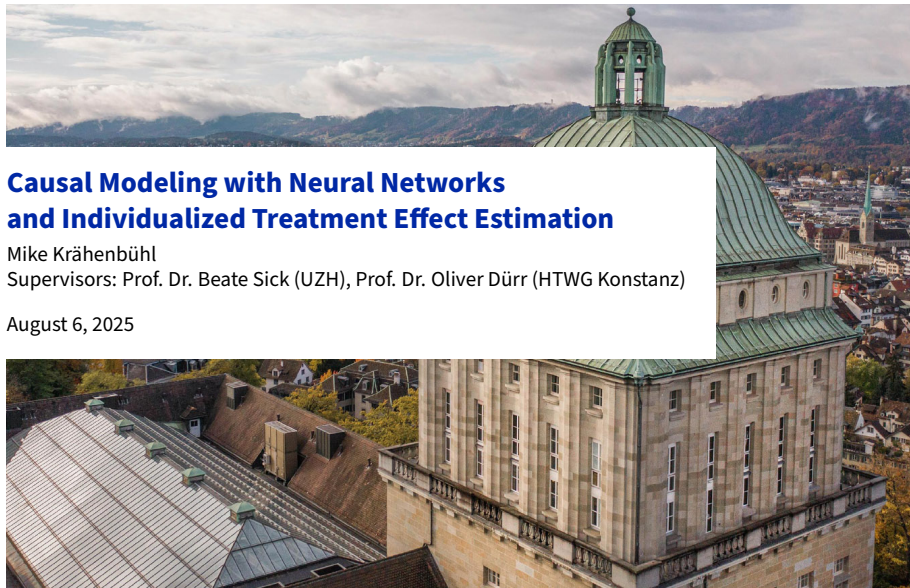




Universität
Zürich^{UZH}

Master Program in Biostatistics www.biostat.uzh.ch
Master Exam



Causal Modeling with Neural Networks and Individualized Treatment Effect Estimation

Mike Krähenbühl

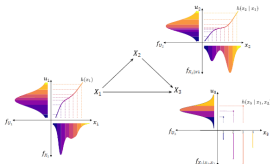
Supervisors: Prof. Dr. Beate Sick (UZH), Prof. Dr. Oliver Dürr (HTWG Konstanz)

August 6, 2025

Background

Paper "*Interpretable Neural Causal Models with TRAM-DAGs*" (Sick and Dürr, 2025):

- Framework to model causal relationships in a known directed acyclic graph (DAG)
- Based on transformation models
- Rely on (deep) neural networks
- Compromise between interpretability and flexibility



They showed on synthetic data, that TRAM-DAGs can be fitted on observational data and tackle causal queries on all three levels of Pearl's causal hierarchy.

Research Questions

In this presentation:

1. TRAM-DAGs

- How to fit the model on observed data and subsequently make observational, interventional and counterfactual queries?

2. Individualized Treatment Effect (ITE) estimation

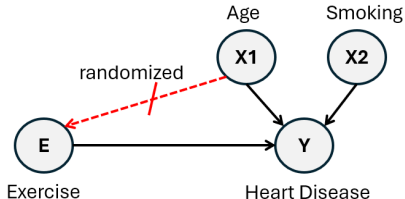
- Does ITE estimation work on real RCT data (International Stroke Trial)?
- When and why does ITE estimation fail (simulation)?
- How to estimate ITEs with TRAM-DAGs in a complicated graph (simulation)?

TRAM-DAGs

TRAM-DAGs: Motivation

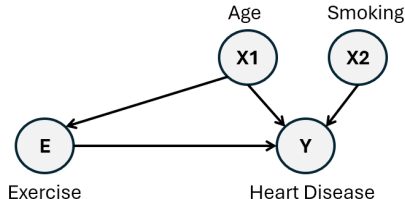
Randomized Controlled Trial:

- Gold standard for estimating causal effect
- Solves problem of confounding



Observational Data:

- Real world, potential confounding
- We assume no unobserved confounding

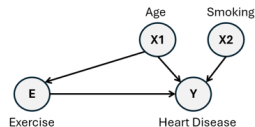


TRAM-DAGs: Motivation

Pearl's causal hierarchy (Pearl, 2009)

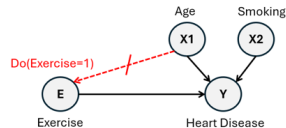
(L1) Observational: $P(Y = 1 \mid E = 1)$

"Probability of heart disease given that the person exercises"



(L2) Interventional: $P(Y = 1 \mid \text{do}(E = 1))$

"Probability of heart disease if we made people start exercising"



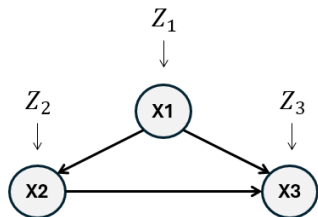
(L3) Counterfactual: $P(Y_{(E=1)} = 1 \mid E = 0, Y = 1)$

"Would someone who does not exercise and has heart disease still have it if they had exercised?"



