

Nonparametric Inference on Dose-Response Curves Without the Positivity Condition

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Joint work with *Professor Yen-Chi Chen*

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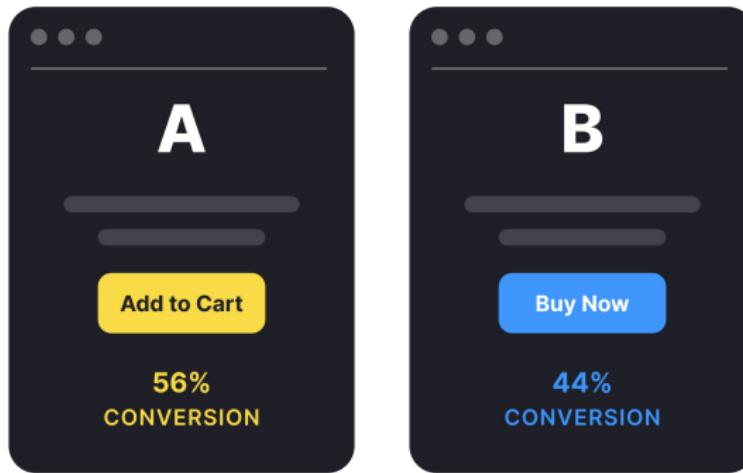
Introduction



Fundamental Problem of Causal Inference

► The Central Problem in Causal Inference:

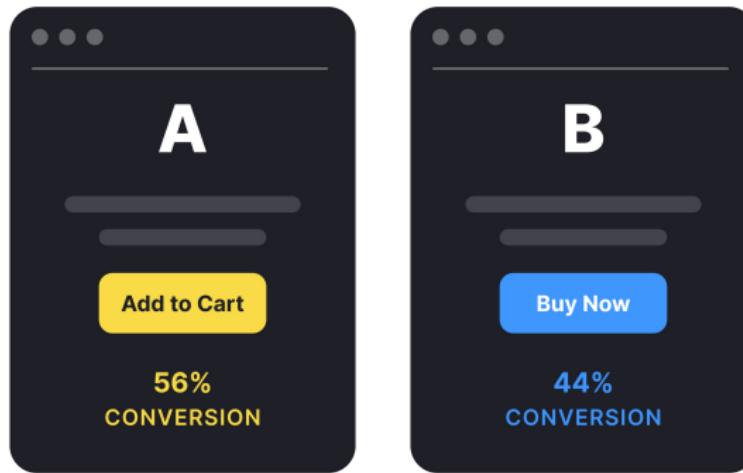
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Fundamental Problem of Causal Inference

► The Central Problem in Causal Inference:

Study the causal effect of a treatment $T \in \mathcal{T}$ on the outcome of interest $Y \in \mathcal{Y}$.



- The treatment is *binary*, i.e., $\mathcal{T} \in \{0, 1\}$.
- Only one potential outcome, $Y(1)$ or $Y(0)$, is observed for each unit.
- The causal estimand is $\mathbb{E}[Y(1)] - \mathbb{E}[Y(0)]$, i.e., average treatment effect.

Effects of PM_{2.5} on Cardiovascular Mortality Rates

► **Motivation:** We want to study the causal effects of PM_{2.5} levels on Cardiovascular Mortality Rates.

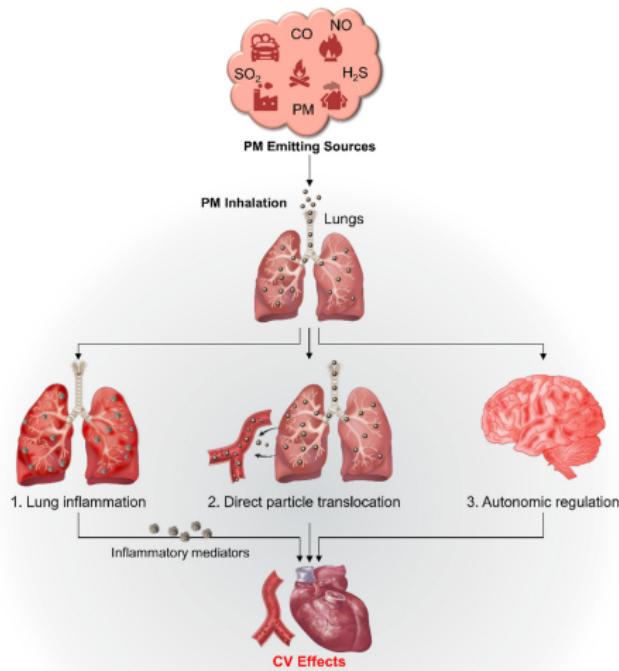


Figure: Biological pathways associated with particulate matter (PM) and cardiovascular disease ([Miller and Newby, 2020](#); [Basith et al., 2022](#)).

County-level PM_{2.5} and CMR Data

We have data for the average annual cardiovascular mortality rates (CMRs) and PM_{2.5} levels across $n = 2132$ U.S. counties over 1990-2010¹.

FIPS	County name	Longitude	Latitude	PM2.5	CMR
1025	Clarke	-87.830772	31.676955	6.766443	379.421713
1061	Geneva	-85.839330	31.094869	8.254272	378.524698
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¹Sources: US National Center for Health Statistics and Community Multiscale Air Quality modeling system; see [Wyatt et al. \(2020\)](#).

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- **Challenge:** The treatment variable, PM_{2.5} level at each county, is *not a binary but continuous variable*.

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Causal Inference For Continuous Treatments

For *binary* treatment (*i.e.*, $\mathcal{T} \in \{0, 1\}$), common causal estimands are

- $\mathbb{E}[Y(t)]$ = mean counterfactual outcome when we set $T = t$.
- $\mathbb{E}[Y(1)] - \mathbb{E}[Y(0)]$ = average treatment effect.

► **Question:** What are the counterparts of the above estimands under *continuous* treatment (*i.e.*, $\mathcal{T} \subset \mathbb{R}$)?

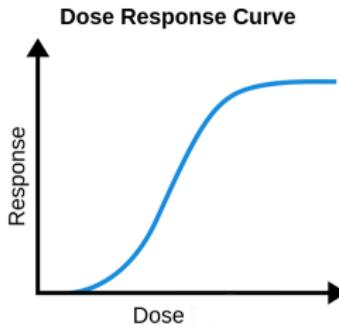
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- $t \mapsto m(t) := \mathbb{E}[Y(t)]$ = (causal) dose-response curve.
- $t \mapsto \theta(t) := m'(t) = \frac{d}{dt}\mathbb{E}[Y(t)]$ = (causal) derivative effect.



Identification of Dose-Response Curves in RCTs

In randomized controlled trials (RCTs),

$$m(t) = \mathbb{E}[Y(t)] = \mathbb{E}(Y|T=t) \quad \text{and} \quad \theta(t) = \frac{d}{dt} \mathbb{E}(Y|T=t).$$

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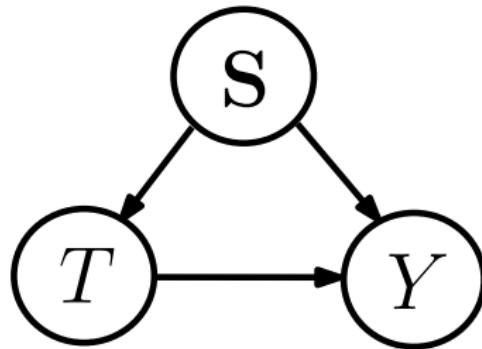
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- Some identification assumptions are required to estimate $m(t)$ and $\theta(t)$ from the observable data $\{(Y_i, T_i, S_i)\}_{i=1}^n$.

Assumption

- ① (Consistency) $Y = Y(t)$ whenever $T = t \in \mathcal{T}$.
- ② (Ignorability or Unconfoundedness) $Y(t) \perp\!\!\!\perp T \mid S$ for all $t \in \mathcal{T}$.
- ③ (Positivity or Overlap) The conditional density $p(t|s)$ is uniformly bounded away from zero for all $(t, s) \in \mathcal{T} \times \mathcal{S}$.

