotonic Subgroup Selection

Key idea: logical relationships of hypotheses $H_0(x_i)$, $i \in [m]$, induce DAG with vertex set [m]. Careful α -budget allocation and sequential rejections are then performed.

Example: None of the remaining three nodes (coincidentally, the leaf nodes), have a *p*-value smaller than their respective α -budgets.



Nodes 1, 5, 6 and 7 have been rejected.

Given $d \in \mathbb{N}$, $\tau \in \mathbb{R}$, $\theta > 1$, $\gamma > 0$ and $\lambda \in (0, 1)$, we let $\mathcal{P}_{\operatorname{Reg},d}(\tau, \theta, \gamma, \lambda)$ denote the class of all distributions P on $\mathbb{R}^d \times \mathbb{R}$ with marginal μ on \mathbb{R}^d and associated regression function η such that

(i) $\theta^{-1} \cdot r^d \leq \mu \left(B_{\infty}(x,r) \right) \leq \theta \cdot (2r)^d$ for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0,1]$;

(ii) $B_{\infty}(x,r) \cap \mathcal{X}_{\tau+\lambda \cdot r^{\gamma}}(\eta) \neq \emptyset$ for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0,1]$,

where $B_{\infty}(x,r)$ is the closed sup-norm ball around x of radius r.

Given $d \in \mathbb{N}$, $\tau \in \mathbb{R}$, $\theta > 1$, $\gamma > 0$ and $\lambda \in (0, 1)$, we let $\mathcal{P}_{\text{Reg},d}(\tau, \theta, \gamma, \lambda)$ denote the class of all distributions P on $\mathbb{R}^d \times \mathbb{R}$ with marginal μ on \mathbb{R}^d and associated regression function η such that

(i)
$$\theta^{-1} \cdot r^d \le \mu \left(B_{\infty}(x, r) \right) \le \theta \cdot (2r)^d$$
 for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0, 1]$;

(ii) $B_{\infty}(x,r) \cap \mathcal{X}_{\tau+\lambda \cdot r^{\gamma}}(\eta) \neq \emptyset$ for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0,1]$,

where $B_{\infty}(x,r)$ is the closed sup-norm ball around x of radius r.

The first condition ensures that μ is genuinely *d*-dimensional.

Given $d \in \mathbb{N}$, $\tau \in \mathbb{R}$, $\theta > 1$, $\gamma > 0$ and $\lambda \in (0, 1)$, we let $\mathcal{P}_{\operatorname{Reg},d}(\tau, \theta, \gamma, \lambda)$ denote the class of all distributions P on $\mathbb{R}^d \times \mathbb{R}$ with marginal μ on \mathbb{R}^d and associated regression function η such that

(i)
$$\theta^{-1} \cdot r^d \leq \mu \left(B_{\infty}(x,r) \right) \leq \theta \cdot (2r)^d$$
 for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0,1]$;

(ii) $B_{\infty}(x,r) \cap \mathcal{X}_{\tau+\lambda \cdot r^{\gamma}}(\eta) \neq \emptyset$ for $x \in \mathcal{X}_{\tau}(\eta) \cap \operatorname{supp}(\mu)$ and $r \in (0,1]$, where $B_{\infty}(x,r)$ is the closed sup-norm ball around x of radius r.

The first condition ensures that μ is genuinely *d*-dimensional.

The second controls the way in which η grows around the τ -boundary.

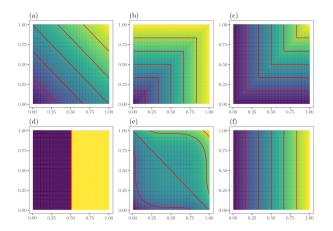
We conduct a simulation study to compare with other choices of multiple testing procedure.

Label	Function f	au	$\gamma(P)$
(a)	$\sum_{j=1}^{d} x^{(j)}$	1/2	1
(b)	$\max_{1 \le j \le d} x^{(j)}$	$1/2^{1/d}$	1
(c)	$\min_{1 \le j \le d} x^{(j)}$	$1 - 1/2^{1/d}$	1
(d)	$\mathbb{1}_{(0.5,1]}(x^{(1)})$	1/2	0
(e)	$\sum_{j=1}^{d} \left(x^{(j)} - 0.5 \right)^3$	1/2	3
(f)	$x^{(1)}$	1/2	1

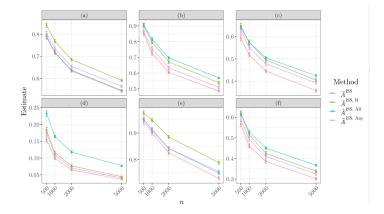
Our regression functions η are obtained by rescaling f.

Simulations: multiple testing procedure

We conduct a simulation study to compare with other choices of multiple testing procedure.



Simulations: multiple testing procedure



Presented is the MC-based estimate of $\mathbb{E}_P\{\mu(\mathcal{X}_\tau(\eta) \setminus \hat{A})\}$ for $\hat{A} \in \{\hat{A}^{\text{ISS}}, \hat{A}^{\text{ISS},\text{H}}, \hat{A}^{\text{ISS},\text{All}}, \hat{A}^{\text{ISS},\text{Any}}\}$. The last two use methods due to Meijer and Goeman (2015).