TRAM-DAGs: Background

Structural Causal Model: Describes the causal mechanism and probabilistic uncertainty (Pearl, 2009)



$$Z \sim F_{Z_1}, Z_2 \sim F_{Z_2}, Z_3 \sim F_{Z_3}$$

$$X_1 = f_1(Z_1)$$

$$X_2 = f_2(Z_2, X_1)$$

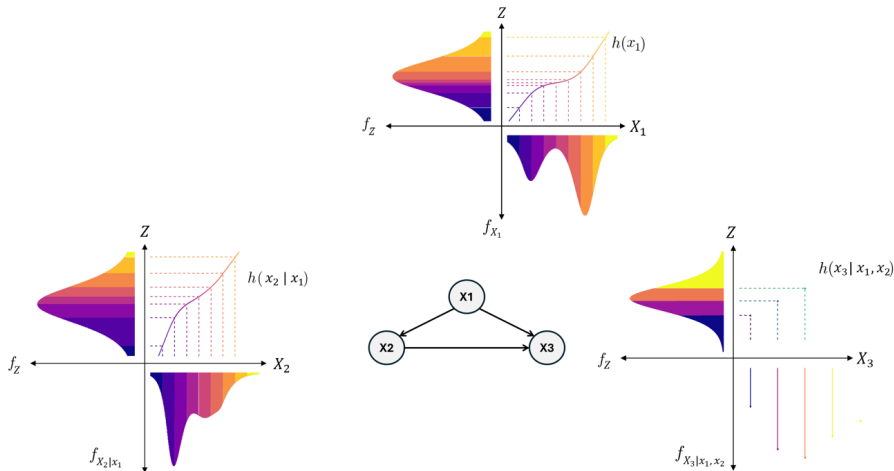
$$X_3 = f_3(Z_3, X_1, X_2)$$

- X_i : observed variable
- Z_i : exogenous (latent) variable
- f_i : deterministic function: $X_i = f_i(Z_i, \text{pa}(X_i))$

→ We want a model that estimates $X_i = f_i(Z_i, \text{pa}(X_i))$ in a flexible and interpretable way!

TRAM-DAGs: Background

Proposed framework: TRAM-DAGs (Sick and Dürr, 2025)



TRAM-DAGs: Background

Transformation Models: Flexible distributional regression method
(Hothorn et al., 2014)

Continuous $Y \in \mathbb{R}$:

$$F_{Y|\mathbf{X}=\mathbf{x}}(y) = F_Z(h(y | \mathbf{x})) = F_Z(h(y) + \mathbf{x}^\top \beta)$$

Discrete $Y \in \{y_1, y_2, \dots, y_K\}$:

$$P(Y \leq y_k | \mathbf{X} = \mathbf{x}) = F_Z(\vartheta_k + \mathbf{x}^\top \beta), \quad k = 1, 2, \dots, K - 1$$

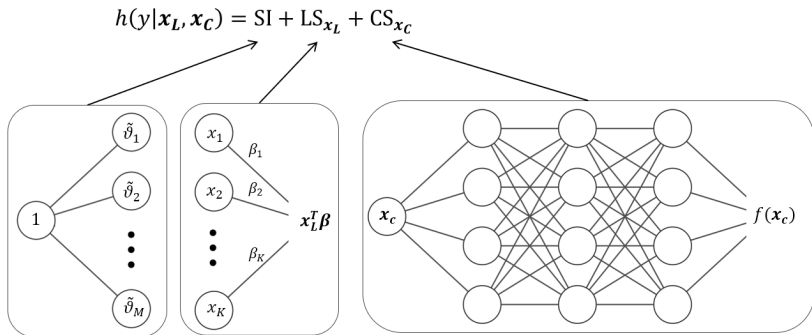
- F_Z : CDF of the latent distribution (e.g. standard logistic)
- h : Transformation function, monotonically increasing
- \mathbf{x} : Predictors

TRAM-DAGs: Background

Extended to Deep TRAMs (Sick et al., 2021)

- Customizable transformation model using neural networks (NNs)
- Minimizing negative log-likelihood (NLL) via NN optimization

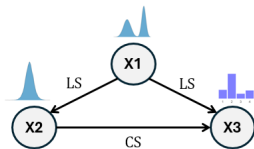
Effects of predictors: LS (Linear Shift), CS (Complex Shift), CI (Complex Intercept)



TRAM-DAGs: Experiment 1 (simulation)

Setup:

- We have:
 - Observational data (simulated)
 - Predefined DAG
- We want:
 - Estimate $Z_i = h_i(X_i \mid \text{pa}(X_i))$ of each variable i
 - Sample from conditional distributions to make causal queries



$$X_1 \sim F_Z(h(x_1))$$

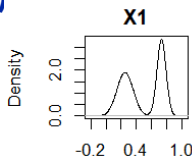
$$X_2 \sim F_Z(h(x_2) + \text{LS}_{x_1})$$

$$X_3 \sim F_Z(h(x_3) + \text{LS}_{x_1} + \text{CS}_{x_2})$$

TRAM-DAGs: Experiment 1 (simulation)

Data-generating process (DGP):

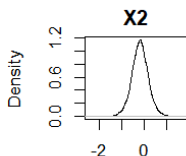
X_1 : Continuous, bimodal. *Source node* (independent).



