Day 2, Lecture 2

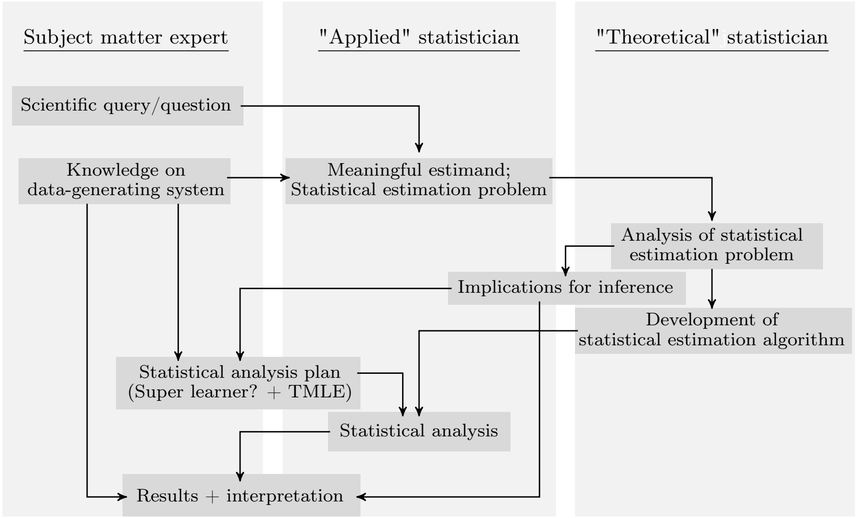
# Targeting: Changing the target

# Targeted learning framework

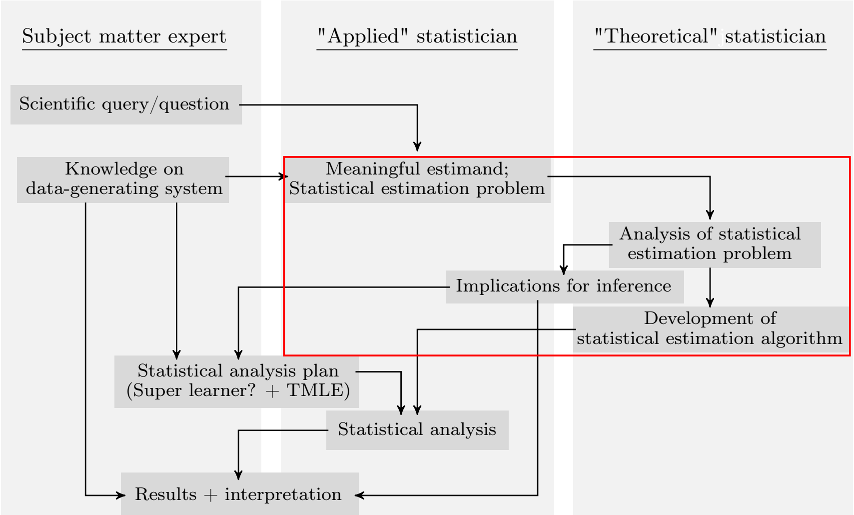
In this lecture, our goal is to:

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

$O_1, \ldots, O_n \overset{iid}{\sim} P_0$, $O_i$ 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.

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 $A$
- $\mu_X$ 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 $f, \pi$

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 $f, \pi$

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 $\pi$ 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.

# Targeting step: Average treatment effect on the treated

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

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

## Targeting step: Average treatment effect on the treated

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

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

EXAMPLE: Average treatment effect among the treated (ATT)

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

EXAMPLE: Average treatment effect among the treated (ATT)

The efficient influence function:

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

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) $f_{\varepsilon=0} = f, \pi_\varepsilon = \pi$  (2) $\left.\frac{d}{d\varepsilon}\right|_{\varepsilon=0} \mathscr{L}(f_\varepsilon, \pi_\varepsilon)(O) = \tilde{\phi}^*(f, \pi, \bar{\pi})(O)$

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

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 $\varepsilon$:
   $$f_\varepsilon(A,X) = \mathrm{expit}\big(\mathrm{logit}(\hat{f}_n^k(A,X)) + \varepsilon H_1(\hat{\pi}_n^k,\bar{\pi})(A,X)\big)$$
   (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 $\varepsilon$:
   $$\pi_\varepsilon(X) = \mathrm{expit}\big(\mathrm{logit}(\hat{\pi}_n^k(1 \mid X)) + \varepsilon H_2(\hat{f}_n^{k+1},\hat{\pi}_n^k,\bar{\pi})(A,X)\big)$$
   (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: $\hat{\pi}_n^{k+1} := \hat{\pi}^k_{n,\hat{\varepsilon}_A^k}$.

## Targeting step: Average treatment effect on the treated

This is continued until we solve:

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

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

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

and,

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

note that we already solve:

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

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

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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 $\pi$.

# 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/`.