Day 2, Lecture 3

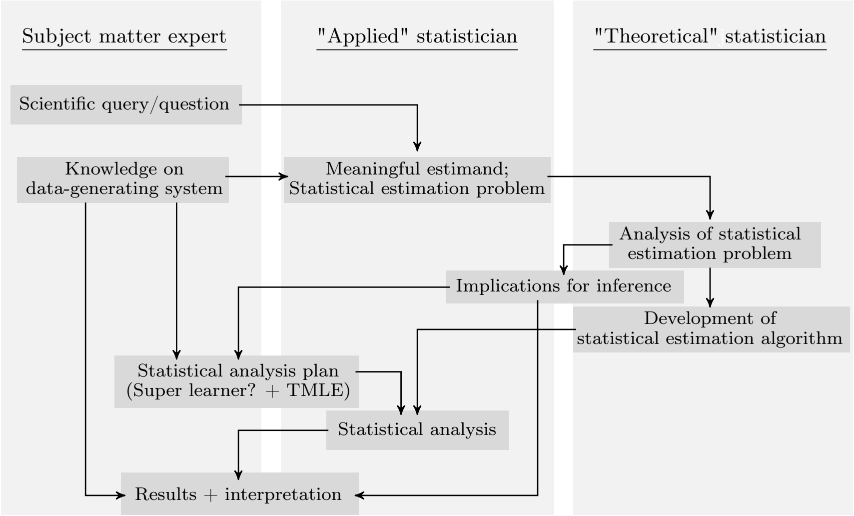
Targeting: Changing the target

Targeted learning framework

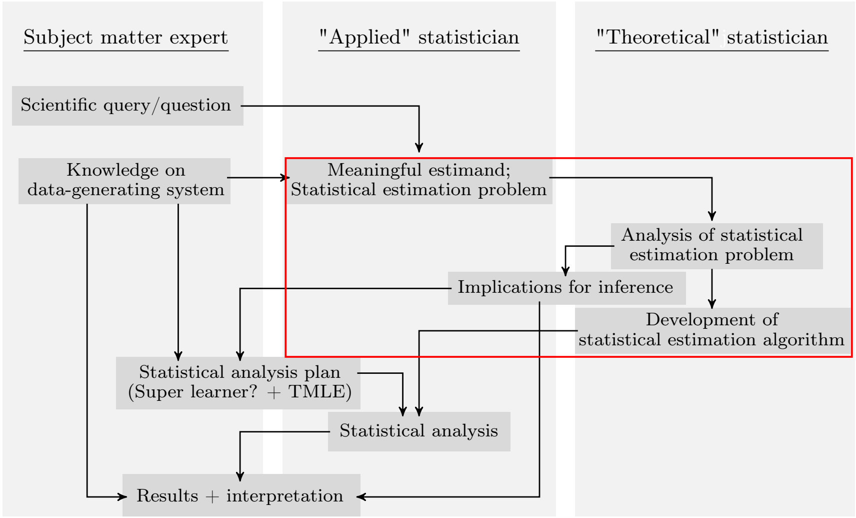
In this lecture, our goal is to:

1. Summarize the steps involved in analyzing and constructing Targeted Minimum Loss-based Estimation (TMLE) estimators for a new estimation problem, using a specific example as a reference point.

Targeted learning framework



Targeted learning framework



Changing the target

ATE: Statistical estimation problem

$O_1, \dots, O_n \overset{iid}{\sim} P_0$, O_i is the observation for individual i of the dataset, consists of

- Covariates: $X_i \in \mathcal{X} \subseteq \mathbb{R}^d$
- Exposure/treatment: $A_i \in \{0, 1\}$
- Outcome: $Y_i \in \{0, 1\}$ or $Y \in \mathbb{R}$

We are interested in:

$$\Psi(P) = \tilde{\Psi}(f, \mu_X) = \int_{\mathbb{R}} \big(f(1, x) - f(0, x)\big) d\mu_X(x),$$

where $f(a, x) = \mathbb{E}_P[Y \mid A = a, X = x]$.