X_2 : Continuous. Depends on X_1 (linear):

$$\beta_{12} = 2, \quad h_I(X_2) = 5X_2$$

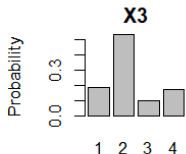
$$h(X_2 | X_1) = h_I(X_2) + \beta_{12}X_1$$



X_3 : Ordinal. Depends on X_1 (linear) and X_2 (complex):

$$\beta_{13} = 0.2, \quad f(X_2) = 0.5 \cdot \exp(X_2), \quad \vartheta_k \in \{-2, 0.42, 1.02\}$$

$$h(X_{3,k} | X_1, X_2) = \vartheta_k + \beta_{13}X_1 + f(X_2)$$



TRAM-DAGs: Experiment 1 (simulation)

Construct Model: Modular Neural Network

Inputs: Observations + assumed structure

Outputs:

- Simple Intercepts (SI): ϑ
- Linear Shifts (LS): $\beta_{12}X_1, \beta_{13}X_1$
- Complex Shift (CS): $f(X_2)$

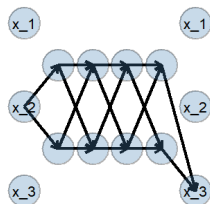
Assemble transformation functions:

$$h(X_i \mid \text{pa}(X_i)) = \text{SI} + \text{LS} + \text{CS}$$

$$h(X_1) = \vartheta_1(X_1)$$

$$h(X_2 \mid X_1) = \vartheta_2(X_2) + \beta_{12}X_1$$

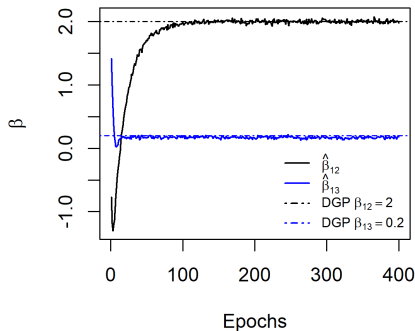
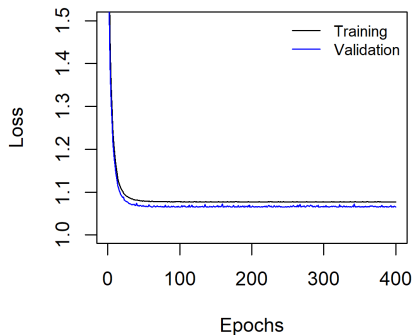
$$h(X_{3,k} \mid X_1, X_2) = \vartheta_k + \beta_{13}X_1 + f(X_2)$$



CS_{X_2} on X_3

TRAM-DAGs: Experiment 1 (simulation)

Model fitting: 20,000 training samples, 400 epochs



Sampling from the Fitted TRAM-DAG (L1)

Nodes $X_i, i \in \{1, 2, 3\}$:

- Sample latent value:

$$z_i \sim F_{Z_i} \quad (\text{e.g., } \text{rlogis}() \text{ in R})$$

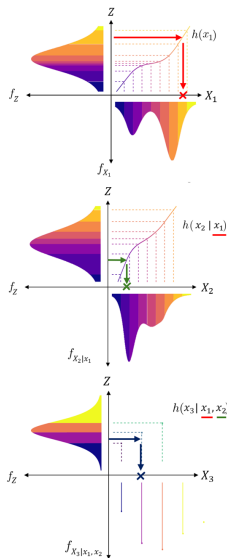
- Determine x_i such that:

- **If X_i is continuous:** Solve for x_i using numerical root-finding:

$$h(x_i \mid \text{pa}(x_i)) - z_i = 0$$

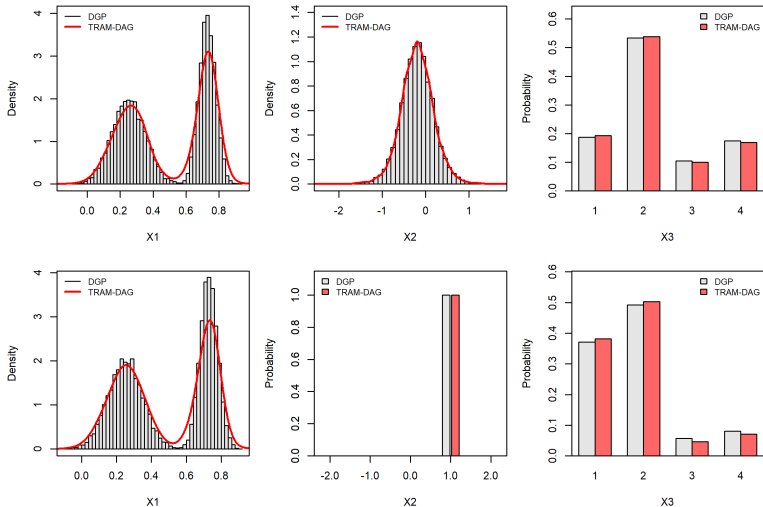
- **If X_i is ordinal:** find the smallest category x_i such that

$$x_i = \max(\{0\} \cup \{x : z_i > h(x \mid \text{pa}(x_i))\}) + 1$$



TRAM-DAGs: Experiment 1 (simulation)

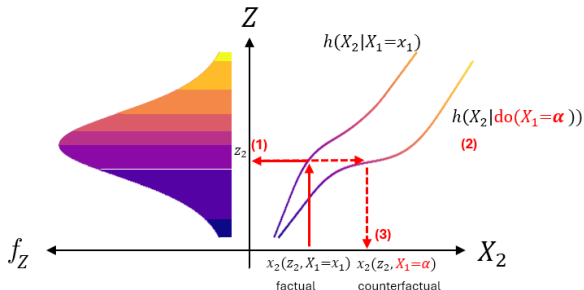
Sampled observational and interventional distributions:



Experiment 1: TRAM-DAGs (Simulation)