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$$\stackrel{(**)}{=} \mathbb{E}\{\mathbb{E}[Y(t)|T=t, S]\} \quad (**)\text{ Ignorability}$$

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- The positivity condition is required in (***) for

$$\mu(t, s) = \mathbb{E}(Y|T=t, S=s)$$

to be well-defined on $\mathcal{T} \times \mathcal{S}$.

Estimation of Dose-Response Curves Under Positivity

There are three major strategies for estimating

$$m(t) = \mathbb{E}[Y(t)] = \mathbb{E}[\mu(t, S)] = \lim_{h \rightarrow 0} \mathbb{E} \left[\frac{Y \cdot K\left(\frac{T-t}{h}\right)}{h \cdot p(T|S)} \right]$$

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► **Issue:** Positivity is a strong assumption with continuous treatments!

Violation of the Positivity Condition

Assumption (Positivity or Overlap Condition)

The conditional density $p(t|s)$ is uniformly bounded away from zero for all $(t, s) \in \mathcal{T} \times \mathcal{S}$.

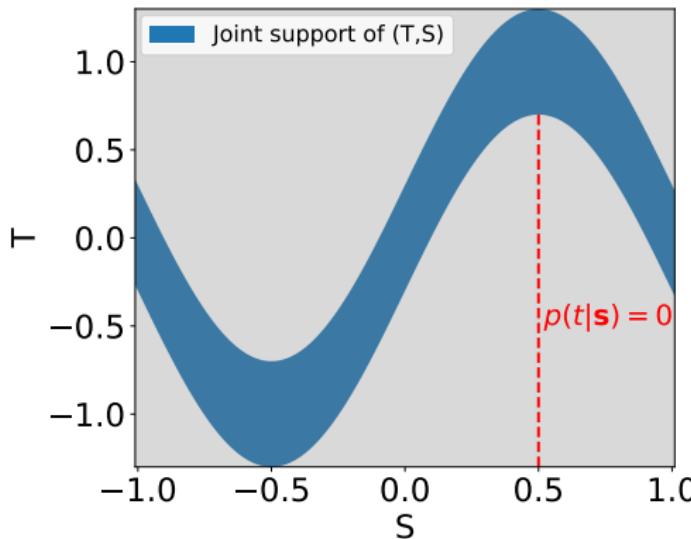
$$T = \sin(\pi S) + E, \quad E \sim \text{Unif}[-0.3, 0.3], \quad S \sim \text{Unif}[-1, 1], \quad \text{and} \quad E \perp\!\!\!\perp S.$$

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► Note: $p(t|s) = 0$ in the gray regions, and the positivity condition fails.

PM_{2.5} Distribution at the County Level

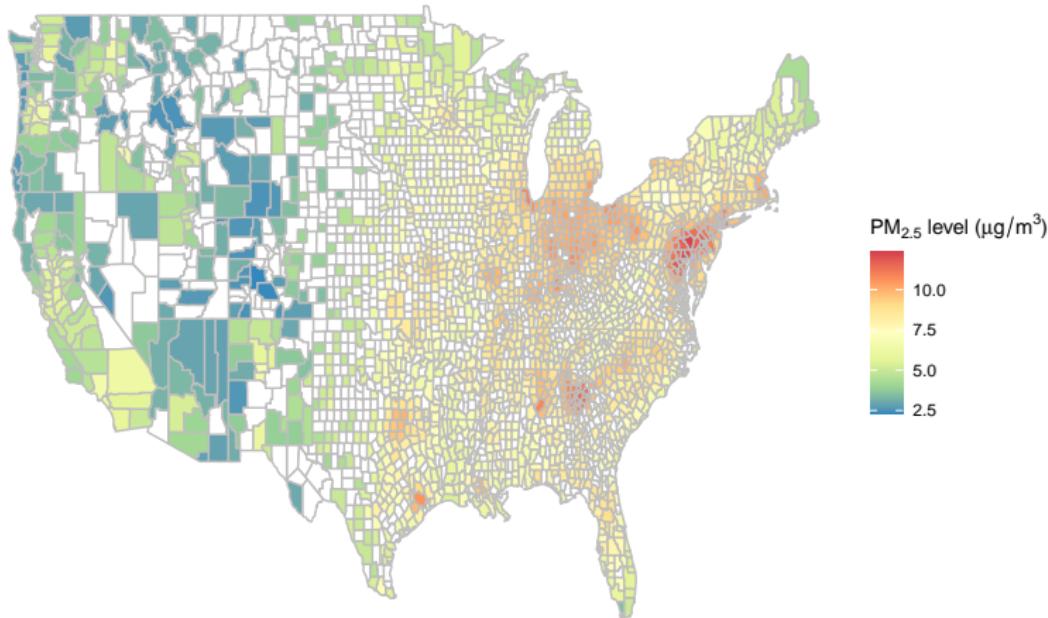


Figure: Average PM_{2.5} levels from 1990 to 2010 in $n = 2132$ counties. T is PM_{2.5} level, while S consists of the county location and some socioeconomic factors.

- **Problem:** Only one PM_{2.5} level is available per county, but causal effects of different PM_{2.5} levels on county-level CMRs are of interest.

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- ① The positivity condition may fail in some regions of $\mathcal{T} \times \mathcal{S}$.
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 - Construct a localized derivative estimator $\hat{\theta}_C(t)$ of $\theta(t) = m'(t)$ around the observations $T_i, i = 1, \dots, n$.
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 - Both $\hat{m}_\theta(t)$ and $\hat{\theta}_C(t)$ are consistent in \mathcal{T} even when the positivity condition is violated.
- ③ Nonparametric bootstrap inference with our proposed estimators for $m(t)$ and $\theta(t)$ is asymptotically valid.

Identification



Identification Strategy Without Positivity

The following identification strategies for $m(t)$ and $\theta(t)$ are not valid without positivity:

$$\begin{cases} m(t) = \mathbb{E}[Y(t)] = \mathbb{E}[\mu(t, S)], \\ \theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)] = \frac{d}{dt}\mathbb{E}[\mu(t, S)] = \mathbb{E}\left[\frac{\partial}{\partial t}\mu(t, S)\right]. \end{cases}$$

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Assumption (Extrapolation condition)

Suppose that at least one of the following conditions are valid.

- ① The function $\mathbb{E}[Y(t)|S = s]$ is continuously differentiable with respect to t for any $(t, s) \in \mathcal{T} \times \mathcal{S}$ with $p(s|t) > 0$ and

$$\theta(t) = \mathbb{E}\left[\frac{\partial}{\partial t}\mathbb{E}[Y(t)|S]\right] = \mathbb{E}\left[\frac{\partial}{\partial t}\mathbb{E}[Y(t)|S] \middle| T = t\right].$$

- ② The potential outcome $Y(t)$ is continuously differentiable with respect to t and

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Additionally, it holds true that $\mathbb{E}(Y) = \mathbb{E}[m(T)]$.

