

# Nonparametric Inference on Dose-Response Curves Without the Positivity Condition

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Yikun Zhang

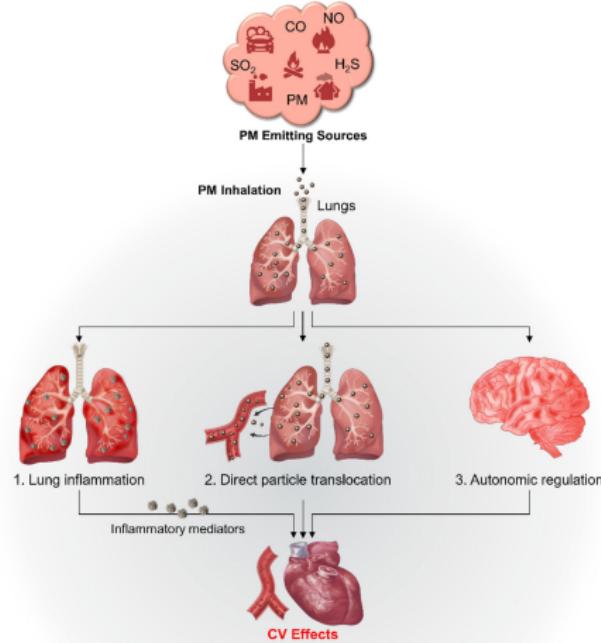
Joint work with *Professor Yen-Chi Chen*

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# Motivation for Continuous Treatments

- We want to study the causal effects of PM<sub>2.5</sub> levels on Cardiovascular Mortality Rates (CMRs).



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

## Motivation for Continuous Treatments

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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5085	Lonoke	-91.887917	34.754412	8.213144	365.061085
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The dataset contains the average annual cardiovascular mortality rates (CMRs) and PM<sub>2.5</sub> levels across  $n = 2132$  U.S. counties from 1990 to 2010 ([Wyatt et al., 2020a,b](#)).

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- The treatment variable  $T$ , i.e., the PM<sub>2.5</sub> level at each county, is a quantitative measure. In other words, it is *not a binary but continuous variable!*

## Causal Inference For Continuous Treatments

For *binary* treatment (*i.e.*,  $\mathcal{T} = \{0, 1\}$ ), 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.*,  $\mathcal{T} \subset \mathbb{R}$ )?

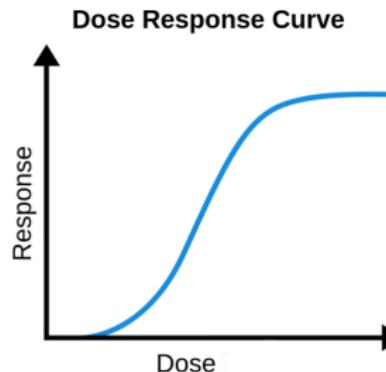
# Causal Inference For Continuous Treatments

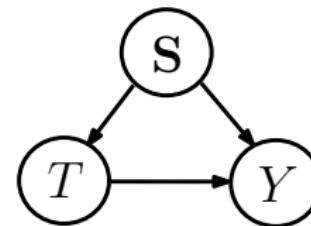
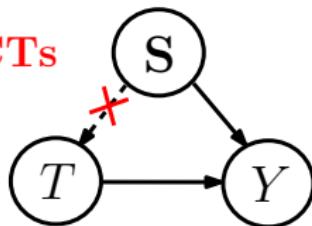
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► **Question:** What are the counterparts of the above estimands under *continuous* treatment (*i.e.*,  $\mathcal{T} \subset \mathbb{R}$ )?

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

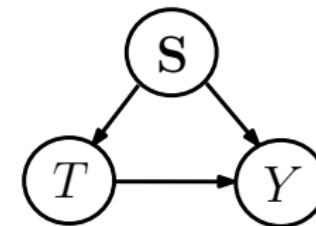
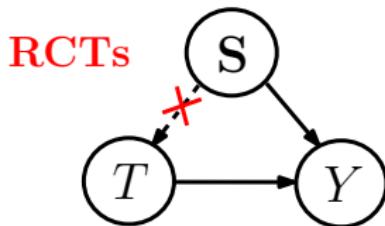


**RCTs**

### Assumption (Identification Conditions)

- ① (*Consistency*)  $Y = Y(t)$  whenever  $T = t \in \mathcal{T}$ .
- ② (*Ignorability*)  $Y(t)$  is conditionally independent of  $T$  given  $S$  for all  $t \in \mathcal{T}$ .
- ③ (*Positivity*) The conditional density satisfies  $p_{T|S}(t|s) \geq p_{\min} > 0$  for all  $(t, s) \in \mathcal{T} \times \mathcal{S}$ .

<sup>1</sup>Some mild interchangeability assumptions are needed; see Theorem 1.1 in [Shao \(2003\)](#).



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$$m(t) = \mathbb{E}[Y(t)] = \mathbb{E}[\mathbb{E}(Y|T=t, S)] \quad \text{and} \quad \theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)] \stackrel{(*)^1}{=} \mathbb{E}\left[\frac{\partial}{\partial t}\mathbb{E}(Y|T=t, S)\right].$$

- The positivity condition is required for  $\mu(t, s) = \mathbb{E}(Y|T = t, S = s)$  and  $\frac{\partial}{\partial t}\mu(t, s) = \frac{\partial}{\partial t}\mathbb{E}(Y|T = t, S = s)$  to be well-defined on  $\mathcal{T} \times \mathcal{S}$ .