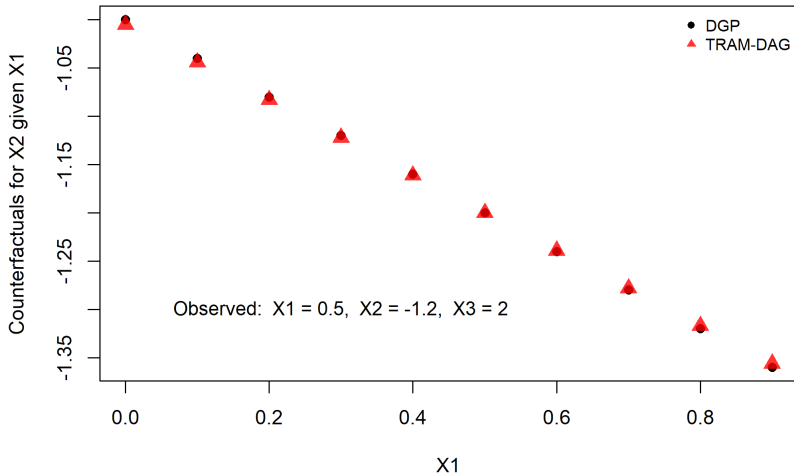
How to determine a counterfactual value for X_2 using Pearl's 3-step procedure (Pearl, 2009):

1. **Abduction:** Infer Z from observed data
2. **Action:** Modify SCM (e.g., $\text{do}(X = \alpha)$)
3. **Prediction:** Infer counterfactual outcome



Experiment 1: TRAM-DAGs (simulation)

Counterfactuals: Counterfactual value of X_2 under varying X_1



Experiment 1: TRAM-DAGs (simulation)

Discussion: With TRAM-DAGs we can

- estimate the functional form of the edges in the DAG
- customize flexibility and interpretability (SI/CI, LS, CS)
- sample from the fitted model (observational/interventional)
- estimate counterfactuals

Individualized Treatment Effects (ITEs)

Individualized Treatment Effect (ITE): Motivation

Why ITE?

- RCTs estimate the Average Treatment Effect (ATE)
- Individuals may respond differently based on covariates
- Important for personalized medicine, targeted marketing, etc.
- Heterogeneity mostly driven by treatment-covariate interactions

Definition: Difference in potential outcomes ([Rubin, 2005](#))

$$Y_i(1) - Y_i(0)$$

where $Y_i(1)$: outcome if treated, $Y_i(0)$: if not treated

Fundamental problem: We never observe both $Y_i(1)$ and $Y_i(0)$ for the same individual ([Holland, 1986](#)).

From Unobservable to Estimable ITE

Goal: Estimate the *individualized treatment effect (ITE)* from observed data (Hoogland et al., 2021).

$$\begin{aligned}\text{ITE}(\mathbf{x}_i) &= \mathbb{E}[Y_i(1) - Y_i(0) \mid \mathbf{X} = \mathbf{x}_i] \\ &= \mathbb{E}[Y_i(1) \mid T = 1, \mathbf{X} = \mathbf{x}_i] - \mathbb{E}[Y_i(0) \mid T = 0, \mathbf{X} = \mathbf{x}_i] \\ &\quad \text{(by ignorability/exchangeability: no unmeasured confounding)} \\ &= \mathbb{E}[Y_i \mid T = 1, \mathbf{X} = \mathbf{x}_i] - \mathbb{E}[Y_i \mid T = 0, \mathbf{X} = \mathbf{x}_i] \\ &\quad \text{(by consistency: observed = potential outcome, e.g. correct label)}\end{aligned}$$

Further assumptions:

- **Positivity:** every individual could receive either treatment (e.g. no deterministic assignment)
- **No interference:** one person's treatment does not affect another's outcome

Individualized Treatment Effect (ITE): Models

How did we estimate the potential outcomes $\mathbb{E}[Y_i \mid T = t, \mathbf{X} = \mathbf{x}_i]$?

— **T-learner:**

1. Fit two separate models on treated and control groups
 2. Predict $\mathbb{E}[Y_i \mid \mathbf{X} = \mathbf{x}_i]$ from each model
- Logistic regression / Random forest (with hyperparameter tuning)

— **S-learner:**

1. Fit one model on all data with treatment as a feature
 2. Predict $\mathbb{E}[Y_i \mid \text{do}(T = t), \mathbf{X} = \mathbf{x}_i]$ by setting $T = 0$ and $T = 1$
- TRAM-DAGs (flexible, interactions, interventions/counterfactuals)

Experiment 2: ITE on International Stroke Trial (IST)

Background/Motivation: [Chen et al. \(2025\)](#) showed that results of models used for ITE estimation did not generalize to the test set.