A plug-in estimator requires an estimator $\hat{f}_n$ for f:

$$\hat{\psi}_n = \tilde{\Psi}(\hat{f}_n, \mathbb{P}_n) = \frac{1}{n} \sum_{i=1}^{n} \big(\hat{f}_n(1, X_i) - \hat{f}_n(0, X_i)\big).$$

Changing the target

What is the interpretation?

Causal interpretation: The risk difference, had everyone in the population been treated versus had everyone in the population been untreated.

Changing the target

In an observational study, the de facto treated and the de facto untreated groups may differ quite a lot.

Sometimes we may be interested in the effect averaged with respect to the distribution of covariates *in the treated population*.

$\Rightarrow$ the average treatment effect among the treated.

Changing the target: Average treatment effect among the treated

Causal interpretation: The risk difference, had everyone in the treated population been treated versus had everyone in the treated population been untreated.

Average treatment effect (ATE)

- $O = (X, A, Y) \in \mathbb{R}^d \times \{0,1\} \times \{0,1\}$
- The ATE is defined for $P \in \mathcal{M}$ as

$$\Psi(P) = \mathbb{E}_P[\mathbb{E}_P[Y \mid A = 1, X] - \mathbb{E}_P[Y \mid A = 0, X]]$$

- Under causal assumptions:

$$\Psi(P) = \mathbb{E}_P[Y^1] - \mathbb{E}_P[Y^0]$$

Changing the target: Average treatment effect among the treated

Average treatment effect among the treated (ATT)

- $O = (X, A, Y) \in \mathbb{R}^d \times \{0,1\} \times \{0,1\}$
- The ATT is defined for $P \in \mathcal{M}$ as

$$\Psi(P) = \mathbb{E}_P[\mathbb{E}_P[Y \mid A = 1, X] - \mathbb{E}_P[Y \mid A = 0, X] \mid A = 1]$$

- Under causal assumptions:

$$\Psi(P) = \mathbb{E}_P[Y^1 \mid A = 1] - \mathbb{E}_P[Y^0 \mid A = 1]$$

This changes the statistical estimation problem and thus the TMLE.

Changing the target: Average treatment effect among the treated

We can identify the causal parameter under the causal assumptions (consistency, exchangeability and positivity):

$$\begin{aligned}
\Psi(P) &= \mathbb{E}[Y^1 \mid A = 1] - \mathbb{E}[Y^0 \mid A = 1] \\
&= \mathbb{E}_P[\mathbb{E}_P[Y \mid A = 1, X] - \mathbb{E}_P[Y \mid A = 0, X] \mid A = 1] \\
&= \int_{\mathbb{R}^d} \big(f(1,x) - f(0,x)\big) d\mu_{X|A}(x \mid 1) \\
&= \int_{\mathbb{R}^d} \big(f(1,x) - f(0,x)\big) \frac{\pi(1 \mid x)}{\bar{\pi}(1)} d\mu_X(x) \\
&= \tilde{\Psi}(\mu_X, \bar{\pi}, \pi, f)
\end{aligned}$$

Changing the target: Average treatment effect among the treated

Thus, the ATT can be identified as the statistical parameter:

$$
\begin{aligned}
\Psi(P) &= \mathbb{E}_P[\mathbb{E}_P[Y \mid A = 1, X] - \mathbb{E}_P[Y \mid A = 0, X] \mid A = 1] \\
&= \int_{\mathbb{R}^d} \big(f(1,x) - f(0,x)\big) \frac{\pi(1 \mid x)}{\bar{\pi}(1)} d\mu_X(x) \\
&= \tilde{\Psi}(\mu_X, \bar{\pi}, \pi, f)
\end{aligned}
$$

where:

- $f(a,x) = \mathbb{E}_P[Y \mid A = a, X = x]$
- $\pi(a \mid x) = P(A = a \mid X = x)$
- $\bar{\pi}(a) = P(A = a)$ is the marginal distribution of A
- μ_X is the marginal distribution of X

Changing the target: Average treatment effect among the treated

A substitution estimator:

$$\hat{\psi}_n = \tilde{\Psi}(\hat{\mu}_X, \hat{\hat{\pi}}_n, \hat{\pi}_n, \hat{f}_n) = \frac{1}{n}\sum_{i=1}^{n} \frac{1\{A_i = 1\}}{\hat{\hat{\pi}}_n(1)}\big(\hat{f}_n(1, X_i) - \hat{f}_n(0, X_i)\big),$$

where, $\hat{\hat{\pi}}_n(1) = \dfrac{1}{n}\displaystyle\sum_{i=1}^{n} A_i$.