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# 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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① **Regression Adjustment** ([Robins, 1986; Gill and Robins, 2001](#)):

$$\hat{m}_{RA}(t) = \frac{1}{n} \sum_{i=1}^n \hat{\mu}(t, S_i).$$

② **Inverse Probability Weighting** ([Hirano and Imbens, 2004](#)):

$$\hat{m}_{IPW}(t) = \frac{1}{nh} \sum_{i=1}^n \frac{K\left(\frac{T_i-t}{h}\right)}{\hat{p}(T_i|S_i)} \cdot Y_i.$$

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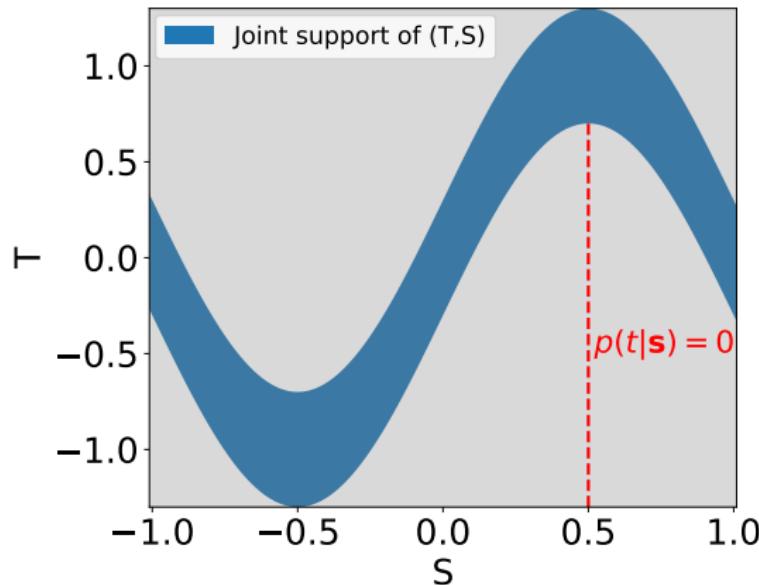
► **Issue:** Positivity is a strong assumption with continuous treatments!

# Violation of the Positivity Condition

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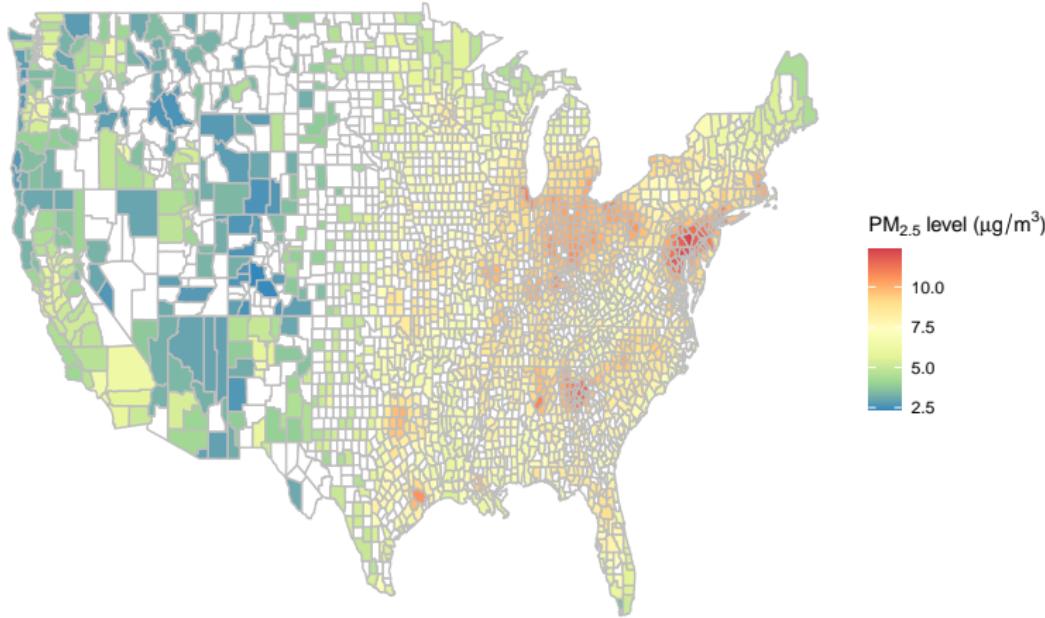
The conditional density  $p(t|s)$  is uniformly bounded away from zero for all  $(t, s) \in \mathcal{T} \times \mathcal{S}$ .

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



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

# PM<sub>2.5</sub> Distribution at the County Level



Average PM<sub>2.5</sub> levels from 1990 to 2010 in  $n = 2132$  counties.

- $T$  is PM<sub>2.5</sub> level, and  $S$  consists of the county location and socioeconomic factors.
- Only one or several PM<sub>2.5</sub> levels are available per county in the dataset, and the positivity condition is violated!

## Highlight of Today's Talk

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

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  - Both  $\widehat{m}_\theta(t)$  and  $\widehat{\theta}_C(t)$  are consistent in  $\mathcal{T}$  even when the positivity condition fails.
- ③ Nonparametric bootstrap inference with our proposed estimators  $\widehat{m}_\theta(t)$  and  $\widehat{\theta}_C(t)$  for  $m(t)$  and  $\theta(t)$  is asymptotically valid.