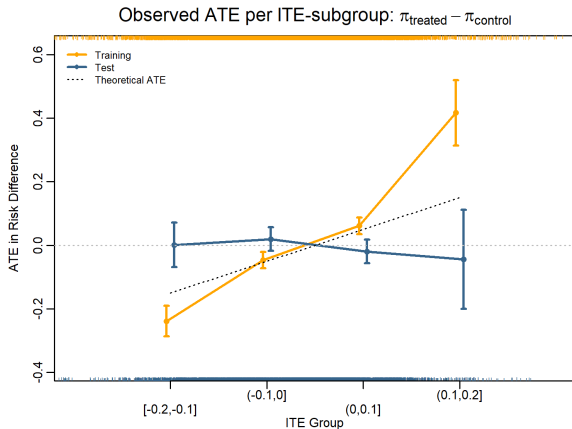
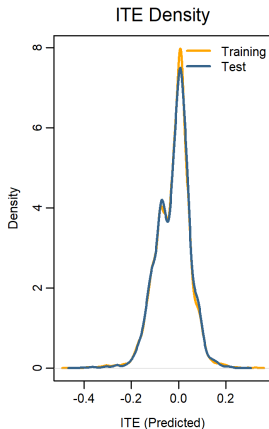
International Stroke Trial (IST):

- Large RCT on stroke patients (19,435 patients, 21 baseline covariates)
- Evaluated the effects of aspirin on death or dependence at 6 months
- Binary treatment and outcome

Research question: Do we reach similar conclusion as [Chen et al. \(2025\)](#) when estimating ITEs with T-learners (logistic regression, tuned random forest) and an S-learner (TRAM-DAGs) on the IST dataset.

Experiment 2: ITE on International Stroke Trial (IST)

Results: with T-learner tuned random forest using the comets package (Kook, 2024):



Experiment 2: ITE on International Stroke Trial (IST)

Discussion:

- We obtained similar results as [Chen et al. \(2025\)](#)
- Some models suggest moderate treatment effect heterogeneity, but the ITEs do not generalize to the test set (no effect)
- We do not certainly know why, since ground truth is unknown

Experiment 3: ITE model robustness in RCTs (simulation)

Motivation: ITE estimation did not generalize to the test data on the real-world RCT of the International Stroke Trial (IST). We want to know why!

Research question: What factors contribute to the failure of ITE estimation in causal models?

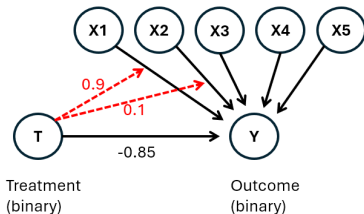
Setup:

- Simulate different RCT scenarios to understand when ITE estimation fails
- Apply simple model (logistic regression; matching DGP) and non-parametric model (tuned random forest)

Simulation Case 1: Fully Observed

Setup:

- $n = 20,000$
- $T \sim \text{Bernoulli}(0.5)$
- $\mathbf{X} = (X_1, \dots, X_5)^\top \sim \mathcal{N}(\mathbf{0}, \Sigma)$
- $\mathbf{X}_{TX} = (X_1, X_2)^\top$ **interaction**



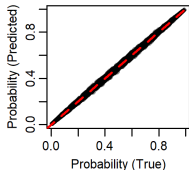
Outcome model:

$$\mathbb{P}(Y = 1 \mid \mathbf{X}, T) = \text{logit}^{-1} \left(\beta_0 + \beta_T T + \beta_X^\top \mathbf{X} + T \cdot \beta_{TX}^\top \mathbf{X}_{TX} \right)$$

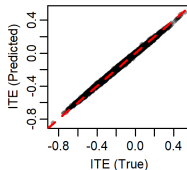
Simulation Case 1: Fully Observed

Results with T-learner logistic regression (glm):

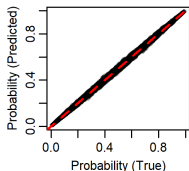
Train: $P(Y = 1 | X, T)$



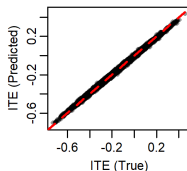
Train: ITE



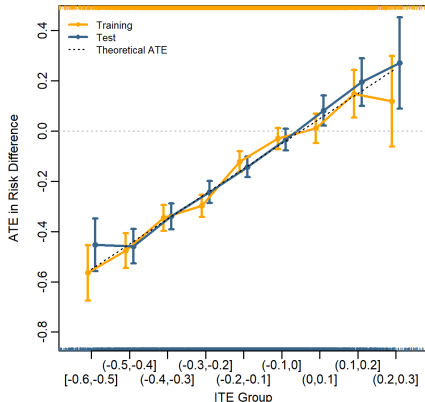
Test: $P(Y = 1 | X, T)$



Test: ITE



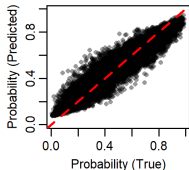
Observed ATE per ITE-subgroup: $\pi_{\text{treated}} - \pi_{\text{control}}$



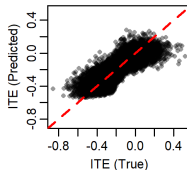
Simulation Case 1: Fully Observed

Results with T-learner tuned random forest (comets package):

