

Day 2, Lecture 1

Targeted Minimum Loss-based Estimation (TMLE)

Overview of today

Before lunch (9 – 12):

- ▶ Targeted Minimum Loss-based Estimation (TMLE).
- ▶ The targeting step: updating/modifying initial nuisance parameter estimators.
- ▶ The ATE as a concrete example; the ATT as a different example.
- ▶ Valid inference still requires strong initial learners.

- * TMLE as a two-step procedure with involving an initial estimation step followed by a targeting step.
- * Implementation of the targeting step.
- * The link between the theoretical decomposition from yesterday, and TMLE as a practical estimation method.

After lunch (13 – 15): Super learning.

Targeted Minimum Loss-based Estimation (TMLE)

In this lecture, our goal is to:

1. Explain the relationship between the two-step procedure of Targeted Minimum Loss-based Estimation (TMLE) and the decomposition guiding the construction of asymptotically linear estimators.
2. Describe the process of constructing the targeting step in TMLE, highlighting the role of the efficient influence curve, and differentiate TMLE from other estimation methods solving the efficient influence curve.

Targeted Minimum Loss-based Estimation (TMLE)

For a particular target parameter $\Psi : \mathcal{M}$ (and a particular statistical model \mathcal{M}),

we have seen that —

Conditions (asymptotic linearity and efficiency)

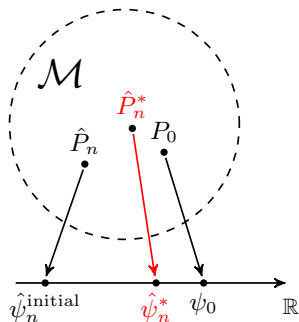
(C1) Solve the efficient influence curve equation: $\mathbb{P}_n \phi^*(\hat{P}_n) = o_P(n^{-1/2})$

(C2) Remainder $R(\hat{P}_n, P_0) = o_P(n^{-1/2})$

(C3) Donsker class conditions for $\{\phi^*(P) : P \in \mathcal{M}\}$

Then: $\Psi(\hat{P}_n) \overset{as}{\approx} N(\Psi(P_0), P_0 \phi^*(P_0)^2 / n)$

Targeted Minimum Loss-based Estimation (TMLE)



TMLE is a two-step procedure:

Step 1 Construct initial estimator \hat{P}_n for P .

Step 2 Update the estimator $\hat{P}_n \mapsto \hat{P}_n^*$ such that \hat{P}_n^* solves the efficient influence curve equation, i.e.,

$$\mathbb{P}_n \phi^*(\hat{P}_n^*) = \frac{1}{n} \sum_{i=1}^n \phi^*(\hat{P}_n^*)(O_i) \approx 0.$$

Step 1 = "initial estimation step"

Step 2 = "targeting step"

Targeted Minimum Loss-based Estimation (TMLE)

$$\begin{aligned}\Psi(\hat{P}_n) - \Psi(P_0) &= \mathbb{P}_n \phi^*(P_0) + o_P(n^{-1/2}) \\ &\quad + R(\hat{P}_n, P_0) \\ &\quad - \mathbb{P}_n \phi^*(\hat{P}_n)\end{aligned}$$

- ▶ The role of the targeting step (Step 2):
 - ▶ Gain double robustness in consistency.
 - ▶ Easier to achieve asymptotic linearity (amounts to getting rid of second-order remainder).
- ▶ The role of the initial estimation step (Step 1):
 - ▶ This should be done well enough to get rid of the second-order remainder.

Targeted Minimum Loss-based Estimation (TMLE)

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

A **loss function** $\mathcal{L}(f)(O)$ measuring the distance between an estimator f and the observed outcome Y , e.g., the negative log-likelihood:

$$\mathcal{L}(\hat{f}_n)(Y_i, A_i, X_i) = -(Y_i \log(\hat{f}_n(A_i, X_i)) + (1 - Y_i) \log(1 - \hat{f}_n(A_i, X_i))).$$

- ▶ The estimator \hat{f}_n closest to the true f_0 minimizes the risk:

$$\mathbb{E}_{P_0}[\mathcal{L}(\hat{f}_n)(Y_i, A_i, X_i)].$$

- ▶ Loss-based super learning: Minimizing the cross-validated empirical risk with respect to the loss function \mathcal{L} over the statistical model.