Targeting step: Average treatment effect on the treated

EXAMPLE: Average treatment effect (ATE)

Step 1 Construct initial estimators $\hat{f}_n, \hat{\pi}_n$ for f, π

Step 2 Update the estimator $\hat{f}_n \mapsto \hat{f}_n^*$ for f such that $\hat{f}_n^*$ for the fixed $\hat{\pi}_n$ solves the efficient influence curve equation

For the ATE, Step 2 is simply just an additional logistic regression step.

Targeting step: Average treatment effect on the treated

EXAMPLE: Average treatment effect among the treated (ATT)

Step 1 Construct initial estimators $\hat{f}_n, \hat{\pi}_n$ for f, π

Step 2 Update the estimator $\hat{f}_n \mapsto \hat{f}_n^*$ for f and the estimator $\hat{\pi}_n \mapsto \hat{\pi}_n^*$ for π such that $\hat{f}_n^*, \hat{\pi}_n^*$ solves the efficient influence curve equation

For the ATE, Step 2 is simply just an additional logistic regression step.

For the ATT, Step 2 is an iterative algorithm with recursive steps of additional logistic regressions.

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

$$\tilde{\phi}^*(f,\pi,\bar{\pi})(O) = \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1 \mid X)}{\bar{\pi}(1)\pi(0 \mid X)}\right)\big(Y - f(A,X)\big) + \frac{A}{\bar{\pi}(1)}\big(f(1,X) - f(0,X) - \Psi(P)\big)$$

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

$$
\begin{aligned}
\tilde{\phi}^*(f,\pi,\bar{\pi})(O) &= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1\,|\,X)}{\bar{\pi}(1)\pi(0\,|\,X)}\right)\big(Y - f(A,X)\big) \\
&\quad + \frac{A}{\bar{\pi}(1)}\big(f(1,X) - f(0,X) - \Psi(P)\big) \\
&= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1\,|\,X)}{\bar{\pi}(1)\pi(0\,|\,X)}\right)\big(Y - f(A,X)\big) \\
&\quad + \frac{f(1,X) - f(0,X) - \Psi(P)}{\bar{\pi}(1)}\big(A - \pi(1\,|\,X)\big) \\
&\quad + \frac{\pi(1\,|\,X)}{\bar{\pi}(1)}\big(f(1,X) - f(0,X) - \Psi(P)\big)
\end{aligned}
$$

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

$$
\begin{aligned}
\tilde{\phi}^*(f,\pi,\bar{\pi})(O) &= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1 \mid X)}{\bar{\pi}(1)\pi(0 \mid X)} \right) \big(Y - f(A,X) \big) \\
&\quad + \frac{A}{\bar{\pi}(1)} \big(f(1,X) - f(0,X) - \Psi(P) \big) \\
&= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1 \mid X)}{\bar{\pi}(1)\pi(0 \mid X)} \right) \big(Y - f(A,X) \big) \\
&\quad + \frac{f(1,X) - f(0,X) - \Psi(P)}{\bar{\pi}(1)} \big(A - \pi(1 \mid X) \big) \\
&\quad + \frac{\pi(1 \mid X)}{\bar{\pi}(1)} \big(f(1,X) - f(0,X) - \Psi(P) \big)
\end{aligned}
$$

Targeting step: Average treatment effect on the treated

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

$$
\begin{aligned}
\tilde{\phi}^*(f,\pi,\bar{\pi})(O) &= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1\mid X)}{\bar{\pi}(1)\pi(0\mid X)}\right)\big(Y - f(A,X)\big) \\
&\quad + \frac{A}{\bar{\pi}(1)}\big(f(1,X) - f(0,X) - \Psi(P)\big) \\
&= \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1\mid X)}{\bar{\pi}(1)\pi(0\mid X)}\right)\big(Y - f(A,X)\big) \\
&\quad + \frac{f(1,X) - f(0,X) - \Psi(P)}{\bar{\pi}(1)}\big(A - \pi(1\mid X)\big) \\
&\quad + \frac{\pi(1\mid X)}{\bar{\pi}(1)}\big(f(1,X) - f(0,X) - \Psi(P)\big)
\end{aligned}
$$