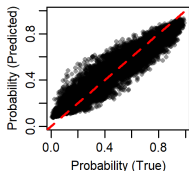
Train: $P(Y = 1 | X, T)$



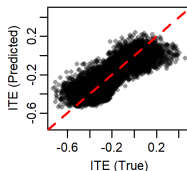
Train: ITE



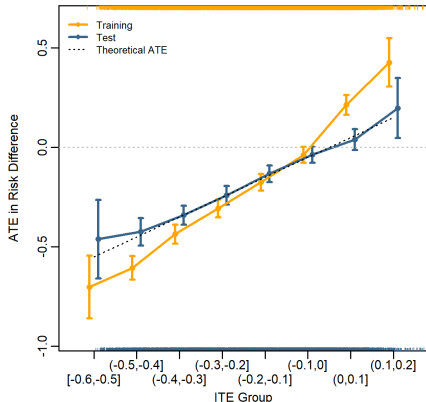
Test: $P(Y = 1 | X, T)$



Test: ITE

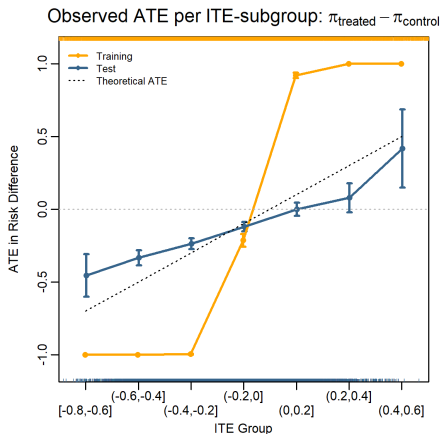
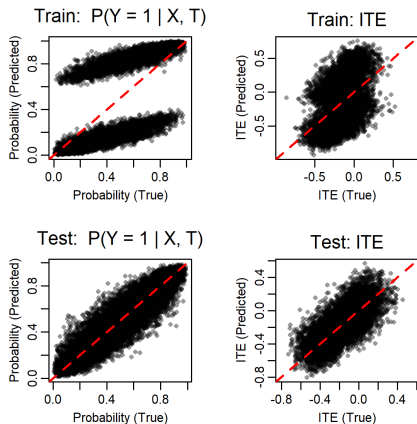


Observed ATE per ITE-subgroup: $\pi_{\text{treated}} - \pi_{\text{control}}$



Simulation Case 1: Fully Observed

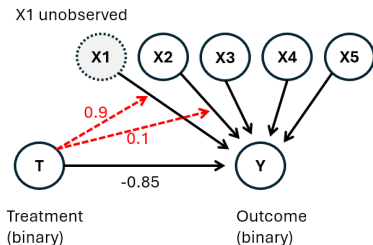
Results with (untuned) T-learner random forest using the randomForest package (Breiman, 2001):



Simulation Case 2: Unobserved Interaction

Setup:

- $n = 20,000$
- $T \sim \text{Bernoulli}(0.5)$
- $\mathbf{X} = (X_1, \dots, X_5)^\top \sim \mathcal{N}(\mathbf{0}, \Sigma)$
- $\mathbf{X}_{\text{TX}} = (X_1, X_2)^\top$ **interaction**



Outcome model:

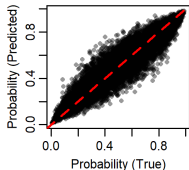
$$\mathbb{P}(Y = 1 \mid \mathbf{X}, T) = \text{logit}^{-1} \left(\beta_0 + \beta_T T + \beta_X^\top \mathbf{X} + T \cdot \beta_{\text{TX}}^\top \mathbf{X}_{\text{TX}} \right)$$

Note: Same DGP, but X_1 is not observed!

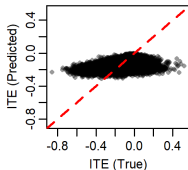
Simulation Case 2: Unobserved Interaction

Results with T-learner logistic regression (glm):

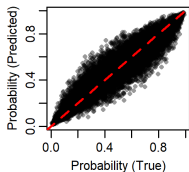
Train: $P(Y = 1 \mid X, T)$



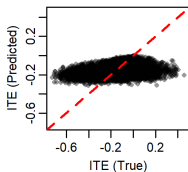
Train: ITE



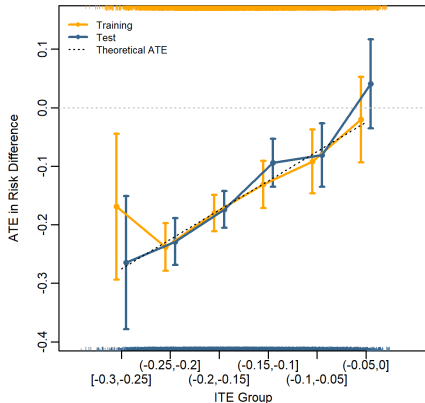
Test: $P(Y = 1 \mid X, T)$



Test: ITE



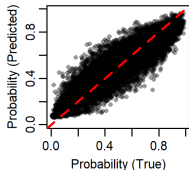
Observed ATE per ITE-subgroup: $\pi_{\text{treated}} - \pi_{\text{control}}$



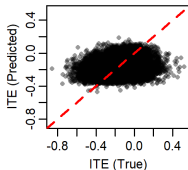
Simulation Case 2: Unobserved Interaction

Results with T-learner tuned random forest (comets package):

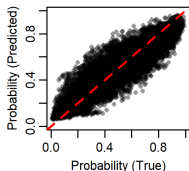
Train: $P(Y = 1 | X, T)$



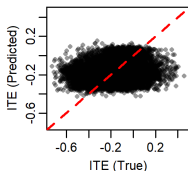
Train: ITE



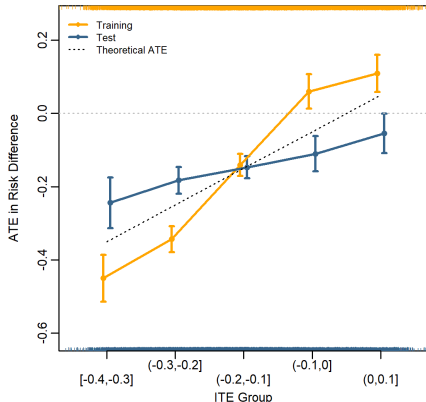
Test: $P(Y = 1 | X, T)$



Test: ITE



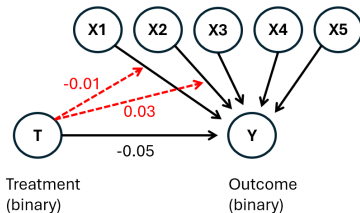
Observed ATE per ITE-subgroup: $\pi_{\text{treated}} - \pi_{\text{control}}$