# Identification and Estimation



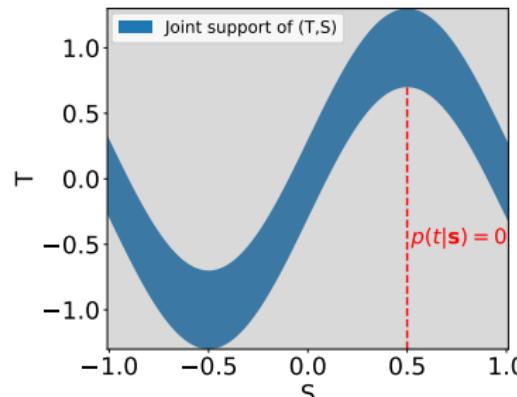
# Why Do We Need Positivity?

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The RA (or G-computation) formulae are given by

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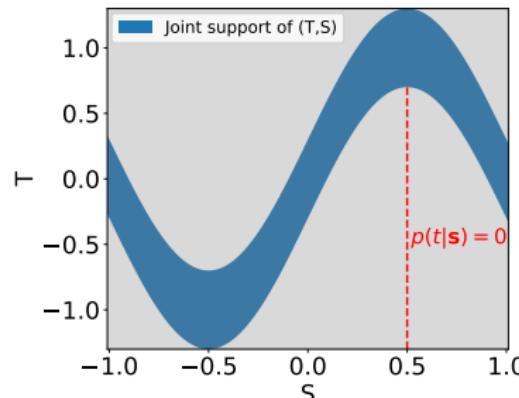
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► **Identification Issue:** Without positivity,

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

is *not well-defined* outside the support  $\mathcal{E} \subset \mathcal{T} \times \mathcal{S}$  of the joint density  $p(t, s)$ .

## Key Example: Additive Confounding Model

Consider the additive confounding model, which is commonly assumed in spatial statistics ([Paciorek, 2010](#); [Schnell and Papadogeorgou, 2020](#); [Gilbert et al., 2023](#)):

$$Y(t) = \bar{m}(t) + \eta(S) + \epsilon \quad \text{or} \quad Y = \bar{m}(T) + \eta(S) + \epsilon. \quad (1)$$

- $\bar{m} : \mathcal{T} \rightarrow \mathbb{R}$  and  $\eta : \mathcal{S} \rightarrow \mathbb{R}$  are deterministic functions.
- $\epsilon \in \mathbb{R}$  is an independent noise variable with  $\mathbb{E}(\epsilon) = 0$  and  $\text{Var}(\epsilon) > 0$ .
- $m(t) = \mathbb{E}[Y(t)] = \bar{m}(t) + \mathbb{E}[\eta(S)]$  and  $\theta(t) = m'(t) = \frac{d}{dt}\mathbb{E}[Y(t)] = \bar{m}'(t)$ .

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

Under the additive confounding model (1), we have that

$$\theta(t) = \mathbb{E} \left[ \frac{\partial}{\partial t} \mu(t, S) \middle| T = t \right] := \theta_C(t) \quad \text{and} \quad \mathbb{E}(Y) = \mathbb{E} [\bar{m}(t) + \eta(S)] = \mathbb{E} [m(T)].$$

► **Identification:** By the fundamental theorem of calculus,

$$m(t) = \mathbb{E} \left[ Y + \int_{u=T}^{u=t} \theta_C(u) du \right] = \mathbb{E}(Y) + \mathbb{E} \left\{ \int_{u=T}^{u=t} \mathbb{E} \left[ \frac{\partial}{\partial t} \mu(T, S) \middle| T = u \right] du \right\} \quad \text{for any } t \in \mathcal{T}.$$

## Proposed Estimators of $m(t)$ and $\theta(t)$

Recall our identification formulae

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

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Our **integral estimator** of  $m(t)$  is given by

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

and our **localized derivative** estimator of  $\theta(t)$  is

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

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

## Some Remarks on Proposed Estimators $\widehat{m}_\theta(t)$ and $\widehat{\theta}_C(t)$

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

- ① Other methods can be applied to estimate  $\frac{\partial}{\partial t} \mu(t, s)$  and  $P(s|t)$ .
  - $\widehat{m}_\theta(t)$  and  $\widehat{\theta}_C(t)$ , under our kernel-based estimators, are *linear smoothers*.

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  - We provide a fast computing recipe via Riemann sum approximation.
  - The approximation error is at most  $O_P(\frac{1}{n})$ , which is *asymptotically negligible*.
- ③ We can construct (simultaneous) inference on  $m(t)$  and  $\theta(t)$  with the proposed estimators  $\widehat{m}_\theta(t)$  and  $\widehat{\theta}_C(t)$  via *nonparametric bootstrap*.