Targeted Minimum Loss-based Estimation (TMLE)

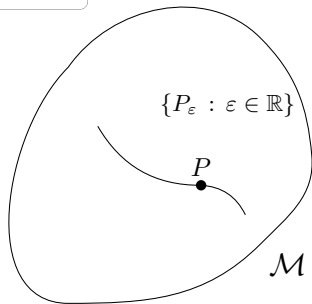
This is all about constructing a good estimator for the conditional expectation f ;

- ▶ does not necessarily yield a good estimator for the particular feature of interest, the target parameter.

This is Step 1.

Targeted Minimum Loss-based Estimation (TMLE)

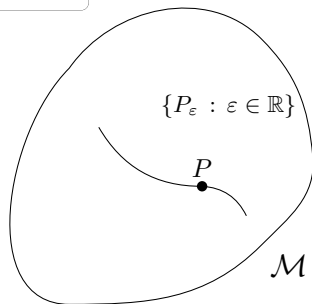
Step 2: We can minimize along a loss function in a certain way *that results in a good estimator for the target*.



Loss function $\mathcal{L}(f)(O)$ + clever choice of a **parametric submodel** $\{P_\epsilon : \epsilon \in \mathbb{R}\} \subset \mathcal{M}$.

Targeted Minimum Loss-based Estimation (TMLE)

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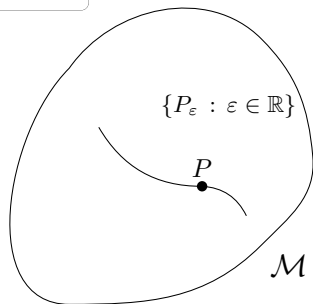


Loss function $\mathcal{L}(f)(O)$ + clever choice of a parametric submodel $\{P_\epsilon : \epsilon \in \mathbb{R}\} \subset \mathcal{M}$.

\Rightarrow minimize the loss along the submodel, given the estimator \hat{f}_n from **Step 1**.

Targeted Minimum Loss-based Estimation (TMLE)

Step 2: We can minimize along a loss function in a certain way *that results in a good estimator for the target*.



Loss function $\mathcal{L}(f)(O)$ + clever choice of a parametric submodel $\{P_\epsilon : \epsilon \in \mathbb{R}\} \subset \mathcal{M}$.

- \Rightarrow minimize the loss along the submodel, given the estimator \hat{f}_n from **Step 1**.
- \Rightarrow update \hat{f}_n along the path defined by P_ϵ : moving by $\hat{\epsilon}_n$ that minimizes the loss.

The targeting step (Step 2)

Construction of the targeting step for a given target parameter $\Psi : \mathcal{M} \rightarrow \mathbb{R}$ with efficient influence function $\phi^*(P)$ requires:

- (i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$
- (ii) A loss function $(O, P) \mapsto \mathcal{L}(P)(O)$

such that: (1) $P_{\varepsilon=0} = P$, and, (2) $\left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \mathcal{L}(P_\varepsilon)(O) = \phi^*(P)(O)$

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- ▶ Initial estimator \hat{P}_n^0
- ▶ Minimizer $\hat{\varepsilon}_{n,0}$ of $\varepsilon \mapsto \mathbb{P}_n \mathcal{L}(\hat{P}_{n,\varepsilon}^0)$
- ▶ Update: $\hat{P}_n^1 := \hat{P}_{\hat{\varepsilon}_{n,0}}^0$

Then: $\mathbb{P}_n \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=\hat{\varepsilon}_{n,0}} \mathcal{L}(\hat{P}_{n,\varepsilon}^0)(O) = 0$

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- ▶ Updated estimator \hat{P}_n^1
- ▶ Minimizer $\hat{\varepsilon}_{n,1}$ of $\varepsilon \mapsto \mathbb{P}_n \mathcal{L}(\hat{P}_{n,\varepsilon}^1)$
- ▶ Update: $\hat{P}_n^2 := \hat{P}_{\hat{\varepsilon}_{n,1}}^1$

Then: $\mathbb{P}_n \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=\hat{\varepsilon}_{n,1}} \mathcal{L}(\hat{P}_{n,\varepsilon}^1)(O) = 0$

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- ▶ k th updated estimator \hat{P}_n^k
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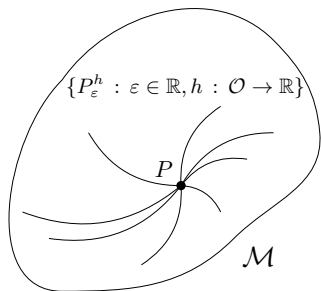
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The targeting step (Step 2) *ASIDE*

What happens?