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- For any $t \in \mathcal{T}$, the fundamental theorem of calculus reveals that

$$m(t) = m(T) + \int_{\tilde{t}=T}^{\tilde{t}=t} m'(\tilde{t}) d\tilde{t} = m(T) + \int_{\tilde{t}=T}^{\tilde{t}=t} \theta(\tilde{t}) d\tilde{t}.$$

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- Taking the expectation on both sides of the above equality yields that

$$m(t) = \mathbb{E}(Y) + \mathbb{E}\left\{\int_{\tilde{t}=T}^{\tilde{t}=t} \mathbb{E}\left[\frac{\partial}{\partial t} \mu(\tilde{t}, S) \middle| T=\tilde{t}\right] d\tilde{t}\right\}.$$

Validity of Our Identification Strategies Without Positivity

We identify $\theta(t)$ through

$$\theta_C(t) = \mathbb{E} \left[\frac{\partial}{\partial t} \mathbb{E}(Y|T=t, S) \middle| T=t \right] = \mathbb{E} \left[\frac{\partial}{\partial t} \mu(t, S) \middle| T=t \right].$$

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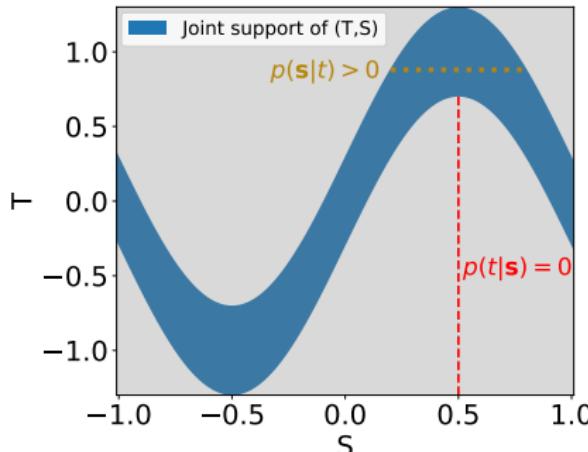
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- In contrast to the identification via $\mathbb{E} \left[\frac{\partial}{\partial t} \mu(t, S) \right]$ under positivity, we only need

$$\frac{\partial}{\partial t} \mu(t, s) = \frac{\partial}{\partial t} \mathbb{E}(Y|T=t, s)$$

to be well-defined when $p(s|t) > 0$.



Example: Additive Confounding Model

Consider the following additive confounding model

$$Y = \bar{m}(T) + \eta(S) + \epsilon, \quad \text{or} \quad Y(t) = \bar{m}(t) + \eta(S) + \epsilon,$$

where $m(t) = \mathbb{E}[Y(t)] = \bar{m}(t) + \mathbb{E}[\eta(S)]$ and $\theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)] = \bar{m}'(t)$.

- This is a common working model in spatial confounding problems ([Paciorek, 2010](#); [Schnell and Papadogeorgou, 2020](#); [Gilbert et al., 2023](#))².
- It is also known as the geoadditive structural equation model ([Kammann and Wand, 2003](#); [Thaden and Kneib, 2018](#)).

²Indeed, our paper is inspired by Professor Ogburn's talk at UW in Feb, 2023.

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Consider the following additive confounding model

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where $m(t) = \mathbb{E}[Y(t)] = \bar{m}(t) + \mathbb{E}[\eta(S)]$ and $\theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)] = \bar{m}'(t)$.

- This is a common working model in spatial confounding problems ([Paciorek, 2010](#); [Schnell and Papadogeorgou, 2020](#); [Gilbert et al., 2023](#))².
- It is also known as the geoadditive structural equation model ([Kammann and Wand, 2003](#); [Thaden and Kneib, 2018](#)).

Proposition (Proposition 2 in [Zhang et al. 2024](#))

Under the additive confounding model,

① $\theta(t) = \mathbb{E}\left[\frac{\partial}{\partial t}\mu(t, S)\right] = \mathbb{E}\left[\frac{\partial}{\partial t}\mu(t, S) \mid T = t\right] = \theta_C(t).$

② $\mathbb{E}(Y) = \mathbb{E}[\mu(T, S)] = \mathbb{E}[m(T)].$

²Indeed, our paper is inspired by Professor Ogburn's talk at UW in Feb, 2023.

Estimation and Inference



Proposed Integral Estimator of $m(t)$

Recall our identification formulae

$$m(t) = \mathbb{E} \left[Y + \int_{\tilde{t}=T}^{\tilde{t}=t} \theta_C(\tilde{t}) d\tilde{t} \right],$$
$$\theta_C(t) = \mathbb{E} \left[\frac{\partial}{\partial t} \mu(t, s) \middle| T = t \right] = \int \frac{\partial}{\partial t} \mu(t, s) dP(s|t).$$

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These imply our **integral estimator** of $m(t)$ as:

$$\hat{m}_\theta(t) = \frac{1}{n} \sum_{i=1}^n \left[Y_i + \int_{\tilde{t}=T_i}^{\tilde{t}=t} \hat{\theta}_C(\tilde{t}) d\tilde{t} \right],$$

where $\hat{\theta}_C(t) = \int \hat{\beta}_2(t, s) d\hat{P}(s|t)$ is our localized derivative estimator.

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- $\beta_2(t, s) := \frac{\partial}{\partial t} \mu(t, s)$ is fitted by (partial) local polynomial regression.
- $P(s|t)$ is estimated by Nadaraya-Watson conditional cumulative distribution function (CDF) estimator.

Estimation of Nuisance Functions

- ① **Order q (Partial) Local Polynomial Regression** ([Fan and Gijbels, 1996](#)): Let $\hat{\beta}(t, s) \in \mathbb{R}^{q+1}$ and $\hat{\alpha}(t, s) \in \mathbb{R}^d$ be the minimizer of

$$\arg \min_{(\beta, \alpha)^T \in \mathbb{R}^{q+1+d}} \sum_{i=1}^n \left[Y_i - \sum_{j=0}^q \beta_j (T_i - t)^j - \sum_{\ell=1}^d \alpha_\ell (S_{i,\ell} - s_\ell) \right]^2 K_T \left(\frac{T_i - t}{h} \right) K_S \left(\frac{S_i - s}{b} \right).$$

- $K_T : \mathbb{R} \rightarrow [0, \infty)$, $K_S : \mathbb{R}^d \rightarrow [0, \infty)$ are two symmetric kernel functions, and $h, b > 0$ are smoothing bandwidth parameters.
- The second component $\hat{\beta}_2(t, s)$ is a consistent estimator of $\beta_2(t, s) = \frac{\partial}{\partial t} \mu(t, s)$.

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- ② **Nadaraya-Watson conditional CDF Estimator** ([Hall et al., 1999](#)):

$$\hat{P}_{\hbar}(s|t) = \frac{\sum_{i=1}^n \mathbb{1}_{\{S_i \leq s\}} \cdot \bar{K}_T \left(\frac{T_i - t}{\hbar} \right)}{\sum_{j=1}^n \bar{K}_T \left(\frac{T_j - t}{\hbar} \right)}.$$

- $\bar{K}_T : \mathbb{R} \rightarrow [0, \infty)$ is a kernel function and $\hbar > 0$ is its smoothing bandwidth parameter.

Proposed Localized Derivative Estimator of $\theta(t)$

Combining two nuisance function estimators $\widehat{\beta}_2(t, s)$ and $\widehat{P}(s|t)$, we derive our **localized derivative estimator** of $\theta(t)$ as:

$$\widehat{\theta}_C(t) = \int \widehat{\beta}_2(t, s) d\widehat{P}_{\hbar}(s|t) = \frac{\sum_{i=1}^n \widehat{\beta}_2(t, S_i) \cdot \bar{K}_T\left(\frac{T_i-t}{\hbar}\right)}{\sum_{j=1}^n \bar{K}_T\left(\frac{T_j-t}{\hbar}\right)}.$$

Our integral estimator takes the form

$$\widehat{m}_\theta(t) = \frac{1}{n} \sum_{i=1}^n \left[Y_i + \int_{\tilde{t}=T_i}^{\tilde{t}=t} \widehat{\theta}_C(\tilde{t}) d\tilde{t} \right].$$

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- Other methods can be applied to estimate $\frac{\partial}{\partial t} \mu(t, s)$ and $P(s|t)$.
 - $\widehat{m}_\theta(t)$, under our kernel-based estimators, is a *linear smoother*.
- **Issue:** The integral could be analytically difficult to compute.