Average treatment effect on the treated

We need:

(i) Parametric submodel $\{f_\varepsilon, \pi_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) Loss function $(O, (f, \pi)) \mapsto \mathscr{L}(f, \pi)(O)$

such that

$$(1) \quad f_{\varepsilon=0} = f, \pi_\varepsilon = \pi \qquad (2) \quad \frac{d}{d\varepsilon}\bigg|_{\varepsilon=0} \mathscr{L}(f_\varepsilon, \pi_\varepsilon)(O) = \tilde{\phi}^*(f, \pi, \bar{\pi})(O)$$

Targeting step: Average treatment effect on the treated

$$\mathrm{logit}(p) = \mathrm{expit}^{-1}(p) = \log\left(\frac{p}{1-p}\right)$$

(i) Sum loss function $\mathscr{L}(f, \pi) = \mathscr{L}_1(f) + \mathscr{L}_2(\pi)$, where

$$\mathscr{L}_1(f)(O) = -\big(Y \log(f(A, X)) + (1 - Y) \log(1 - f(A, X))\big)$$
$$\mathscr{L}_2(\pi)(O) = -\big(A \log(\pi(1 \mid X)) + (1 - A) \log(1 - \pi(1 \mid X))\big)$$

(ii) Logistic regression models:

$$f_\varepsilon(A, X) = \mathrm{expit}\big(\mathrm{logit}(f(A, X)) + \varepsilon H_1(\pi, \bar{\pi})(A, X)\big)$$
$$\pi_\varepsilon(X) = \mathrm{expit}\big(\mathrm{logit}(\pi(1 \mid X)) + \varepsilon H_2(f, \pi, \bar{\pi})(A, X)\big)$$

with the "clever covariates":

$$H_1(\pi, \bar{\pi})(A, X) = \left(\frac{A}{\bar{\pi}(1)} - \frac{(1-A)\pi(1 \mid X)}{\bar{\pi}(1)\pi(0 \mid X)}\right), \quad \text{and,}$$
$$H_2(f, \pi, \bar{\pi})(A, X) = \frac{f(1, X) - f(0, X) - \Psi(P)}{\bar{\pi}(1)}$$

Targeting step: Average treatment effect on the treated

Iterative algorithm:

1. Given initial estimators $\hat{f}_n^0, \hat{\pi}_n^0$:
   - Obtain estimate $\hat{\varepsilon}_Y^0$ for ε:
   $$f_\varepsilon(A,X) = \mathrm{expit}\big(\mathrm{logit}(\hat{f}_n^0(A,X)) + \varepsilon H_1(\hat{\pi}_n^0, \bar{\pi})(A,X)\big)$$
   (i.e., regress Y on covariate $H_1(\hat{\pi}_n^0, \bar{\pi})(A,X)$ with offset $\mathrm{logit}(\hat{f}_n^0(A,X))$)
   - Update: $\hat{f}_n^1 := \hat{f}^0_{n,\hat{\varepsilon}_Y^0}$.
   - Obtain estimate $\hat{\varepsilon}_A^0$ for ε:
   $$\pi_\varepsilon(X) = \mathrm{expit}\big(\mathrm{logit}(\hat{\pi}_n^0(1 \mid X)) + \varepsilon H_2(\hat{f}_n^1, \hat{\pi}_n^0, \bar{\pi})(A,X)\big)$$
   (i.e., regress A on covariate $H_2(\hat{f}_n^1, \hat{\pi}_n^0, \bar{\pi})(A,X)$ with offset $\mathrm{logit}(\hat{\pi}_n^0(1 \mid X))$)
   - Update: $\hat{\pi}_n^1 := \hat{\pi}^0_{n,\hat{\varepsilon}_A^0}$.