Parametric submodels $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$ are also what we use to:

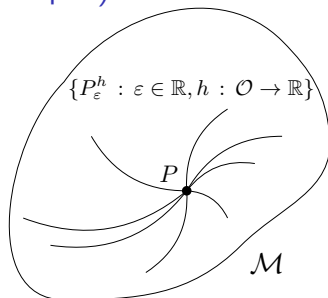
- ▶ define pathwise differentiability:¹

$$\left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \Psi(P_\varepsilon) = \int \phi(P)(o) b(o) dP(o), \quad (1)$$

- ▶ derive a nonparametric lower bound on the variance.

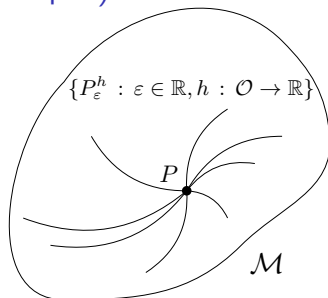
¹(1) should hold across any smooth submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$.

The targeting step (Step 2) *ASIDE*



- ▶ Index submodel by its score function: $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}, h : \mathcal{O} \rightarrow \mathbb{R}\}$.
 - ▶ i.e., $\left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \log p_\varepsilon^h(o) = h(o)$.
- ▶ Easier to estimate Ψ in the smaller model $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}\}$ than in \mathcal{M} .
- ▶ The supremum over Cramér-Rao bounds over all submodels $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}\}$ for estimating $\varepsilon \mapsto \Psi(P_\varepsilon^h)$ at $\varepsilon = 0$ provides a lower bound on the variance for estimating Ψ in \mathcal{M} :

The targeting step (Step 2) *ASIDE*

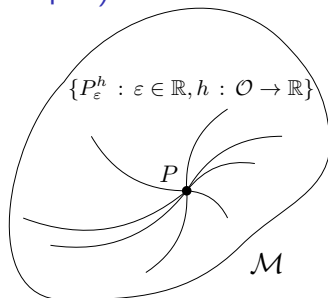


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$$\frac{\left(\left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \Psi(P_\varepsilon^h) \right)^2}{Ph^2}$$

(*)

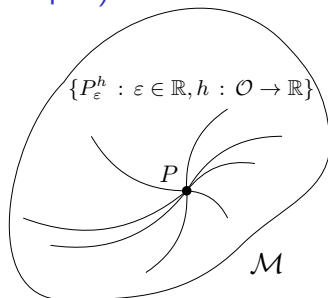
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$$\frac{\left(\left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \Psi(P_\varepsilon^h) \right)^2}{Ph^2} \stackrel{\text{PD}}{=} \frac{(P\phi^*(P)h)^2}{Ph^2} \quad (*)$$

The targeting step (Step 2) *ASIDE*



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The targeting step (Step 2) *ASIDE*

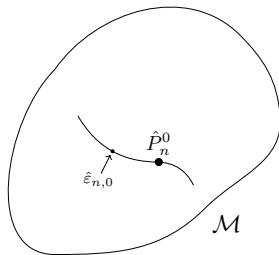
The submodel which attains the supremum of the Cramér-Rao bounds over all parametric submodels is called the **least favorable submodel**;

- ▷ It is the submodel for which the score is equal to the efficient influence function $\phi^*(P)$.

The targeting step (Step 2) *ASIDE*

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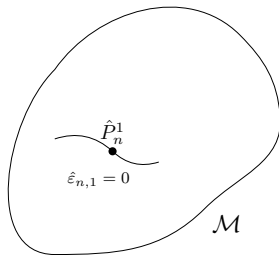
The TMLE step uses the **least favorable submodel** as a fluctuation model

- ▶ given a current estimator \hat{P}_n^k the updated estimator is found by fluctuating along the least favorable submodel;
- ▶ when no further fluctuation is needed ($\varepsilon \approx 0$), the estimator **solves the efficient influence curve equation**.