Simulation Case 3: Fully Observed, Small Effects

Setup:

- $n = 20,000$
- $T \sim \text{Bernoulli}(0.5)$
- $\mathbf{X} = (X_1, \dots, X_5)^\top \sim \mathcal{N}(\mathbf{0}, \Sigma)$
- $\mathbf{X}_{\text{TX}} = (X_1, X_2)^\top$ **interaction**



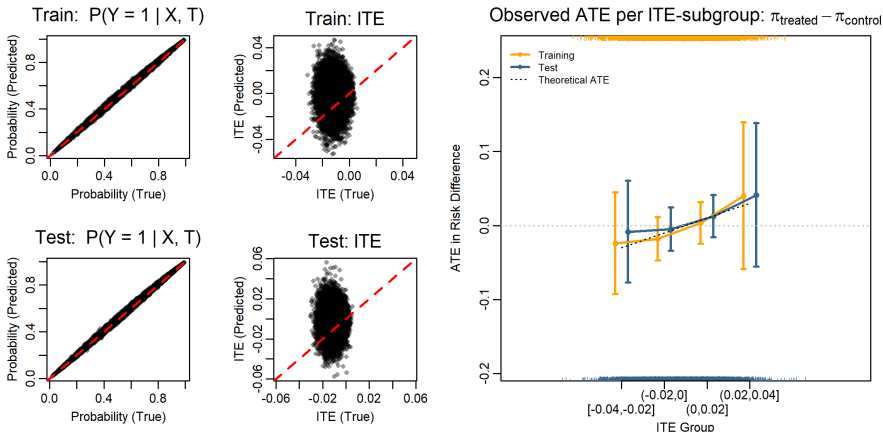
Outcome model:

$$\mathbb{P}(Y = 1 \mid \mathbf{X}, T) = \text{logit}^{-1} \left(\beta_0 + \beta_T T + \beta_X^\top \mathbf{X} + T \cdot \beta_{\text{TX}}^\top \mathbf{X}_{\text{TX}} \right)$$

Note: Same DGP, but weak treatment effects!

Simulation Case 3: Fully Observed, Small Effects

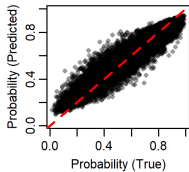
Results with T-learner logistic regression (glm):



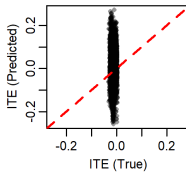
Simulation Case 3: Fully Observed, Small Effects

Results with T-learner Random Forest (comets package):

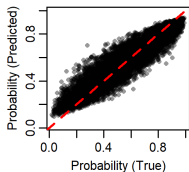
Train: $P(Y = 1 | X, T)$



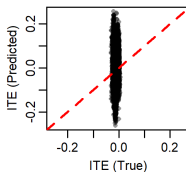
Train: ITE



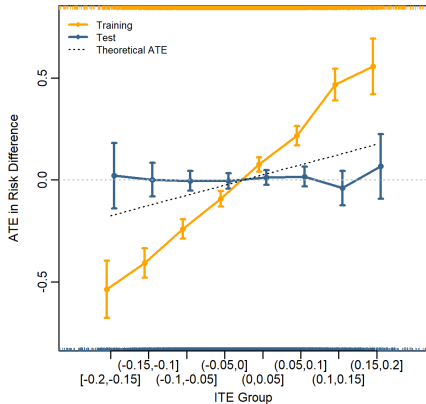
Test: $P(Y = 1 | X, T)$



Test: ITE



Observed ATE per ITE-subgroup: $\pi_{\text{treated}} - \pi_{\text{control}}$



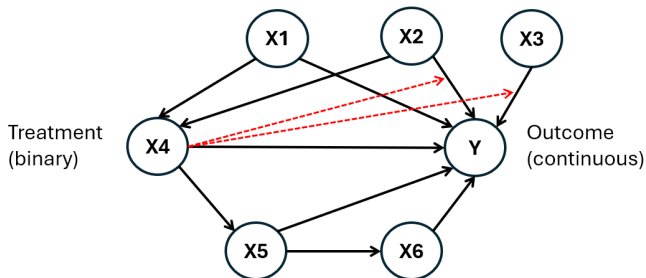
Experiment 3: ITE model robustness in RCTs (simulation)

Key Insights:

- **Calibration** and tuning of models are crucial for reliable ITE estimation
- Ignorability alone may not guarantee unbiased ITEs if important **effect modifiers are unobserved**
- **Low true heterogeneity** may be mistaken for model failure

These factors may explain the limited ITE performance in the IST dataset.