Targeting step: Average treatment effect on the treated

Iterative algorithm:

2. Iteratively from k to $k+1$, given current estimators $\hat{f}_n^k, \hat{\pi}_n^k$:
   - Obtain estimate $\hat{\varepsilon}_Y^k$ for ε:
   $$f_\varepsilon(A,X) = \mathrm{expit}\big(\mathrm{logit}(\hat{f}_n^k(A,X)) + \varepsilon H_1(\hat{\pi}_n^k, \bar{\pi})(A,X)\big)$$
   (i.e., regress Y on covariate $H_1(\hat{\pi}_n^k, \bar{\pi})(A,X)$ with offset $\mathrm{logit}(\hat{f}_n^k(A,X))$)
   - Update: $\hat{f}_n^{k+1} := \hat{f}^k_{n,\hat{\varepsilon}_Y^k}$.
   - Obtain estimate $\hat{\varepsilon}_A^k$ for ε:
   $$\pi_\varepsilon(X) = \mathrm{expit}\big(\mathrm{logit}(\hat{\pi}_n^k(1 \mid X)) + \varepsilon H_2(\hat{f}_n^{k+1}, \hat{\pi}_n^k, \bar{\pi})(A,X)\big)$$
   (i.e., regress A on covariate $H_2(\hat{f}_n^{k+1}, \hat{\pi}_n^k, \bar{\pi})(A,X)$ with offset $\mathrm{logit}(\hat{\pi}_n^k(1 \mid X))$)
   - Update: $\hat{\pi}_n^{k+1} := \hat{\pi}^k_{n,\hat{\varepsilon}_A^k}$.

This is continued until we solve:

$$\frac{1}{n}\sum_{i=1}^{n}\left(\frac{A_i}{\hat{\hat{\pi}}_n(1)} - \frac{(1-A_i)\hat{\pi}_n^{k^*}(1\mid X_i)}{\hat{\hat{\pi}}_n(1)\hat{\pi}_n^{k^*}(0\mid X_i)}\right)\big(Y - \hat{f}_n^{k^*}(A_i, X_i)\big) \approx 0$$

and,

$$\frac{1}{n}\sum_{i=1}^{n}\frac{\hat{f}_n^{k^*}(1, X_i) - \hat{f}_n^{k^*}(0, X_i) - \tilde{\Psi}(\hat{\mu}_X, \hat{\hat{\pi}}_n, \hat{\pi}_n^{k^*}, \hat{f}_n^{k^*})}{\hat{\hat{\pi}}_n(1)}\big(A_i - \hat{\pi}_n^{k^*}(1\mid X_i)\big) \approx 0;$$

These are the different parts of the efficient influence curve equation.

Targeting step: Average treatment effect on the treated

This is continued until we solve:

$$\frac{1}{n}\sum_{i=1}^{n}\left(\frac{A_i}{\hat{\hat{\pi}}_n(1)} - \frac{(1-A_i)\hat{\pi}_n^{k^*}(1 \mid X_i)}{\hat{\hat{\pi}}_n(1)\hat{\pi}_n^{k^*}(0 \mid X_i)}\right)\left(Y - \hat{f}_n^{k^*}(A_i, X_i)\right) \approx 0$$

and,

$$\frac{1}{n}\sum_{i=1}^{n}\frac{\hat{f}_n^{k^*}(1, X_i) - \hat{f}_n^{k^*}(0, X_i) - \tilde{\Psi}(\hat{\mu}_X, \hat{\hat{\pi}}_n, \hat{\pi}_n^{k^*}, \hat{f}_n^{k^*})}{\hat{\hat{\pi}}_n(1)}\left(A_i - \hat{\pi}_n^{k^*}(1 \mid X_i)\right) \approx 0;$$

note that we already solve:

$$\frac{1}{n}\sum_{i=1}^{n}\frac{\hat{\pi}_n^{k^*}(1 \mid X_i)}{\hat{\hat{\pi}}_n(1)}\left(\hat{f}_n^{k^*}(1, X_i) - \hat{f}_n^{k^*}(0, X_i) - \tilde{\Psi}(\hat{\mu}_X, \hat{\hat{\pi}}_n, \hat{\pi}_n^{k^*}, \hat{f}_n^{k^*})\right) = 0.$$

These are the different parts of the efficient influence curve equation.