The targeting step (Step 2) *ASIDE*

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The targeting step (Step 2)

Conditions (asymptotic linearity and efficiency)

(C1) Solve the efficient influence curve equation: $\mathbb{P}_n \phi^*(\hat{P}_n) = o_P(n^{-1/2})$

(C2) Remainder $R(\hat{P}_n, P_0) = o_P(n^{-1/2})$

(C3) Donsker class conditions for $\{\phi^*(P) : P \in \mathcal{M}\}$

Then: $\Psi(\hat{P}_n) \overset{as}{\approx} N(\Psi(P_0), P_0 \phi^*(P_0)^2 / n)$

- ▶ The targeting step ensures that (C1) holds.
- ▶ Assume that (C2)^a and (C3) hold.

We can use the efficient influence function to compute an estimator for the standard error of the TMLE estimator:

$$\hat{\sigma}_n = \sqrt{\frac{\mathbb{P}_n \{\phi^*(\hat{P}_n)\}^2}{n}}$$

^aWith (C2) depending on how well we do for the initial estimation step.

Targeting the average treatment effect (ATE)

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EXAMPLE: Average treatment effect (ATE)

Observed data $O = (X, A, Y) \in \mathbb{R}^d \times \{0, 1\} \times \{0, 1\} = \mathcal{O}$

- * $X \in \mathbb{R}^d$ are covariates
- * $A \in \{0, 1\}$ is a binary exposure variable (treatment decision)
- * $Y \in \{0, 1\}$ is a binary outcome variable

$O \sim P_0$ where P_0 assumed to belong to nonparametric model \mathcal{M} .

We are interested in estimating the ATE:

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

Targeting the average treatment effect (ATE)

EXAMPLE: Average treatment effect (ATE)

For the ATE, as we have seen, we can also write the target parameter $\Psi : \mathcal{M} \rightarrow \mathbb{R}$ as

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

where

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

and μ_X is the marginal distribution of X .

I.e., $\hat{\psi}_n = \tilde{\Psi}(\hat{f}_n, \hat{\mu}_n)$.

Targeting the average treatment effect (ATE)

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 the average treatment effect (ATE)

EXAMPLE: Average treatment effect (ATE)

We need:

0. The efficient influence function:

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

Targeting the average treatment effect (ATE)

EXAMPLE: Average treatment effect (ATE)

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Further, we need:

- (i) A parametric submodel $\{f_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$
- (ii) A loss function $(O, f) \mapsto \mathcal{L}(f)(O)$

such that

$$(1) \quad f_{\varepsilon=0} = f \qquad (2) \quad \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \mathcal{L}(f_\varepsilon)(O) = \tilde{\phi}_f^*(f, \pi)(O)$$

Targeting the average treatment effect (ATE)

(i) Log-likelihood loss function:

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

$$\mathcal{L}(f)(O) = -(Y \log(f(A, X)) + (1 - Y) \log(1 - f(A, X)))$$

(ii) Logistic regression model:

$$f_{\varepsilon}(A, X) = \text{expit}(\text{logit}(f(A, X)) + \varepsilon H(A, X))$$

with the so-called "clever covariate": $H(A, X) := \frac{2A - 1}{\pi(A | X)}$.

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To show this, we verify that (i)–(ii) fulfill

$$(1) \quad f_{\varepsilon=0} = f \quad (2) \quad \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \mathcal{L}(f_{\varepsilon})(O) = \tilde{\phi}_f^*(f, \pi)(O)$$

Targeting the average treatment effect (ATE)

(i) Log-likelihood loss function:

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with the so-called "clever covariate": $H(A, X) := \frac{2A - 1}{\pi(A | X)}$.

SMALL EXERCISE: To show this, we verify that (i)–(ii) fulfill

$$(1) \quad f_{\varepsilon=0} = f \quad (2) \quad \left. \frac{d}{d\varepsilon} \right|_{\varepsilon=0} \mathcal{L}(f_{\varepsilon})(O) = \tilde{\phi}_f^*(f, \pi)(O)$$

Targeting the average treatment effect (ATE)

- ▶ Initial estimators $\hat{f}_n, \hat{\pi}_n$.
- ▶ Estimate clever covariate by:

$$\hat{H}_n(A, X) = \frac{2A - 1}{\hat{\pi}_n(A | X)}.$$

- ▶ The minimizer $\hat{\varepsilon}_n$ of $\varepsilon \mapsto \mathbb{P}_n \mathcal{L}(\hat{f}_{n,\varepsilon})$ equals the maximum likelihood estimator for ε in the fixed-intercept logistic regression:

$$\text{logit } \mathbb{E}[Y | A, X] = \text{logit}(\hat{f}_n(A, X)) + \varepsilon \hat{H}_n(A, X)$$

- ▶ Update: $\hat{f}_n^* := \hat{f}_{n,\hat{\varepsilon}_n}$.