# Asymptotic Theory



# Uniform Consistencies of Proposed Estimators

Combining with the consistency of  $\widehat{P}_\hbar(s|t)$  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  $p_T(t) \geq p_{T,\min} > 0$  for all  $t \in \mathcal{T}'$ . When  $q = 2$  and  $h, b, \hbar, \frac{\max\{h,b\}^4}{h} \rightarrow 0$  and  $\frac{n \max\{h, \hbar\} b^d}{\log n}, \frac{n \hbar}{\log n} \rightarrow \infty$ ,

$$\sup_{t \in \mathcal{T}'} |\widehat{\theta}_C(t) - \theta_C(t)| = \underbrace{O\left(h^2 + b^2 + \frac{\max\{b, h\}^4}{h}\right)}_{\text{Bias term}} + \underbrace{O_P\left(\sqrt{\frac{\log n}{nh^3}} + \hbar^2 + \sqrt{\frac{\log n}{n\hbar}}\right)}_{\text{Stochastic variation}},$$
$$\sup_{t \in \mathcal{T}'} |\widehat{m}_\theta(t) - m(t)| = O\left(h^2 + b^2 + \frac{\max\{b, h\}^4}{h}\right) + O_P\left(\frac{1}{\sqrt{n}} + \sqrt{\frac{\log n}{nh^3}} + \hbar^2 + \sqrt{\frac{\log n}{n\hbar}}\right).$$

# Uniform Rate of Convergence For the Integral Estimator

$$\widehat{m}_\theta(t) = \frac{1}{n} \sum_{i=1}^n Y_i + \frac{1}{n} \sum_{i=1}^n \int_{u=T_i}^{u=t} \widehat{\theta}_C(u) du \quad \text{and} \quad \widehat{\theta}_C(t) = \frac{\sum_{i=1}^n \widehat{\beta}_2(t, s_i) \cdot \bar{K}_T\left(\frac{T_i-t}{\hbar}\right)}{\sum_{j=1}^n \bar{K}_T\left(\frac{T_j-t}{\hbar}\right)}.$$

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

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# Case Study: PM<sub>2.5</sub> on CMR



## PM<sub>2.5</sub> and CMRs Data Recap

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
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8045	Garfield	-107.903621	39.599420	2.601772	250.781477

- 1 The dataset ([Wyatt et al., 2020a,b](#)) contains the average annual CMRs ( $Y$ ) and PM<sub>2.5</sub> levels ( $T$ ) across  $n = 2132$  U.S. counties over 1990-2010.

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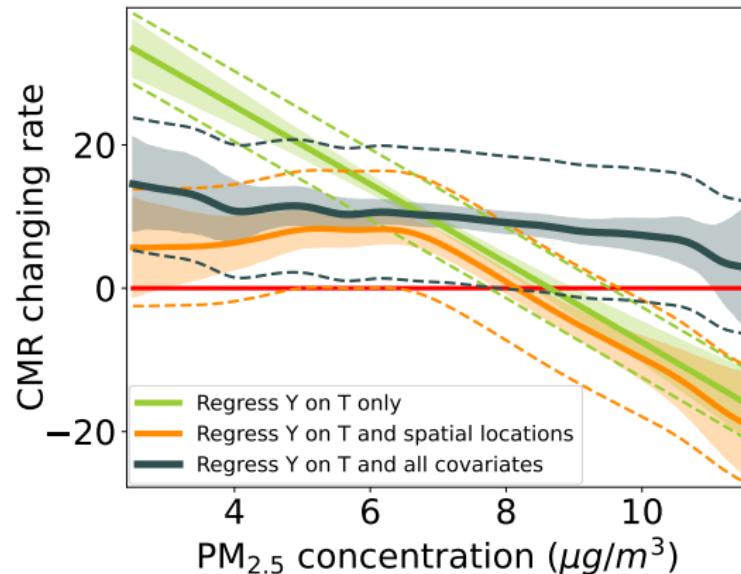
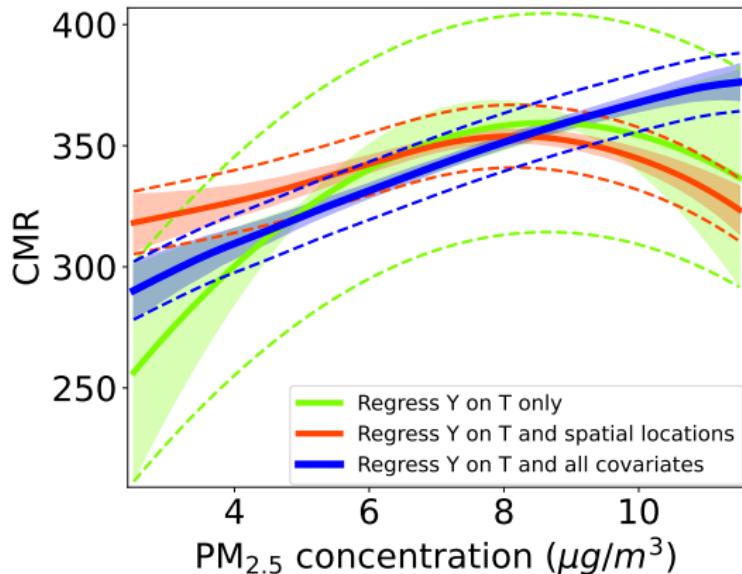
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  - 8 county-level socioeconomic factors acquired from the US census.
- ③ Focus on the values of PM<sub>2.5</sub> between 2.5  $\mu\text{g}/\text{m}^3$  and 11.5  $\mu\text{g}/\text{m}^3$  to avoid boundary effects ([Takatsu and Westling, 2022](#)).

