Average treatment effects (ATE) are at the heart of clinical and policy decision making, used to derive incremental cost-effectiveness ratio and incremental net benefits. More nuanced decision-making accounting for heterogeneity in treatment effect may yield greater population health gains [1-3].

Clinicians and payers have focused more on considerations at the subgroup- and individual-levels.

Patients and clinicians want to know what the outcomes of a treatment is for them, not for an average individual.

The individualized treatment effect (ITE) for individual i with a vector of individual-specific predictors $x_i$ can be defined as:

$$ITE(x_i) = E[Y(x_i)|X = x_i] - E[Y(x_i)|X = \bar{x}_i]$$

The ATE($E[Y(x_i)|X = x_i]$) is equal to the average of the ITE($E[Y(x_i)|X = x_i] - E[Y(x_i)|X = \bar{x}_i]$).

Identification Assumptions of ITEs are the same as ATE, including consistency, conditional exchangeability, positivity, no interference.

Challenges in Estimating ITE

1. What Data is Required for ITE Estimation?

ITE is essentially a highly conditional average treatment effect and can be realistically derived from large, well-designed, real-world studies.

2. Why use machine learning (ML) to estimate ITE?

ML identify potential subgroups and select covariates (NICE real world evidence framework June 2022). ML flexibly model complex interactions between treatment and high-dimensional individual characteristics. ML are not substitutes for content knowledge and clinicians’ opinions.

3. Uncertainty Quantification

makes ML more trustworthy and facilitate safer and more consistent treatment decisions.

4. Parameters

focus on ITE outcome, baseline risk, related measures of treatment effects, HRQoL, and costs.

Risk of Bias in Causal Inference

• General to All Observational Studies
  1. Selection Bias
  2. Confounding
  3. Collider Bias
  4. Measurement Error

• Specific to Longitudinal Analysis
  1. Loss to Follow-Up
  2. Exposure Affected Time-varying Confounding
  3. Immortal Time Bias

We extract data based on:

• the available data (cross-sectional or longitudinal);
• the outcome of interest (continuous, binary or ITE);
• whether hand observed or unobserved confounders;
• whether quantity uncertainties of treatment effects or predicted outcomes;
• software implementation (R, Python, Stata).

ML Methods to Estimate ITE in Static Setting

Most ML methods:

• are designed for binary or continuous outcomes, require large samples;
• handle baseline confounding, assume no hidden confounding;

• not quantify uncertainty of both the predicted outcomes and treatment.

Table 1: Methods to Estimate ITE in Static Setting

ML Methods to Estimate ITE in Longitudinal Setting

Survival model should account for potential bias from:

• non-randomised treatment assignment (confounding);
• informative censoring,
• event-induced covariate shift [17].

Modeling competing risks is another challenge.

Table 2: Methods to Estimate ITE in Longitudinal Setting

ML Methods to Estimate ITE for ITE Outcomes

1. Most ML for ITE estimation can handle confounding at baseline but not time-varying or hidden confounding.
2. ML accounting for time-varying confounding are developed mostly for use with continuous or binary outcomes.
3. Most ML methods do not quantify uncertainty of treatment effects estimates or predicted outcomes, especially in longitudinal settings.
4. Modeling assumptions should be properly assessed before making causal conclusions.
5. No ML can estimate ITE for ITE outcomes AND account for time-varying confounders.