Then: $\mathbb{P}_n \frac{d}{d\varepsilon} \bigg|_{\varepsilon=\hat{\varepsilon}_n} \mathcal{L}(\hat{f}_{n,\varepsilon}) = 0, \quad \text{i.e.,}$

$$\mathbb{P}_n \tilde{\phi}_f^*(\hat{f}_{n,\hat{\varepsilon}_n}, \hat{\pi}_n) = \mathbb{P}_n \tilde{\phi}_f^*(\hat{f}_n^*, \hat{\pi}_n) = 0.$$

Targeting the average treatment effect (ATE)

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

Per construction we already have: $\mathbb{P}_n \phi_{\mu}^*(\hat{f}_n^*) = 0$,

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

The targeting step thus yields:

$$\mathbb{P}_n \tilde{\phi}^*(\hat{f}_n^*, \hat{\pi}_n) = \mathbb{P}_n \tilde{\phi}_f^*(\hat{f}_n^*, \hat{\pi}_n) + \mathbb{P}_n \phi_{\mu}^*(\hat{f}_n^*) = 0.$$

Targeting the average treatment effect (ATE)

Doing the targeting in practice using the simulated dataset:

```
set.seed(5)
n <- 500
X <- runif(n, -2, 2)
A <- rbinom(n, 1, prob=plogis(-0.25 + 1.2*X))
Y <- rbinom(n, 1, prob=plogis(-0.9 + 1.9*X^2 + 0.5*A))
(sim.data <- data.table(id=1:n,X=X,A=A,Y=Y))
```

	id	X	A	Y
1:	1	-1.1991422	0	1
2:	2	0.7408744	1	1
3:	3	1.6675031	1	1
4:	4	-0.8624022	0	1
5:	5	-1.5813995	0	1

496:	496	-0.3978523	1	0
497:	497	-1.5069379	0	1
498:	498	1.8340120	1	1
499:	499	0.6349484	1	0
500:	500	-0.5214807	0	1

Targeting the average treatment effect (ATE)

Initial estimation:

```
#-- treatment distribution;
glm.A <- glm(A~X, data=sim.data, family=binomial)
pi.1 <- predict(glm.A, type="response")

#-- outcome distribution (misspecified);
glm.Y <- glm(Y~A+X, data=sim.data, family=binomial)
sim.data[, f:=predict(glm.Y, type="response")]
sim.data[, f.A1:=predict(glm.Y, type="response",
                        newdata=copy(sim.data)[, A:=1])]
sim.data[, f.A0:=predict(glm.Y, type="response",
                        newdata=copy(sim.data)[, A:=0])]

#-- initial estimate of the ATE;
fit.ate.initial <- sim.data[, mean(f.A1 - f.A0)]
```


Targeting the average treatment effect (ATE)

Targeting step:

```
#-- tmle;  
sim.data[, clever.covariate:=((A==1)/pi.1 - (A==0)/(1-pi.1))]  
eps <- coef(glm(Y ~ offset(qlogis(f))+clever.covariate-1,  
               data=sim.data, family=binomial()))
```

eps = -0.0157708436790858

Targeting the average treatment effect (ATE)

Targeting step:

```
#-- tmle;  
sim.data[, clever.covariate:=((A==1)/pi.1 - (A==0)/(1-pi.1))]  
eps <- coef(glm(Y ~ offset(qlogis(f))+clever.covariate-1,  
                data=sim.data, family=binomial()))
```

eps = -0.0157708436790858

```
#-- tmle update;  
sim.data[, f.A1.tmle:=plogis(qlogis(f.A1) + eps/pi.1)]  
sim.data[, f.A0.tmle:=plogis(qlogis(f.A0) - eps/(1-pi.1))]
```

i.e., `f.A1.tmle` is the estimate of $f(1, X) = \mathbb{E}[Y \mid A = 1, X]$, obtained via the submodel:

$$\hat{f}_n^*(1, X) = \hat{f}_{n, \hat{\epsilon}_n}(1, X) = \text{expit}(\text{logit}(\hat{f}_n(1, X)) + \hat{\epsilon}_n \hat{H}_n(1, X)),$$

and likewise with `f.A0.tmle`.