Fast Computing Algorithm for the Integral Estimator

Our integral estimator takes the form

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- **Riemann Sum Approximation:** Let $T_{(1)} \leq \dots \leq T_{(n)}$ be the order statistics of T_1, \dots, T_n and $\Delta_j = T_{(j+1)} - T_{(j)}$ for $j = 1, \dots, n-1$.
- Approximate $\hat{m}_\theta(T_{(j)})$ for each $j = 1, \dots, n$ as:

$$\hat{m}_\theta(T_{(j)}) \approx \frac{1}{n} \sum_{i=1}^n Y_i + \frac{1}{n} \sum_{i=1}^{n-1} \Delta_i \left[i \cdot \hat{\theta}_C(T_{(i)}) \mathbb{1}_{\{i < j\}} - (n-i) \cdot \hat{\theta}_C(T_{(i+1)}) \mathbb{1}_{\{i \geq j\}} \right].$$

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- Evaluate $\hat{m}_\theta(t)$ at any $t \in [T_{(j)}, T_{(j+1)}]$ by a linear interpolation between $\hat{m}_\theta(T_{(j)})$ and $\hat{m}_\theta(T_{(j+1)})$.
- The approximation error is at most $O_P\left(\frac{1}{n}\right)$.

Nonparametric Bootstrap Inference

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- ③ Let $\alpha \in (0, 1)$ be a pre-specified significance level.
 - For pointwise inference at $t_0 \in \mathcal{T}$, calculate the $1 - \alpha$ quantile $\zeta_{1-\alpha}^*(t_0)$ of $\{D_1(t_0), \dots, D_B(t_0)\}$, where $D_b(t_0) = \left| \hat{m}_\theta^{*(b)}(t_0) - \hat{m}_\theta(t_0) \right|$ for $b = 1, \dots, B$.
 - For uniform inference on $m(t)$, compute the $1 - \alpha$ quantile $\xi_{1-\alpha}^*$ of $\{D_{\text{sup},1}, \dots, D_{\text{sup},B}\}$, where $D_{\text{sup},b} = \sup_{t \in \mathcal{T}} \left| \hat{m}_\theta^{*(b)}(t) - \hat{m}_\theta(t) \right|$ for $b = 1, \dots, B$.

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- ④ Define the $1 - \alpha$ confidence interval for $m(t_0)$ as:

$$[\hat{m}_\theta(t_0) - \zeta_{1-\alpha}^*(t_0), \hat{m}_\theta(t_0) + \zeta_{1-\alpha}^*(t_0)]$$

and the simultaneous $1 - \alpha$ confidence band for every $t \in \mathcal{T}$ as:

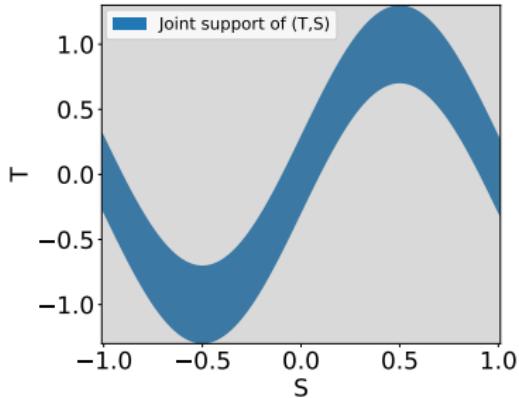
$$[\hat{m}_\theta(t) - \xi_{1-\alpha}^*, \hat{m}_\theta(t) + \xi_{1-\alpha}^*].$$

Asymptotic Theory



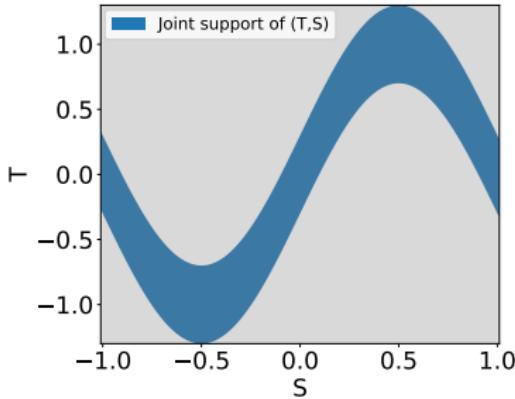
Uniform Consistency of Local Polynomial Regression

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Uniform Consistency of Local Polynomial Regression

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- The localized derivative estimator $\widehat{\theta}_C(t) = \int \widehat{\beta}_2(t, s) d\widehat{P}_h(s|t)$ only requires $\widehat{\beta}_2(t, s)$ to be consistent in \mathcal{E} .

Lemma (Lemma 3 in Zhang et al. 2024)

Under some regularity conditions, as $h, b, \frac{\max\{h, b\}^4}{h} \rightarrow 0$ and $\frac{|\log(hb^d)|}{nh^3b^d} \rightarrow \infty$,

$$\sup_{(t,s) \in \mathcal{E}} \left| \widehat{\beta}_2(t, s) - \frac{\partial}{\partial t} \mu(t, s) \right| = O \left(h^q + b^2 + \frac{\max\{h, b\}^4}{h} \right) + O_P \left(\sqrt{\frac{|\log(hb^d)|}{nh^3b^d}} \right).$$

Uniform Consistencies of Proposed Estimators

Combining with the consistency of $\hat{P}_\hbar(s|t)$ via the technique in [Fan et al. \(1998\)](#), we have the following results.

Theorem (Theorem 4 in [Zhang et al. 2024](#))

Let $\mathcal{T}' \subset \mathcal{T}$ be a compact set so that $p_{\mathcal{T}}(t) \geq p_{\mathcal{T},\min} > 0$ for all $t \in \mathcal{T}'$. When $q = 2$ and h, b, \hbar , $\frac{\max\{h, b\}^4}{h} \rightarrow 0$ and $\frac{n \max\{h, \hbar\} b^d}{\log n}, \frac{n \hbar}{\log n} \rightarrow \infty$,

$$\sup_{t \in \mathcal{T}'} |\hat{\theta}_C(t) - \theta_C(t)| = O \underbrace{\left(h^2 + b^2 + \frac{\max\{b, h\}^4}{h} \right)}_{\text{Bias term}} + O_P \underbrace{\left(\sqrt{\frac{\log n}{nh^3}} + \hbar^2 + \sqrt{\frac{\log n}{n\hbar}} \right)}_{\text{Stochastic variation}},$$

$$\sup_{t \in \mathcal{T}'} |\hat{m}_\theta(t) - m(t)| = O \left(h^2 + b^2 + \frac{\max\{b, h\}^4}{h} \right) + O_P \left(\frac{1}{\sqrt{n}} + \sqrt{\frac{\log n}{nh^3}} + \hbar^2 + \sqrt{\frac{\log n}{n\hbar}} \right).$$

Uniform Rate of Convergence For the Integral Estimator

$$\begin{aligned} & \sup_{t \in \mathcal{T}'} |\hat{m}_\theta(t) - m(t)| \\ &= O \left(h^2 + b^2 + \frac{\max\{b, h\}^4}{h} \right) + O_P \left(\frac{1}{\sqrt{n}} + \sqrt{\frac{\log n}{nh^3}} + \hbar^2 + \sqrt{\frac{\log n}{n\hbar}} \right). \end{aligned}$$

- **Blue term:** the estimation bias of local polynomial estimator $\hat{\beta}_2(t, s)$.
- **Orange term:** additional bias of $\hat{\beta}_2(t, s)$ at the boundary $\partial\mathcal{E}$.

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- **Cyan term:** asymptotic rate from the Nadaraya-Watson conditional CDF estimator $\hat{P}_\hbar(s|t)$.