Experiment 4: ITE estimation with TRAM-DAGs



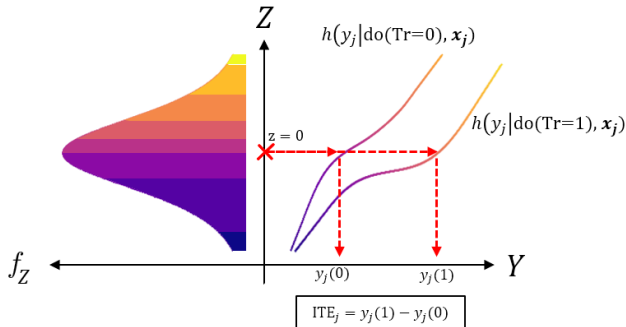
DGP:

- $X_1, X_2, X_3 \sim \mathcal{N}(\mathbf{0}, \Sigma)$
- X_4 (treatment) depends probabilistically on X_1 and X_2 via a logistic model
- $X_5 = h_5^{-1}(Z_5 - 0.8X_4) \rightarrow$ (depends on treatment)
- $X_6 = h_6^{-1}(Z_6 + 0.5X_5) \rightarrow$ (depends on treatment through X_5)
- $Y = h_7^{-1}(Z_7 - \beta_1X_1 - \beta_2X_2 - \beta_3X_3 - \beta_4X_4 - \beta_5X_5 - \beta_6X_6 - X_4 \cdot (\beta_{2,Tr}X_2 + \beta_{3,Tr}X_3))$

Experiment 4: ITE estimation with TRAM-DAGs

We define the ITE as the difference in medians of potential outcomes:

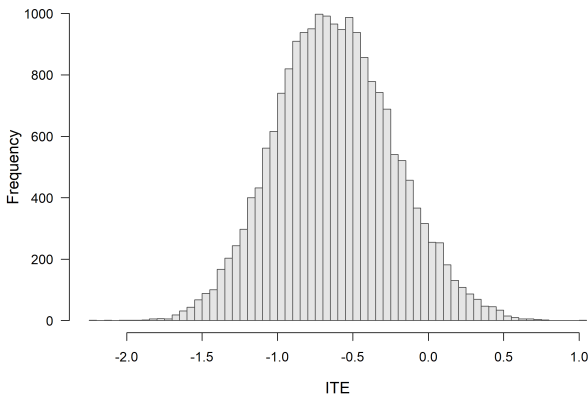
$$\text{ITE} = \text{median}(Y \mid \text{do}(T = 1), \mathbf{X}) - \text{median}(Y \mid \text{do}(T = 0), \mathbf{X})$$



Experiment 4: ITE estimation with TRAM-DAGs

Resulting ITEs from the DGP in terms of difference in medians of potential outcomes:

$$\text{ITE} = \text{median}(Y \mid \text{do}(T = 1), \mathbf{X}) - \text{median}(Y \mid \text{do}(T = 0), \mathbf{X})$$

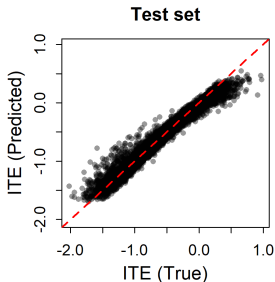
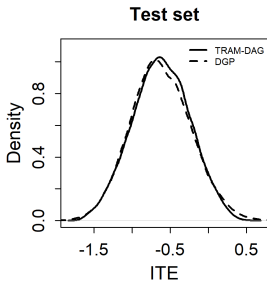
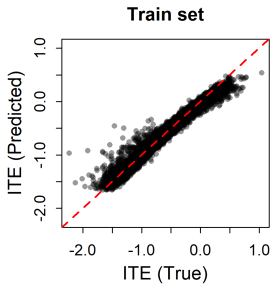
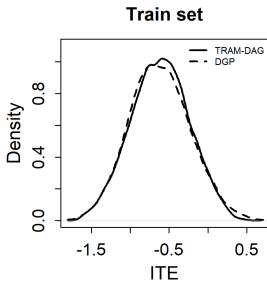


Experiment 4: ITE Estimation with TRAM-DAGs

Estimate ITEs with TRAM-DAGs (S-learner approach) from observed data:

1. Fit the TRAM-DAG on the training set (fully flexible – CI – to allow for interactions)
2. Compute potential outcomes as $\text{median}(Y \mid \text{do}(T = t), \mathbf{X}_t)$ for $t \in \{0, 1\}$
3. $\text{ITE} = \text{median}(Y \mid \text{do}(T = 1), \mathbf{X}_1) - \text{median}(Y \mid \text{do}(T = 0), \mathbf{X}_0)$

ITE estimation with TRAM-DAGs (Results)



Key Findings

Findings: TRAM-DAGs

- Customizable; accurately recovers causal relationships in known DAG; allows sampling of L1-L3
- Can model interactions between variables

Findings: Individualized treatment effects (ITE)

- Calibration is important for ITE prediction
- Missing effect modifiers (or weak heterogeneity) are problematic
- TRAM-DAGs yield unbiased ITEs when DAG is correct and heterogeneity exists

Outlook

Limitations

- Simulations may not reflect real-world complexity
- TRAM-DAGs are computationally expensive (long training time)
- TRAM-DAGs require correct model specification for interpretability
- ITE estimation for continuous outcomes used medians of potential outcomes instead of expected values

Recommendations

- Apply TRAM-DAGs to real-world datasets, including semi-structured data
- Investigate ITE estimation under unobserved effect modifiers

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Heterogeneity

Heterogeneity despite no interaction effects in logistic model (Hoogland et al., 2021).