Targeting the average treatment effect (ATE)

	id		X	A	Y	f.A1	f.A0	f.A1.tmle	f.A0.tmle
1:	1	-1.1991422	0	1	0.7655621	0.6713853	0.7488795	0.6755825	
2:	2	0.7408744	1	1	0.7396070	0.6399080	0.7349584	0.6504368	
3:	3	1.6675031	1	1	0.7265721	0.6244167	0.7228545	0.6481588	
4:	4	-0.8624022	0	1	0.7611886	0.6660214	0.7488197	0.6705960	
5:	5	-1.5813995	0	1	0.7704590	0.6774205	0.7463439	0.6813231	

496:	496	-0.3978523	1	0	0.7550638	0.6585507	0.7464799	0.6639337	
497:	497	-1.5069379	0	1	0.7695108	0.6762494	0.7471142	0.6802008	
498:	498	1.8340120	1	1	0.7241872	0.6216047	0.7205492	0.6495635	
499:	499	0.6349484	1	0	0.7410712	0.6416611	0.7362345	0.6513868	
500:	500	-0.5214807	0	1	0.7567041	0.6605467	0.7472996	0.6656728	

Targeting the average treatment effect (ATE)

	id		X	A	Y	f.A1	f.A0	f.A1.tmle	f.A0.tmle
1:	1	-1.1991422	0	1	0.7655621	0.6713853	0.7488795	0.6755825	
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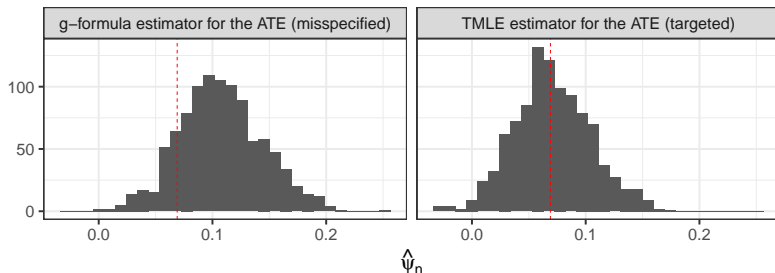
```
fit.ate.tmle <- sim.data[, mean(f.A1.tmle - f.A0.tmle)]
```

```
initial ate est = 0.0975
```

```
tmle ate est    = 0.0768
```

Targeting the average treatment effect (ATE)

With 500 repeated simulations:



Practical 1: Implementing the targeting step

Practical Part 1 Implementing the targeting step.

Practical Part 2 Computing the variances of the ATE, the log RR and the log OR.

Practical Part 3 Large-sample properties (simulation study).

The exercise is described in detail in: **day2-practical1.pdf**.

[More comments on the following slides].

Comments for practical

We focused on the ATE as an example of a causal parameter.

But note that other simple causal parameters can be constructed from $\mathbb{E}_P[Y^1]$ and $\mathbb{E}_P[Y^0]$.

Like:

$$\psi_{\text{RR}}(P) = \frac{\mathbb{E}_P[Y^1]}{\mathbb{E}_P[Y^0]},$$

or,

$$\psi_{\text{OR}}(P) = \frac{\mathbb{E}_P[Y^1]/(1 - \mathbb{E}_P[Y^1])}{\mathbb{E}_P[Y^0]/(1 - \mathbb{E}_P[Y^0])},$$

Comments for practical

For the targeting step, we can choose to target $\psi_1(P) = \mathbb{E}_P[Y^1]$ and $\psi_0(P) = \mathbb{E}_P[Y^0]$ separately.

Comments for practical

For the targeting step, we can choose to target $\Psi_1(P) = \mathbb{E}_P[Y^1]$ and $\Psi_0(P) = \mathbb{E}_P[Y^0]$ separately.