Asymptotic Linearity of Proposed Estimators

Lemma (Lemma 5 in Zhang et al. 2024)

Under the same regularity conditions, if $h \asymp n^{-\frac{1}{\gamma}}$ and $\hbar \asymp n^{-\frac{1}{\varpi}}$ for some $\gamma \geq \varpi > 0$ such that $\frac{nh^5}{\log n} \rightarrow c_1$ and $\frac{n\hbar^5}{\log n} \rightarrow c_2$ for some $c_1, c_2 \geq 0$ and $\frac{n \max\{h, \hbar\} b^d}{\log n}, \frac{n\hbar}{\log n}, \frac{h^3 \log n}{\hbar}, \frac{nh^3\hbar^4}{\log n} \rightarrow \infty$ as $n \rightarrow \infty$, then for any $t \in \mathcal{T}'$,

$$\sqrt{nh^3} [\widehat{\theta}_C(t) - \theta(t)] = \mathbb{G}_n \bar{\varphi}_t + o_P(1),$$

$$\sqrt{nh^3} [\widehat{m}_\theta(t) - m(t)] = \mathbb{G}_n \varphi_t + o_P(1),$$

where

$$\bar{\varphi}_t(Y, T, S) = \frac{C_{K_T} [Y - \mu(T, S)]}{\sqrt{h} \cdot p_T(t)} \left(\frac{T-t}{h} \right) K_T \left(\frac{T-t}{h} \right)$$

and $\varphi_t(Y, T, S) = \mathbb{E}_{T_1} \left[\int_{T_1}^t \bar{\varphi}_t(Y, T, S) d\tilde{t} \right]$ with $\mathbb{G}_n = \sqrt{n} (\mathbb{P}_n - P)$, where $C_{K_T} > 0$ is a constant that only depends on K_T .

- **Note:** $\bar{\varphi}_t$ and φ_t may not be efficient influence functions.

Bootstrap Consistency

Theorem (Theorems 6 and 7 in [Zhang et al. 2024](#))

Under the same regularity conditions, if $h \asymp n^{-\frac{1}{\gamma}}$ and $b \lesssim \hbar \asymp n^{-\frac{1}{\varpi}}$ for some $\gamma \geq \varpi > 0$ such that $\frac{nh^{d+5}}{\log n} \rightarrow c_1$ and $\frac{n\hbar^5}{\log n} \rightarrow c_2$ for some $c_1, c_2 \geq 0$ and $\frac{\hbar}{h^3 \log n}, \hbar n^{\frac{1}{3}} \log n, \frac{\sqrt{n}\hbar}{\log n}, \frac{n \max\{h, \hbar\} b^d}{\log n} \rightarrow \infty$ as $n \rightarrow \infty$,

1

$$\left| \sqrt{nh^3} \sup_{t \in \mathcal{T}'} |\hat{m}_\theta(t) - m(t)| - \sup_{t \in \mathcal{T}'} |\mathbb{G}_n \varphi_t| \right| = O_P \left(\sqrt{nh^3 \max\{h, \hbar\}^4} + \sqrt{\frac{h^3 \log n}{\hbar}} + \frac{\log n}{\sqrt{n}\hbar} + \sqrt{\frac{\log n}{nb^d \hbar}} \right).$$

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2 there exists a mean-zero Gaussian process \mathbb{B} such that

$$\sup_{u \geq 0} \left| P \left(\sqrt{nh^3} \sup_{t \in \mathcal{T}'} |\hat{m}_\theta(t) - m(t)| \leq u \right) - P \left(\sup_{f \in \mathcal{F}} |\mathbb{B}(f)| \leq u \right) \right| = O \left(\left(\frac{\log^5 n}{nh^3} \right)^{\frac{1}{8}} + \left(\frac{\log^2 n}{nb^d \hbar} \right)^{\frac{3}{8}} \right).$$

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3

$$\sup_{u \geq 0} \left| P \left(\sqrt{nh^3} \sup_{t \in \mathcal{T}'} |\hat{m}_\theta^*(t) - \hat{m}_\theta(t)| \leq u \middle| \mathbb{U}_n \right) - P \left(\sup_{f \in \mathcal{F}} |\mathbb{B}(f)| \leq u \right) \right| = O_P \left(\left(\frac{\log^5 n}{nh^3} \right)^{\frac{1}{8}} + \left(\frac{\log^2 n}{nb^d \hbar} \right)^{\frac{3}{8}} \right),$$

where

$$\mathcal{F} = \{(v, x, z) \mapsto \varphi_t(v, x, z) : t \in \mathcal{T}'\}.$$

Remarks on Our Asymptotic Results

- ① \mathcal{F} is not Donsker because φ_t is not uniformly bounded as $h \rightarrow 0$.
 - However, $\tilde{\mathcal{F}} = \left\{ (v, x, z) \mapsto \sqrt{h^3} \cdot \varphi_t(v, x, z) : t \in \mathcal{T}' \right\}$ is of VC-type.
 - Gaussian approximation in [Chernozhukov et al. \(2014\)](#) can be applied to bound the difference between $\sup_{f \in \mathcal{F}} |\mathbb{G}_n(f)|$ and $\sup_{f \in \mathcal{F}} |\mathbb{B}(f)|$.

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- ② As long as $\text{Var}(Y|T = t, S = s) \geq \sigma^2 > 0$, $\text{Var}[\varphi_t(Y, T, S)]$ is a positive finite number.
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- ③ For the validity of uniform bootstrap confidence band, one can choose the bandwidths $h \asymp \hbar = O\left(n^{-\frac{1}{5}}\right)$ and $\left(\frac{\log n}{n}\right)^{\frac{4}{5d}} \lesssim b \lesssim n^{-\frac{1}{5}}$.
 - They match up with the outputs by the usual bandwidth selection methods ([Bashtannyk and Hyndman, 2001](#); [Li and Racine, 2004](#)).
 - No explicit undersmoothing is required!!

Case Study: PM_{2.5} on CMR



Effect of PM_{2.5} on the Cardiovascular Mortality Rate (CMR)

FIPS	County name	Longitude	Latitude	PM2.5	CMR
1025	Clarke	-87.830772	31.676955	6.766443	379.421713
1061	Geneva	-85.839330	31.094869	8.254272	378.524698
1073	Jefferson	-86.896571	33.554343	10.825441	352.790427
1077	Lauderdale	-87.654117	34.901500	9.208783	332.594557
5085	Lonoke	-91.887917	34.754412	8.213144	365.061085
8045	Garfield	-107.903621	39.599420	2.601772	250.781477

- ① The data ([Wyatt et al., 2020](#)) cover the average annual CMRs (Y) and PM_{2.5} levels (T) across $n = 2132$ U.S. counties over 1990-2010.