# Effect of PM<sub>2.5</sub> on the Cardiovascular Mortality Rate (CMR)

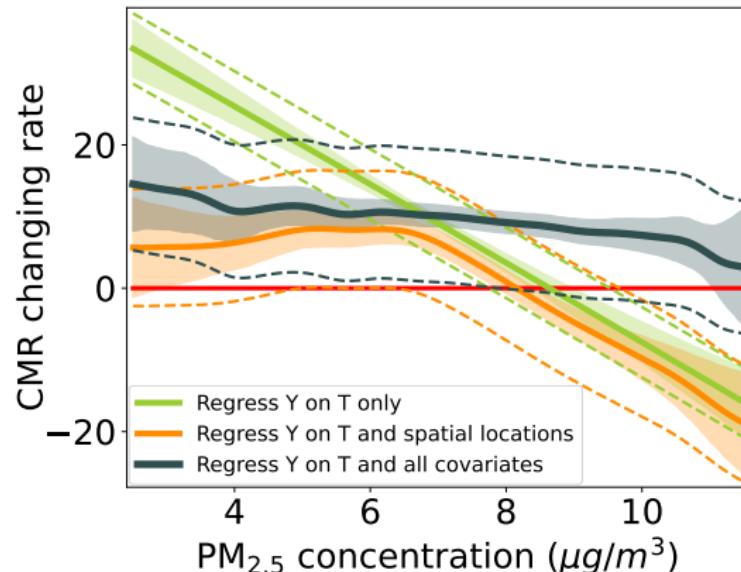
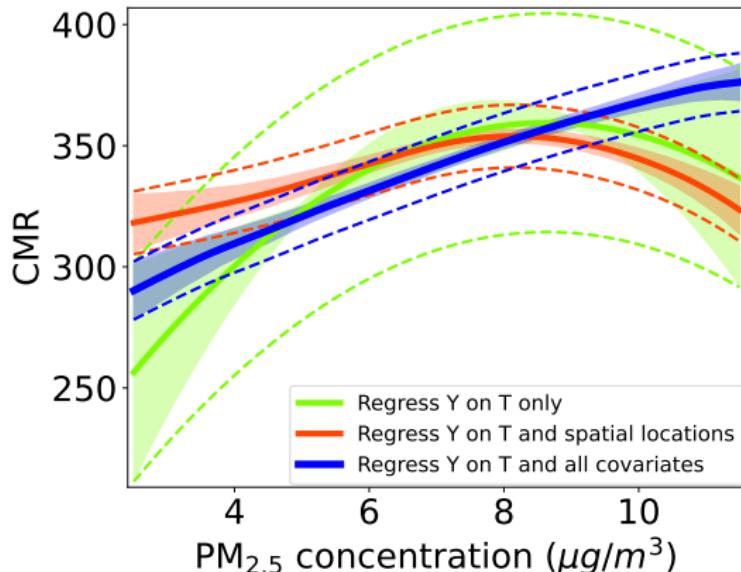


Shaded areas: 95% pointwise confidence intervals; Regions between dashed lines: 95% uniform confidence bands.

- We compare three models:

- 1 Regress  $Y$  on  $T$  alone via local quadratic regression.
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- 3 Regress  $Y$  on  $T$  with both spatial and socioeconomic covariates.

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- 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.
- For model 3, the increasing trends are **significant** when  $\text{PM}_{2.5} < 8 \mu\text{g}/\text{m}^3$ .

# Discussion



## Summary and Future Work

We study nonparametric inference on  $m(t) = \mathbb{E}[Y(t)]$  and  $\theta(t) = \frac{d}{dt}\mathbb{E}[Y(t)]$  without the **positivity** condition.

- Our key technique relies on two pillars in calculus:

$$\underbrace{\theta(t) = \mathbb{E} \left[ \frac{\partial}{\partial t} \mu(t, S) \middle| T = t \right]}_{\text{Differentiation}} \quad \text{and} \quad \underbrace{m(t) = \mathbb{E} \left[ Y + \int_{u=T}^{u=t} \theta(u) du \right]}_{\text{Integration}}.$$

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### ► Ongoing and Future Directions:

- Generalize our proposed estimators to inverse probability weighting and doubly robust forms ([Zhang and Chen, 2025](#)).
- Use additive models ([Guo et al., 2019](#)) to address the high-dimensional covariates.

# 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](#).

I will present the following paper in the invited Session “Advances in Modern Causal Inference” on **Tuesday at 8:30am**.

- [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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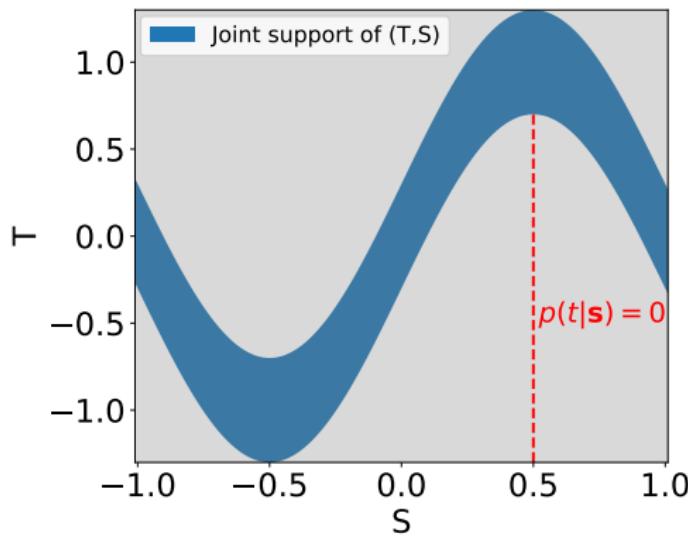
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# Identification Strategy Without Positivity