Average treatment effect on the treated

This was the targeting step: What we need procedurally to carry out the TMLE estimation.

Average treatment effect on the treated

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To finish the analysis, it remains to analyze the remainder term:

$$R(P, P_0) = \Psi(P) - \Psi(P_0) + P_0\phi^*(P).$$

Average treatment effect on the treated

This was the targeting step: What we need procedurally to carry out the TMLE estimation.

To finish the analysis, it remains to analyze the remainder term:

$$R(P, P_0) = \Psi(P) - \Psi(P_0) + P_0\phi^*(P).$$

To derive this: Start from $P_0\phi^*(P) = \mathbb{E}_{P_0}[\phi^*(P)(O)]$ and show that this can be written as [something] plus $\Psi(P_0) - \Psi(P)$. This [something] is the remainder term.

Average treatment effect on the treated

For the ATT we can derive that:

$$\tilde{R}(f, \pi, \bar{\pi}, f_0, \pi_0, \bar{\pi}_n) = \frac{1}{\bar{\pi}(1)}\left(\frac{\pi_0(1 \mid X) - \pi(1 \mid X)}{1 - \pi(1 \mid X)}\right)\big(f_0(0, X) - f(0, X)\big) + \left(\frac{\bar{\pi}_0(1) - \bar{\pi}(1)}{\bar{\pi}(1)}\right)\big(\Psi(P_0) - \Psi(P)\big)$$

Again we see the double robust structure.

Average treatment effect on the treated

For the ATT we can derive that:

$$\tilde{R}(f, \pi, \bar{\pi}, f_0, \pi_0, \bar{\pi}_n) = \frac{1}{\bar{\pi}(1)} \left(\frac{\pi_0(1 \mid X) - \pi(1 \mid X)}{1 - \pi(1 \mid X)} \right) \big(f_0(0, X) - f(0, X) \big) + \left(\frac{\bar{\pi}_0(1) - \bar{\pi}(1)}{\bar{\pi}(1)} \right) \big(\Psi(P_0) - \Psi(P) \big)$$

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Average treatment effect on the treated

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Again we see the double robust structure.

This is a particularly nice result, since the parameter depends on both the outcome regression f and the propensity score π.

Final comments — changing the target

It depends very much on the target parameter and the structure of its efficient influence function how easy/hard estimation, and particularly targeting, becomes.

For many target parameters, all this work has already been done!

Final comments — changing the target

The average treatment effect among the treated is implemented in the `tmle` package:

```
set.seed(15)
sim.data <- sim.fun(n=1000)
```

```
library(tmle)
fit.tmle <- tmle(Y=sim.data$Y, A=sim.data$A,
         cbind(X1=sim.data$X1,X2=sim.data$X2,
               X3=sim.data$X3),
         gform=A~X1+X2+X3, ## treatment model
         Qform=Y~A+X1+X2+X3, ## outcome model
         family="binomial",
         cvQinit=FALSE)
```

Final comments — changing the target

```
Additive Effect
  Parameter Estimate:  0.066263
  Estimated Variance:  0.00085811
             p-value:  0.023694
   95% Conf Interval: (0.0088482, 0.12368)

Additive Effect among the Treated
  Parameter Estimate:  0.072104
  Estimated Variance:  0.0009739
             p-value:  0.020862
   95% Conf Interval: (0.010938, 0.13327)

Additive Effect among the Controls
  Parameter Estimate:  0.059976
  Estimated Variance:  0.0009839
             p-value:  0.055869
   95% Conf Interval: (-0.0015039, 0.12146)

Relative Risk
  Parameter Estimate:  1.0954
```

Final comments — changing the target

Many other (!!) interesting parameters[1]

- Controlled and natural direct and indirect effects (mediation analysis parameters)
- Effects among groups defined by specific covariate characteristics (effect modification)
- Dynamic interventions, stochastic interventions

$\vdots$

We get back to examples of target parameters in longitudinal settings.

[1] Newer software ecosystem: `https://tlverse.org/`.