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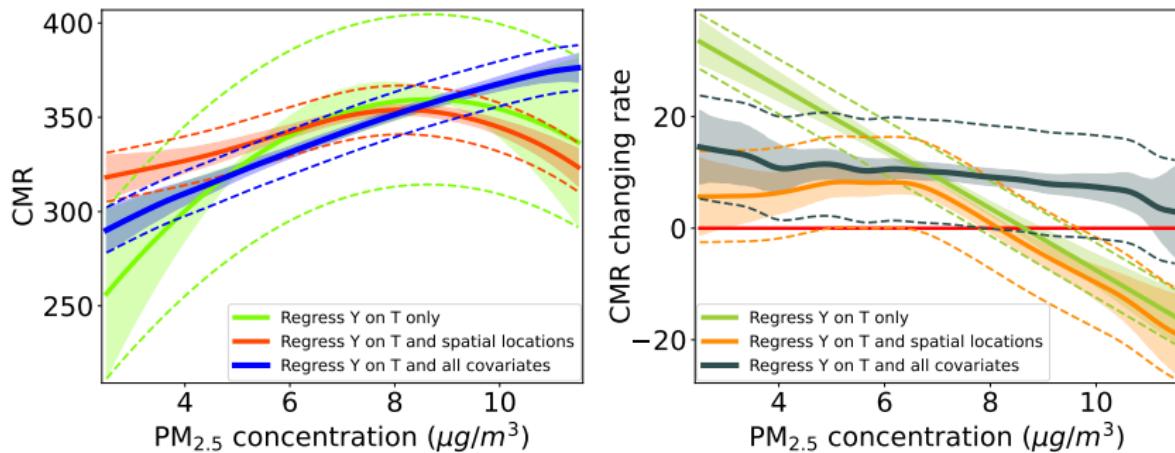
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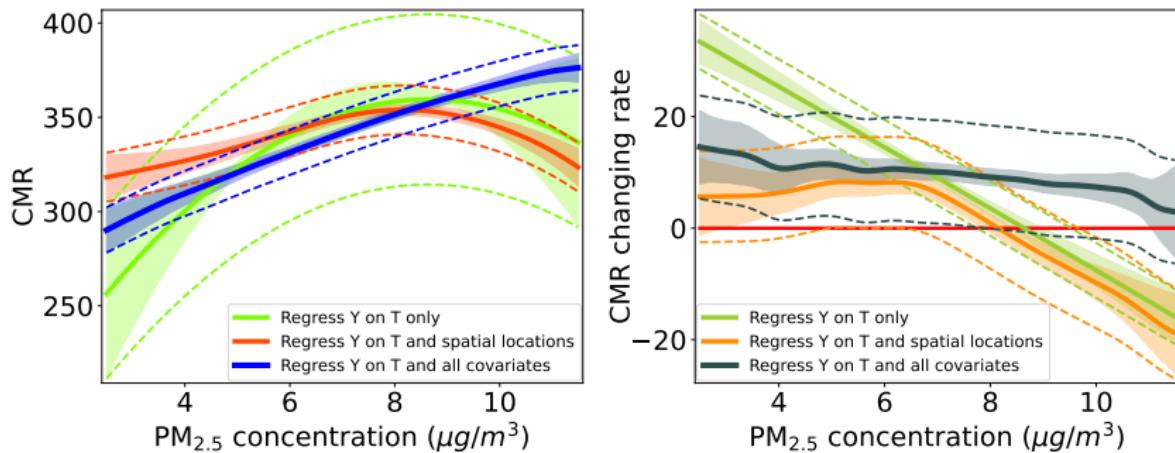
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 - Two spatial confounders, *i.e.*, latitude and longitude of each county.
 - Eight county-level socioeconomic factors acquired from the US census.
- ③ Focus on the values of PM_{2.5} between $2.5 \mu\text{g}/m^3$ and $11.5 \mu\text{g}/m^3$ to avoid boundary effects ([Takatsu and Westling, 2022](#)).

Effect of PM_{2.5} on the Cardiovascular Mortality Rate (CMR)



- We compare three models:
 - ① Regress Y on T alone via local quadratic regression.
 - ② Regress Y on T with spatial locations.
 - ③ Regress Y on T with both spatial and socioeconomic covariates.
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- The shaded areas indicate pointwise 95% confidence intervals, while the dashed lines are uniform 95% confidence bands.
- After adjusting for all covariates, the increasing trends are statistically significant when the PM_{2.5} level is below 8 $\mu\text{g}/\text{m}^3$.

Discussion



Summary of Today's Talk

We study nonparametric inference on the dose-response curve $m(t) = \mathbb{E}[Y(t)]$ and its derivative $\theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)]$.

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- Both estimators are consistent without the positivity condition.
- Our integration idea opens a new direction for causal inference with continuous treatments under violations of positivity!

Ongoing Works and Future Directions

- ① **IPW and Doubly Robust Estimation:** Our estimators are based on a regression adjustment method. Can we generalize them to the IPW and doubly robust approaches ([Zhang and Chen, 2025](#))?

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- ④ **High-Dimensional Confounders:** $\left(\frac{\log n}{n}\right)^{\frac{4}{5d}} \lesssim b \lesssim n^{-\frac{1}{5}}$ only works when $d < 5$. Can we utilize a semi-parametric additive model ([Guo et al., 2019](#)) to resolve the curse of dimensionality?

$$\mathbb{E}(Y|T=t, S=s, Z=z) = m(t) + \eta(s) + \sum_{j=1}^{d'} g_j(z_j) \quad \text{with} \quad z \in \mathbb{R}^{d'}, d' \gg d.$$

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- ⑤ **Semi-parametric Efficiency:** In what sense are the influence functions from our proposed estimators statistically efficient?

$$\bar{\varphi}_t(Y, T, S) = \frac{C_{K_T} [Y - \mu(T, S)]}{\sqrt{h} \cdot p_T(t)} \left(\frac{T-t}{h} \right) K_T \left(\frac{T-t}{h} \right), \quad \varphi_t(Y, T, S) = \mathbb{E}_{T_{i_2}} \left[\int_{T_{i_2}}^t \bar{\varphi}_{\tilde{t}}(Y, T, S) d\tilde{t} \right].$$

Thank you!

More details can be found in

- [1] Y. Zhang, Y.-C. Chen, and A. Giessing. Nonparametric Inference on Dose-Response Curves Without the Positivity Condition. *arXiv preprint*, 2024.
<https://arxiv.org/abs/2405.09003>.

All the code and data are available at

<https://github.com/zhangyk8/npDoseResponse/tree/main>.

Python Package: [npDoseResponse](#) and R Package: [npDoseResponse](#).

- [2] Y. Zhang and Y.-C. Chen. Doubly Robust Inference on Causal Derivative Effects for Continuous Treatments. *arXiv preprint*, 2025. <https://arxiv.org/abs/2501.06969>.

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Regularity Assumptions (Smoothness Conditions)

Let $\mathcal{E} \subset \mathcal{T} \times \mathcal{S}$ be the support of $p(t, s)$, \mathcal{E}° be the interior of \mathcal{E} , and $\partial\mathcal{E}$ be the boundary of \mathcal{E} .

- ① For any $(t, s) \in \mathcal{E}^\circ$, $\mu(t, s)$ is at least $(q + 1)$ times continuously differentiable with respect to t and at least four times continuously differentiable with respect to s . All these partial derivatives of $\mu(t, s)$ are continuous up to the boundary $\partial\mathcal{E}$. Furthermore, $\mu(t, s)$ and the partial derivatives are uniformly bounded on \mathcal{E} . Finally, there exist absolute constants $\sigma, A_0 > 0$ such that $\text{Var}(Y|T = t, S = s) = \sigma^2$ and $\mathbb{E}|Y|^4 < A_0 < \infty$ uniformly in \mathcal{E} .
- ② $p(t, s)$ is bounded and at least twice continuously differentiable with bounded partial derivatives up to the second order on \mathcal{E}° . All these partial derivatives of $p(t, s)$ are continuous up to the boundary $\partial\mathcal{E}$. Furthermore, \mathcal{E} is compact and $p(t, s)$ is uniformly bounded away from 0 on \mathcal{E} . Finally, the marginal density $p_T(t)$ of T is non-degenerate, i.e., its support \mathcal{T} has a nonempty interior.

Regularity Assumptions (Boundary Conditions)

- ③ There exists some constants $r_1, r_2 \in (0, 1)$ such that for any $(t, s) \in \mathcal{E}$ and all $\delta \in (0, r_1]$, there is a point $(t', s') \in \mathcal{E}$ satisfying

$$\mathcal{B}((t', s'), r_2\delta) \subset \mathcal{B}((t, s), \delta) \cap \mathcal{E},$$

where

$$\mathcal{B}((t, s), r) = \left\{ (t_1, s_1) \in \mathbb{R}^{d+1} : \| (t_1 - t, s_1 - s) \|_2 \leq r \right\}$$

with $\|\cdot\|_2$ being the standard Euclidean norm.