The efficient influence function for the treatment-specific mean $\Psi_a(P) = \mathbb{E}_P[Y^a]$:

$$\tilde{\phi}_a^*(f, \pi)(O) = \underbrace{\frac{1\{A=a\}}{\pi(a|X)}}_{\text{clever covar.}} (Y - f(A, X)) + f(a, X) - \Psi_a(P)$$

Comments for practical

For the targeting step, we can choose to target $\Psi_1(P) = \mathbb{E}_P[Y^1]$ and $\Psi_0(P) = \mathbb{E}_P[Y^0]$ separately.

The efficient influence function for the treatment-specific mean $\Psi_a(P) = \mathbb{E}_P[Y^a]$:

$$\tilde{\phi}_a^*(f, \pi)(O) = \underbrace{\frac{1\{A=a\}}{\pi(a|X)}}_{\text{clever covar.}} (Y - f(A, X)) + f(a, X) - \Psi_a(P)$$

If we target $\Psi_1(P)$ and $\Psi_0(P)$ separately, we obtain two sets of updated estimators $\hat{f}_n \mapsto \hat{f}_{n,1}^*$ and $\hat{f}_n \mapsto \hat{f}_{n,0}^*$

- ▶ one to construct a targeted estimator $\hat{\psi}_{1,n}^*$ for $\Psi_1(P)$;
- ▶ and the other to construct a targeted estimator $\hat{\psi}_{0,n}^*$ for $\Psi_0(P)$.

Comments for practical

We can then compute an estimate for the ATE as

$$\hat{\psi}_n^* = \hat{\psi}_{n,1}^* - \hat{\psi}_{n,0}^*,$$

and we can estimate the variance of this estimator by

$$\mathbb{P}_n\{\tilde{\phi}_1^*(\hat{f}_{n,1}^*, \hat{\pi}_n) - \tilde{\phi}_0^*(\hat{f}_{n,0}^*, \hat{\pi}_n)\}^2;$$

since efficient influence function for the ATE is

$$\tilde{\phi}^*(f, \pi) = \tilde{\phi}_1^*(f, \pi) - \tilde{\phi}_0^*(f, \pi).$$

Comments for practical

Similarly we can construct estimators for the RR and the OR by simple plug-in:

$$\hat{\psi}_{\text{RR},n}^* = \frac{\hat{\psi}_{1,n}^*}{\hat{\psi}_{0,n}^*},$$

and,

$$\hat{\psi}_{\text{OR},n}^* = \frac{\hat{\psi}_{1,n}^*/(1 - \hat{\psi}_{1,n}^*)}{\hat{\psi}_{0,n}^*/(1 - \hat{\psi}_{0,n}^*)}.$$

Comments for practical

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$$\hat{\psi}_{\text{RR},n}^* = \frac{\hat{\psi}_{1,n}^*}{\hat{\psi}_{0,n}^*},$$

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$$\hat{\psi}_{\text{OR},n}^* = \frac{\hat{\psi}_{1,n}^*/(1 - \hat{\psi}_{1,n}^*)}{\hat{\psi}_{0,n}^*/(1 - \hat{\psi}_{0,n}^*)}.$$

We can use the **delta method** to derive the efficient influence functions of $\Psi_{\text{RR}}(P)$ and $\Psi_{\text{OR}}(P)$.

Comments for practical

Let $\phi^*(P)$ be the efficient influence function for a parameter $\Psi(P)$. Say that interest is in $h(\Psi(P))$ for a function h .

The delta method yields that:

If the first derivative $h'(\psi) = \frac{d}{d\psi} h(\psi)$ of h exists and is non-zero, then the efficient influence function of $h(\Psi(P))$ is:

$$\phi_h^*(P) = h'(\Psi(P))\phi^*(P).$$

Comments for practical

So, once we have TMLE (targeted) estimators for $\Psi_1(P) = \mathbb{E}[Y^1]$ and $\Psi_0(P) = \mathbb{E}[Y^0]$:

- ▶ We can construct estimators for the ATE, the RR and the OR.
- ▶ We can compute the variance of the ATE estimator, the log RR estimator and the log OR estimator.

Practical 1: Implementing the targeting step

Practical Part 1 Implementing the targeting step.

Practical Part 2 Computing the variances of the ATE, the log RR and the log OR.

Practical Part 3 Large-sample properties (simulation study).

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