## Assumption (Identification Conditions)

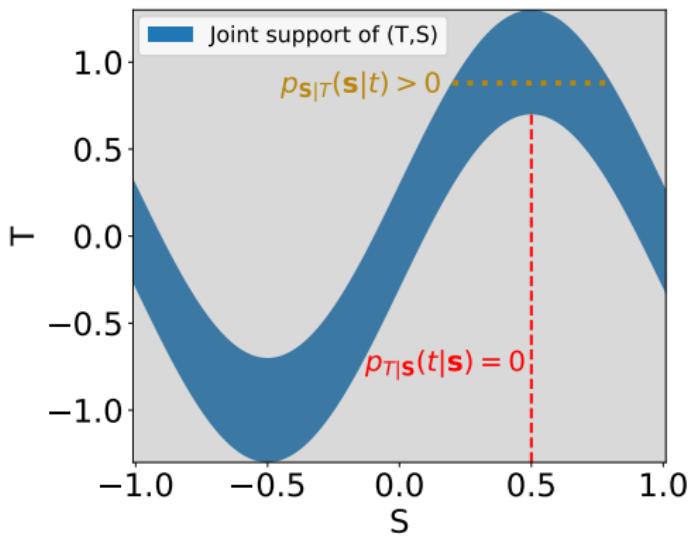
- ① (*Consistency*)  $Y = Y(t)$  whenever  $T = t \in \mathcal{T}$ .
- ② (*Ignorability*)  $Y(t)$  is conditionally independent of  $T$  given  $S$  for all  $t \in \mathcal{T}$ .
- ③ (*Treatment Variation*)  $\text{Var}(T|S = s) > 0$  for all  $s \in \mathcal{S}$ .



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- ③ (Treatment Variation)  $\text{Var}(T|S = s) > 0$  for all  $s \in \mathcal{S}$ .



## Assumption (Extrapolation; Zhang et al. 2024)

Assume  $(t, s) \mapsto \mathbb{E}[Y(t)|S = s]$  to be differentiable w.r.to  $t$  for any  $(t, s) \in \mathcal{T} \times \mathcal{S}$  with  $p_{S|T}(s|t) > 0$  and

$$\begin{aligned}\theta(t) &= \frac{d}{dt} \mathbb{E}[Y(t)] = \mathbb{E} \left[ \frac{\partial}{\partial t} \mathbb{E}[Y(t)|S] \right] \\ &\stackrel{*}{=} \mathbb{E} \left[ \frac{\partial}{\partial t} \mathbb{E}[Y(t)|S] \mid T = t \right].\end{aligned}$$

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

- 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  $\beta_2(t, s) = \frac{\partial}{\partial t} \mu(t, s)$ .

- 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.

# Fast Computing Algorithm for the Integral Estimator

Our integral estimator takes the form

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

► **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:

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

- 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  $O_p(\frac{1}{n})$ , which is *asymptotically negligible*.

# Nonparametric Bootstrap Inference

- ① Compute  $\hat{m}_\theta(t)$  on the original data  $\{(Y_i, T_i, S_i)\}_{i=1}^n$ .
- ② Generate  $B$  bootstrap samples  $\left\{\left(Y_i^{*(b)}, T_i^{*(b)}, S_i^{*(b)}\right)\right\}_{i=1}^n$  by sampling with replacement and compute  $\hat{m}_\theta^{*(b)}(t)$  for each  $b = 1, \dots, B$ .
- 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  $b = 1, \dots, B$ .
- 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:

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

## Regularity Assumptions (Smoothness Conditions)

Let  $\mathcal{E} \subset \mathcal{T} \times \mathcal{S}$  be the support of  $p(t, s)$ ,  $\mathcal{E}^\circ$  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  $\mathcal{E}^\circ$ . 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  $\int s \cdot K_S(s) ds = 0$ . In addition, for all  $j = 1, 2, \dots$ , and  $\ell = 1, \dots, d$ ,

$$\begin{aligned}\kappa_j^{(T)} &:= \int_{\mathbb{R}} u^j K_T(u) du < \infty, & \nu_j^{(T)} &:= \int_{\mathbb{R}} u^j K_T^2(u) du < \infty, \\ \kappa_{j,\ell}^{(S)} &:= \int_{\mathbb{R}^d} u_\ell^j K_S(u) du < \infty, & \text{and} & \nu_{j,k}^{(S)} := \int_{\mathbb{R}^d} u_\ell^j K_S^2(u) du < \infty.\end{aligned}$$

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

# 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  $t \in \mathcal{T}'$ ,

$$\sqrt{nh^3} [\hat{\theta}_C(t) - \theta(t)] = \mathbb{G}_n \bar{\varphi}_t + o_P(1), \quad \text{and} \quad \sqrt{nh^3} [\hat{m}_\theta(t) - m(t)] = \mathbb{G}_n \varphi_t + o_P(1),$$

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  $\varphi_t$  are the IPW components of the *approximated* efficient influence functions.