- ④ For any $(t, s) \in \partial\mathcal{E}$, the boundary of \mathcal{E} , it satisfies that
 $\frac{\partial}{\partial t} p(t, s) = \frac{\partial}{\partial s_j} p(t, s) = 0$ and $\frac{\partial^2}{\partial s_j^2} \mu(t, s) = 0$ for all $j = 1, \dots, d$.
- ⑤ For any $\delta > 0$, the Lebesgue measure of the set $\partial\mathcal{E} \oplus \delta$ satisfies
 $|\partial\mathcal{E} \oplus \delta| \leq A_1 \cdot \delta$ for some absolute constant $A_1 > 0$, where

$$\partial\mathcal{E} \oplus \delta = \left\{ z \in \mathbb{R}^{d+1} : \inf_{x \in \partial\mathcal{E}} \|z - x\|_2 \leq \delta \right\}.$$

Regularity Assumptions (Kernel Conditions)

- ⑥ $K_T : \mathbb{R} \rightarrow [0, \infty)$ and $K_S : \mathbb{R}^d \rightarrow [0, \infty)$ are compactly supported and Lipschitz continuous kernels such that $\int_{\mathbb{R}} K_T(t) dt = \int_{\mathbb{R}^d} K_S(s) ds = 1$, $K_T(t) = K_T(-t)$, and K_S is radially symmetric with $\int s \cdot K_S(s) ds = \mathbf{0}$. In addition, for all $j = 1, 2, \dots$, and $\ell = 1, \dots, d$,

$$\kappa_j^{(T)} := \int_{\mathbb{R}} u^j K_T(u) du < \infty, \quad \nu_j^{(T)} := \int_{\mathbb{R}} u^j K_T^2(u) du < \infty,$$

$$\kappa_{j,\ell}^{(S)} := \int_{\mathbb{R}^d} u_\ell^j K_S(u) du < \infty, \quad \text{and} \quad \nu_{j,k}^{(S)} := \int_{\mathbb{R}^d} u_\ell^j K_S^2(u) du < \infty.$$

Finally, both K_T and K_S are second-order kernels, i.e., $\kappa_2^{(T)} > 0$ and $\kappa_{2,\ell}^{(S)} > 0$ for all $\ell = 1, \dots, d$.

- ⑦ Let $\mathcal{K}_{q,d} = \left\{ (y, z) \mapsto \left(\frac{y-t}{h}\right)^\ell \left(\frac{z_i-s_i}{b}\right)^{k_1} \left(\frac{z_j-s_j}{b}\right)^{k_2} K_T\left(\frac{y-t}{h}\right) K_S\left(\frac{z-s}{b}\right) : (t, s) \in \mathcal{T} \times \mathcal{S}; i, j = 1, \dots, d; \ell = 0, \dots, 2q; k_1, k_2 = 0, 1; h, b > 0 \right\}$. It holds that $\mathcal{K}_{q,d}$ is a bounded VC-type class of measurable functions on \mathbb{R}^{d+1} .

Regularity Assumptions (Kernel Conditions)

- ⑧ The function $\bar{K}_T : \mathbb{R} \rightarrow [0, \infty)$ is a second-order, Lipschitz continuous, and symmetric kernel with a compact support, i.e., $\int_{\mathbb{R}} \bar{K}_T(t) dt = 1$, $\bar{K}_T(t) = \bar{K}_T(-t)$, and $\int_{\mathbb{R}} t^2 \bar{K}_T(t) dt \in (0, \infty)$.
- ⑨ Let $\bar{\mathcal{K}} = \left\{ y \mapsto \bar{K}_T \left(\frac{y-t}{\hbar} \right) : t \in \mathcal{T}, \hbar > 0 \right\}$. It holds that $\bar{\mathcal{K}}$ is a bounded VC-type class of measurable functions on \mathbb{R} .

Recall that the class \mathcal{G} of measurable functions on \mathbb{R}^{d+1} is VC-type if there exist constants $A_2, v_2 > 0$ such that for any $0 < \epsilon < 1$,

$$\sup_Q N \left(\mathcal{G}, L_2(Q), \epsilon \|G\|_{L_2(Q)} \right) \leq \left(\frac{A_2}{\epsilon} \right)^{v_2},$$

where $N \left(\mathcal{G}, L_2(Q), \epsilon \|G\|_{L_2(Q)} \right)$ is the $\epsilon \|G\|_{L_2(Q)}$ -covering number of the (semi-)metric space $(\mathcal{G}, \|\cdot\|_{L_2(Q)})$, Q is any probability measure on \mathbb{R}^{d+1} , G is an envelope function of \mathcal{G} , and $\|G\|_{L_2(Q)}$ is defined as

$$\left[\int_{\mathbb{R}^{d+1}} [G(x)]^2 dQ(x) \right]^{\frac{1}{2}}.$$

Simulation Setup

- Use the Epanechnikov kernel for K_T and K_S (with the product kernel technique) and Gaussian kernel for \bar{K}_T .
- Select the bandwidth parameters $h, b > 0$ by modifying the rule-of-thumb method in [Yang and Tschernig \(1999\)](#).
- Set the bandwidth parameter $\hbar > 0$ to the normal reference rule in [Chacón et al. \(2011\)](#); [Chen et al. \(2016\)](#).
- Set the bootstrap resampling time $B = 1000$ and the significance level $\alpha = 0.05$.
- Compare our proposed estimators with the regression adjustment estimators under the same choices of bandwidth parameters:

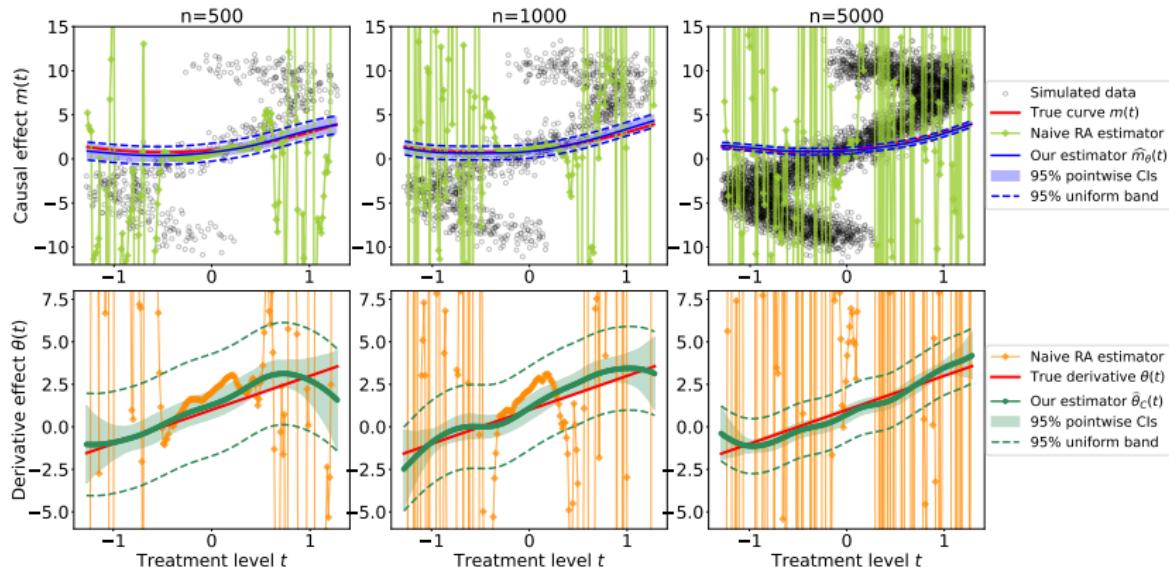
$$\hat{m}_{\text{RA}}(t) = \frac{1}{n} \sum_{i=1}^n \hat{\mu}(t, S_i) \quad \text{and} \quad \hat{\theta}_{\text{RA}}(t) = \frac{1}{n} \sum_{i=1}^n \hat{\beta}_2(t, S_i).$$

Single Confounder Model

Generate i.i.d. observations $\{(Y_i, T_i, S_i)\}_{i=1}^{2000}$ from

$$Y = T^2 + T + 1 + 10S + \epsilon, \quad T = \sin(\pi S) + E, \quad \text{and} \quad S \sim \text{Uniform}[-1, 1].$$

- $E \sim \text{Uniform}[-0.3, 0.3]$ is an independent treatment variation,
- $\epsilon \sim \mathcal{N}(0, 1)$ is an exogenous normal noise.