# Nonparametric 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  $b \lesssim \bar{h} \asymp n^{-\frac{1}{\varpi}}$  for some  $\gamma \geq \varpi > 0$  such that  $\frac{nh^{d+5}}{\log n} \rightarrow c_1$  and  $\frac{n\bar{h}^5}{\log n} \rightarrow c_2$  for some  $c_1, c_2 \geq 0$  and

$$\frac{\bar{h}}{\bar{h}^3 \log n}, \bar{h}n^{\frac{1}{3}} \log n, \frac{\sqrt{n}\bar{h}}{\log n}, \frac{n \max\{h, \bar{h}\} b^d}{\log n} \rightarrow \infty \text{ as } n \rightarrow \infty,$$

1

$$\left| \sqrt{nh^3} \sup_{t \in \mathcal{T}} |\hat{m}_\theta(t) - m(t)| - \sup_{t \in \mathcal{T}} |\mathbb{G}_n \varphi_t| \right| = O_P \left( \sqrt{nh^3 \max\{h, \bar{h}\}^4} + \sqrt{\frac{h^3 \log n}{\bar{h}}} + \frac{\log n}{\sqrt{n}\bar{h}} + \sqrt{\frac{\log n}{nb^d \bar{h}}} \right).$$

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

$$\sup_{u \geq 0} \left| P \left( \sqrt{nh^3} \sup_{t \in \mathcal{T}} |\hat{m}_\theta(t) - m(t)| \leq u \right) - P \left( \sup_{f \in \mathcal{F}} |\mathbb{B}(f)| \leq u \right) \right| = O \left( \left( \frac{\log^5 n}{nh^3} \right)^{\frac{1}{8}} + \left( \frac{\log^2 n}{nb^d \bar{h}} \right)^{\frac{3}{8}} \right).$$

3

$$\sup_{u \geq 0} \left| P \left( \sqrt{nh^3} \sup_{t \in \mathcal{T}} |\hat{m}_\theta^*(t) - \hat{m}_\theta(t)| \leq u \middle| \mathbb{U}_n \right) - P \left( \sup_{f \in \mathcal{F}} |\mathbb{B}(f)| \leq u \right) \right| = O_P \left( \left( \frac{\log^5 n}{nh^3} \right)^{\frac{1}{8}} + \left( \frac{\log^2 n}{nb^d \bar{h}} \right)^{\frac{3}{8}} \right),$$

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  $\varphi_t$  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  $\sup_{f \in \mathcal{F}} |\mathbb{B}(f)|$ .
- 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.
  - The asymptotic linearity (or V-statistic) is non-degenerate.
  - Pointwise bootstrap confidence intervals are asymptotically valid.
- 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  $\left(\frac{\log n}{n}\right)^{\frac{4}{5d}} \lesssim b \lesssim n^{-\frac{1}{5}}$ .
  - These orders align with the outputs from the usual bandwidth selection methods ([Bashtannyk and Hyndman, 2001](#); [Li and Racine, 2004](#)).
  - No explicit undersmoothing is required!!

## Simulation Setup for Estimating $m(t)$ and $\theta(t)$ Without Positivity

- 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 nominal level for confidence intervals or bands to 95%.
- Compare our proposed estimators with the regression adjustment estimators under the same choices of bandwidth parameters:

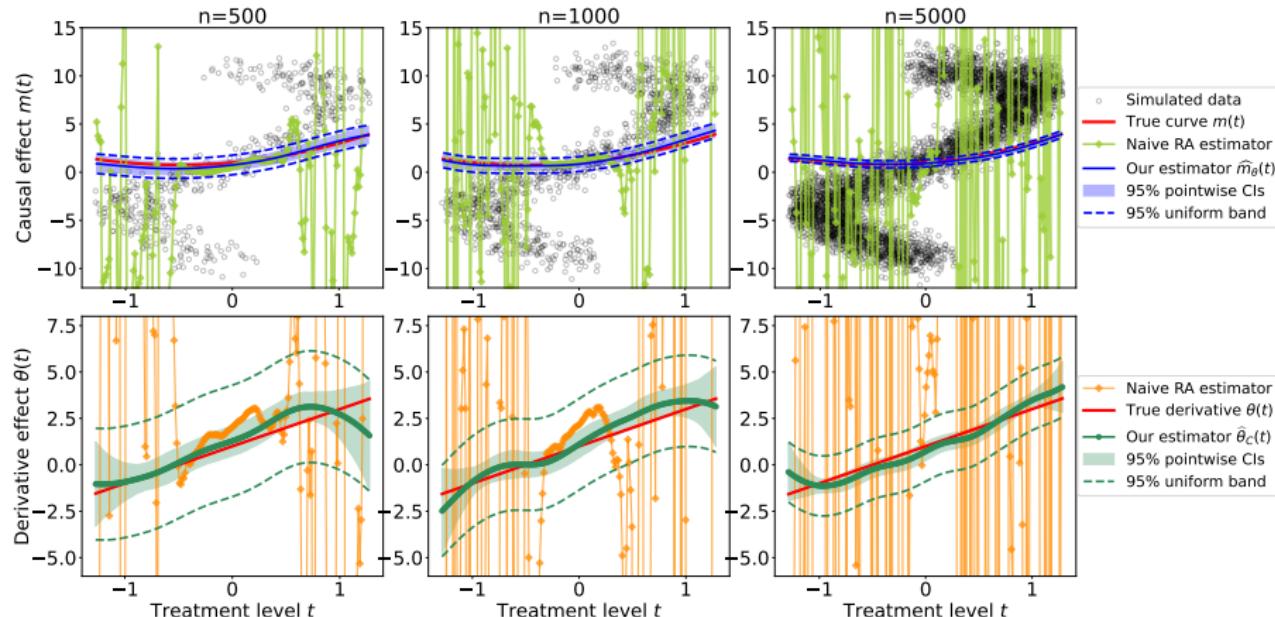
$$\hat{m}_{\text{RA}}(t) = \frac{1}{n} \sum_{i=1}^n \hat{\mu}(t, S_i) \quad \text{and} \quad \hat{\theta}_{\text{RA}}(t) = \frac{1}{n} \sum_{i=1}^n \hat{\beta}_2(t, S_i).$$

# Single Confounder Model Without Positivity

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.