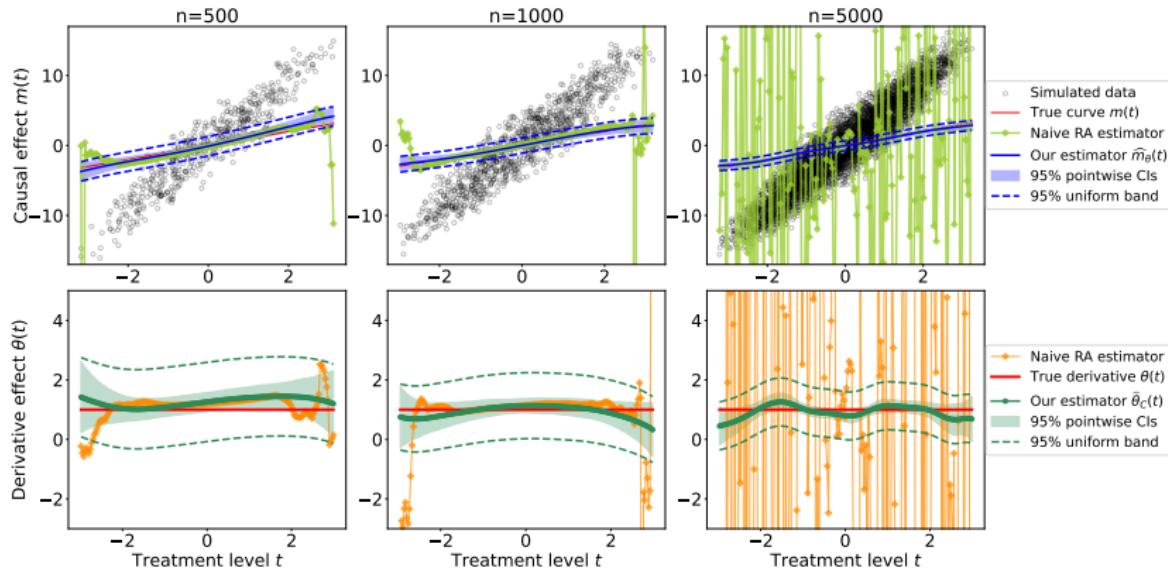


Linear Confounding Model

Generate i.i.d. observations $\{(Y_i, T_i, S_i)\}_{i=1}^{2000}$ from

$$Y = T + 6S_1 + 6S_2 + \epsilon, \quad T = 2S_1 + S_2 + E, \quad \text{and} \quad (S_1, S_2) \sim \text{Uniform}[-1, 1]^2,$$

- $E \sim \text{Uniform}[-0.5, 0.5]$ and $\epsilon \sim \mathcal{N}(0, 1)$.

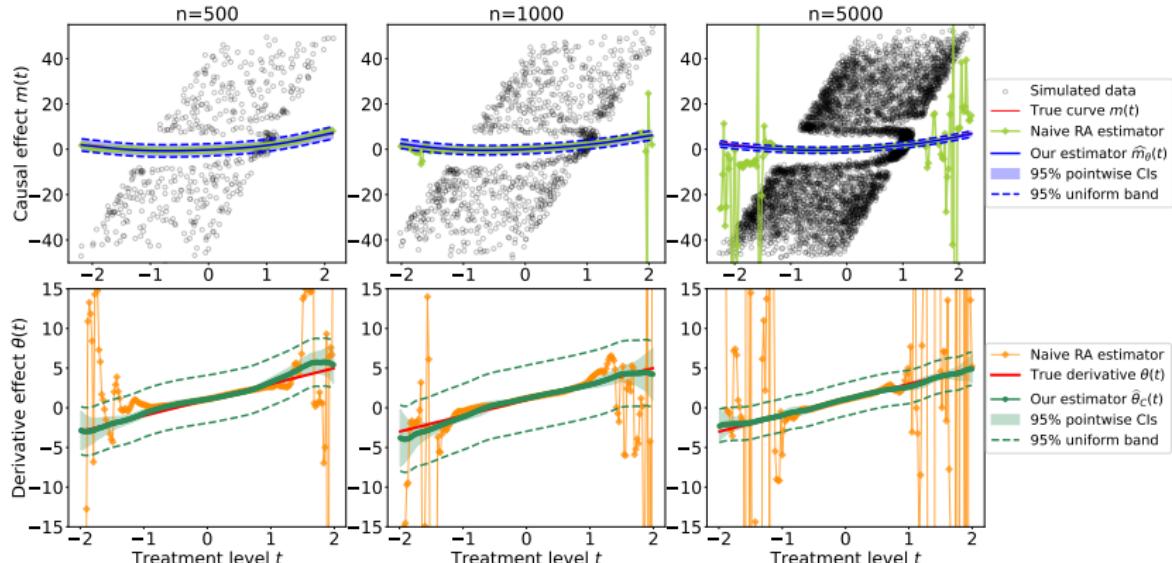


Nonlinear Confounding Model

Generate i.i.d. observations $\{(Y_i, T_i, S_i)\}_{i=1}^{2000}$ from

$$Y = T^2 + T + 10Z + \epsilon, \quad T = \cos(\pi Z^3) + \frac{Z}{4} + E, \quad \text{and} \quad Z = 4S_1 + S_2,$$

- $(S_1, S_2) \sim \text{Uniform}[-1, 1]^2$, $E \sim \text{Uniform}[-0.1, 0.1]$, and $\epsilon \sim \mathcal{N}(0, 1)$.
- Those doubly robust Methods based on pseudo-outcomes ([Kennedy et al., 2017](#); [Takatsu and Westling, 2022](#)) do not work in this example.



Nonparametric Bound on $m(t)$ When $\text{Var}(E) = 0$

For simplicity, we assume the additive confounding model

$$Y = \bar{m}(T) + \eta(S) + \epsilon, \quad T = f(S) + E \quad \text{with} \quad \mathbb{E}[\eta(S)] = 0 \quad \text{and} \quad \mathbb{E}(E) = 0.$$

When $\text{Var}(E) = 0$,

- $\mu(t, s)$ can be identified only on a lower-dimensional surface $\{(t, s) \in \mathcal{T} \times \mathcal{S} : t = f(s)\}$ so that

$$\mu(f(s), s) = \bar{m}(f(s)) + \eta(s) = m(f(s)) + \eta(s). \quad (1)$$

- The relation $T = f(S)$ can be recovered from the data $\{(T_i, S_i)\}_{i=1}^n$.

Assumption (Bounded random effect)

Let $L_f(t) = \{s \in \mathcal{S} : f(s) = t\}$ be a level set of the function $f : \mathcal{S} \rightarrow \mathbb{R}$ at $t \in \mathcal{T}$. There exists a constant $\rho_1 > 0$ such that

$$\rho_1 \geq \max \left\{ \sup_{t \in \mathcal{T}} \sup_{s \in L_f(t)} |\eta(s)|, \frac{\sup_{t \in \mathcal{T}} \sup_{s \in L_f(t)} \mu(f(s), s) - \inf_{t \in \mathcal{T}} \inf_{s \in L_f(t)} \mu(f(s), s)}{2} \right\}.$$

Nonparametric Bound on $m(t)$ When $\text{Var}(E) = 0$

By (1) and the first lower bound on $\rho_1 \geq \sup_{t \in \mathcal{T}} \sup_{s \in L_f(t)} |\eta(s)|$ in the previous assumption, we know that

$$|\mu(f(s), s) - m(t)| = |\eta(s)| \leq \rho_1$$

for any $s \in L_f(t)$. It also implies that

$$\begin{aligned} m(t) &\in \bigcap_{s \in L_f(t)} [\mu(f(s), s) - \rho_1, \mu(f(s), s) + \rho_1] \\ &= \left[\sup_{s \in L_f(t)} \mu(f(s), s) - \rho_1, \inf_{s \in L_f(t)} \mu(f(s), s) + \rho_1 \right], \end{aligned}$$

which is the nonparametric bound on $m(t)$ that contains all the possible values of $m(t)$ for any fixed $t \in \mathcal{T}$ when $\text{Var}(E) = 0$.

- This bound is well-defined and nonempty under the second lower bound on ρ_1 in the previous assumption.