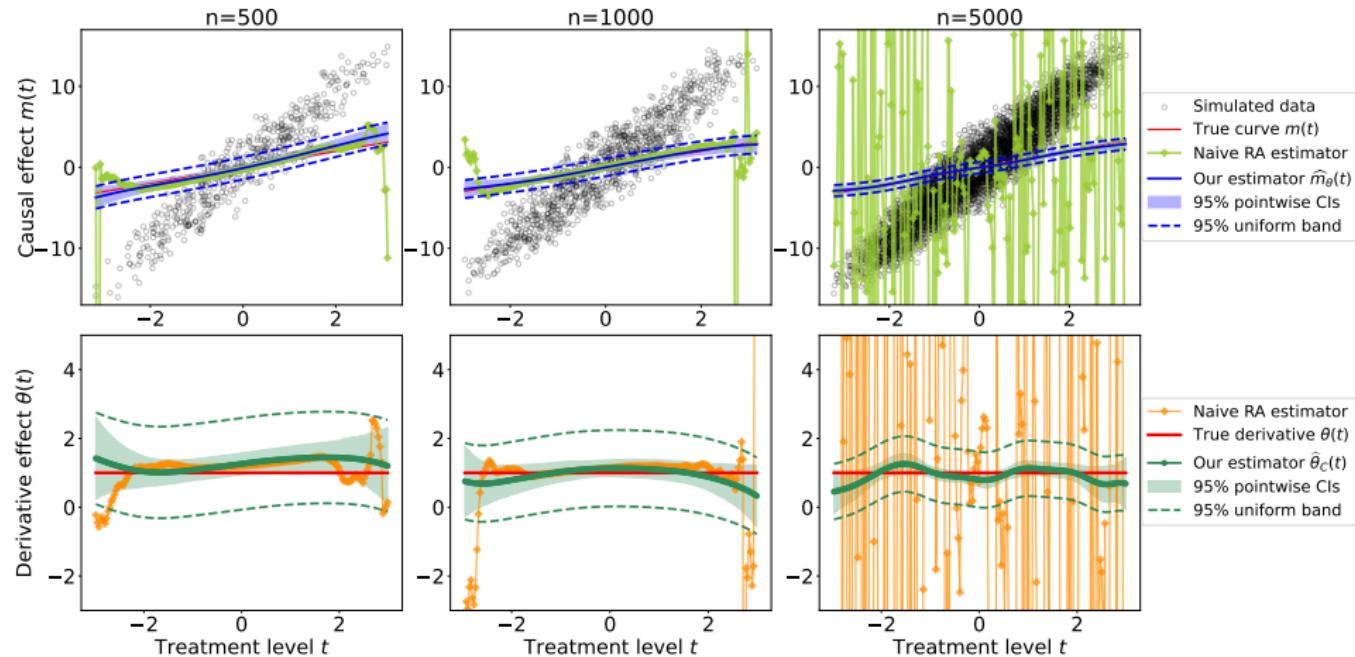


# Linear Confounding Model Without Positivity

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  $\epsilon \sim \mathcal{N}(0, 1)$ .

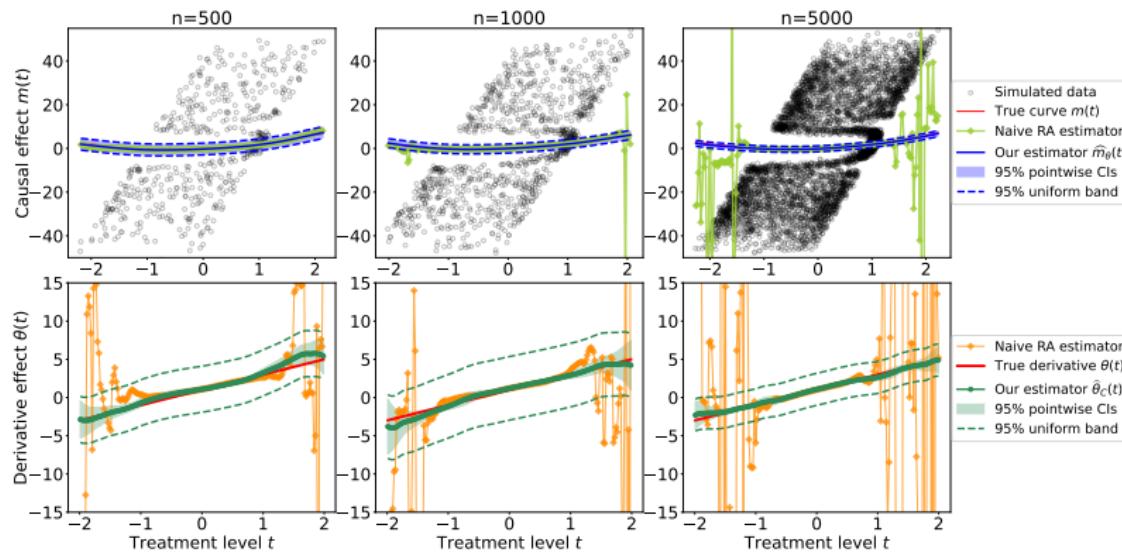


# Nonlinear Confounding Model Without Positivity

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

$$\mu(f(s), s) = \bar{m}(f(s)) + \eta(s) = m(f(s)) + \eta(s). \quad (2)$$

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

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

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

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

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  $\rho_1$  in the previous assumption.