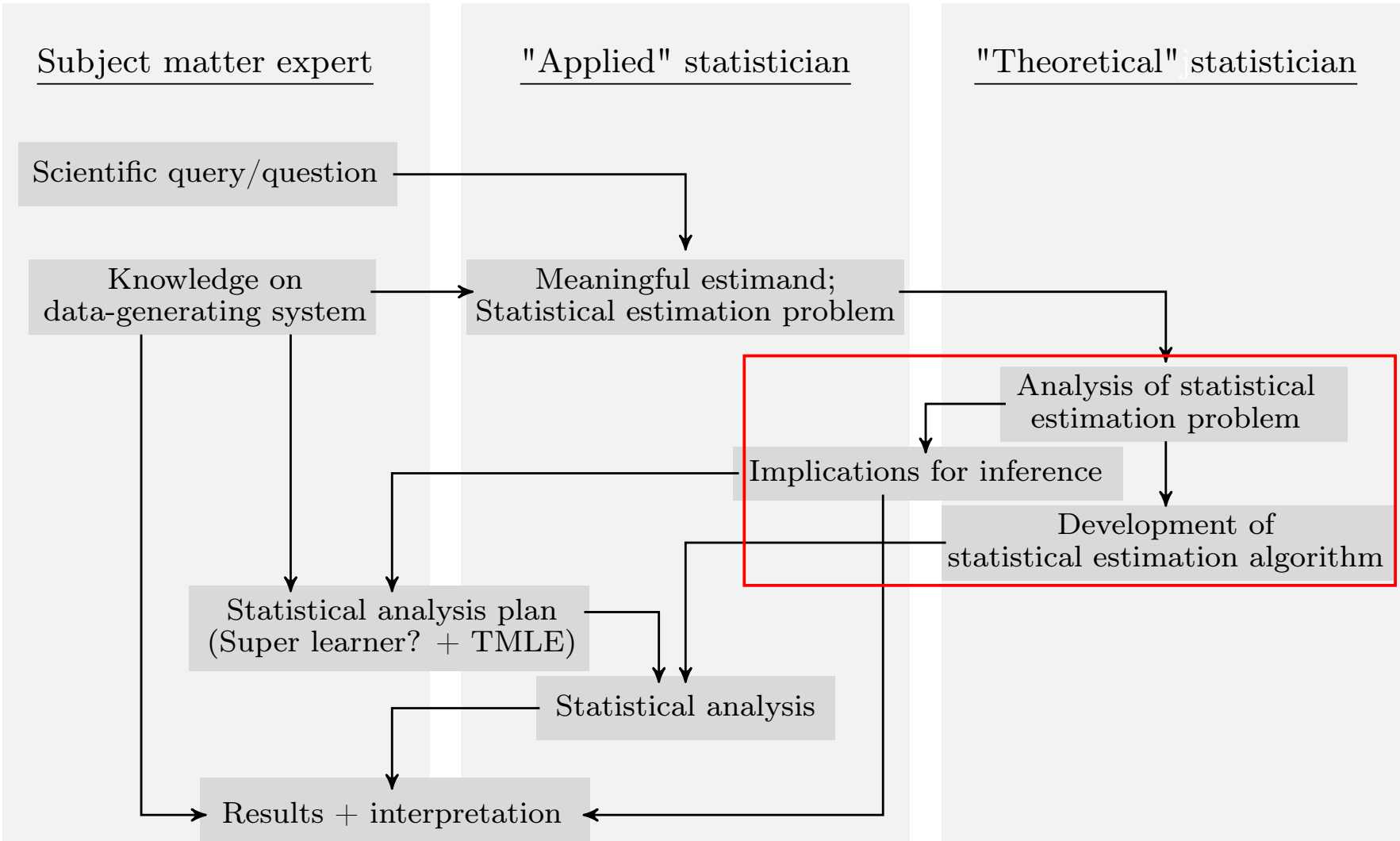
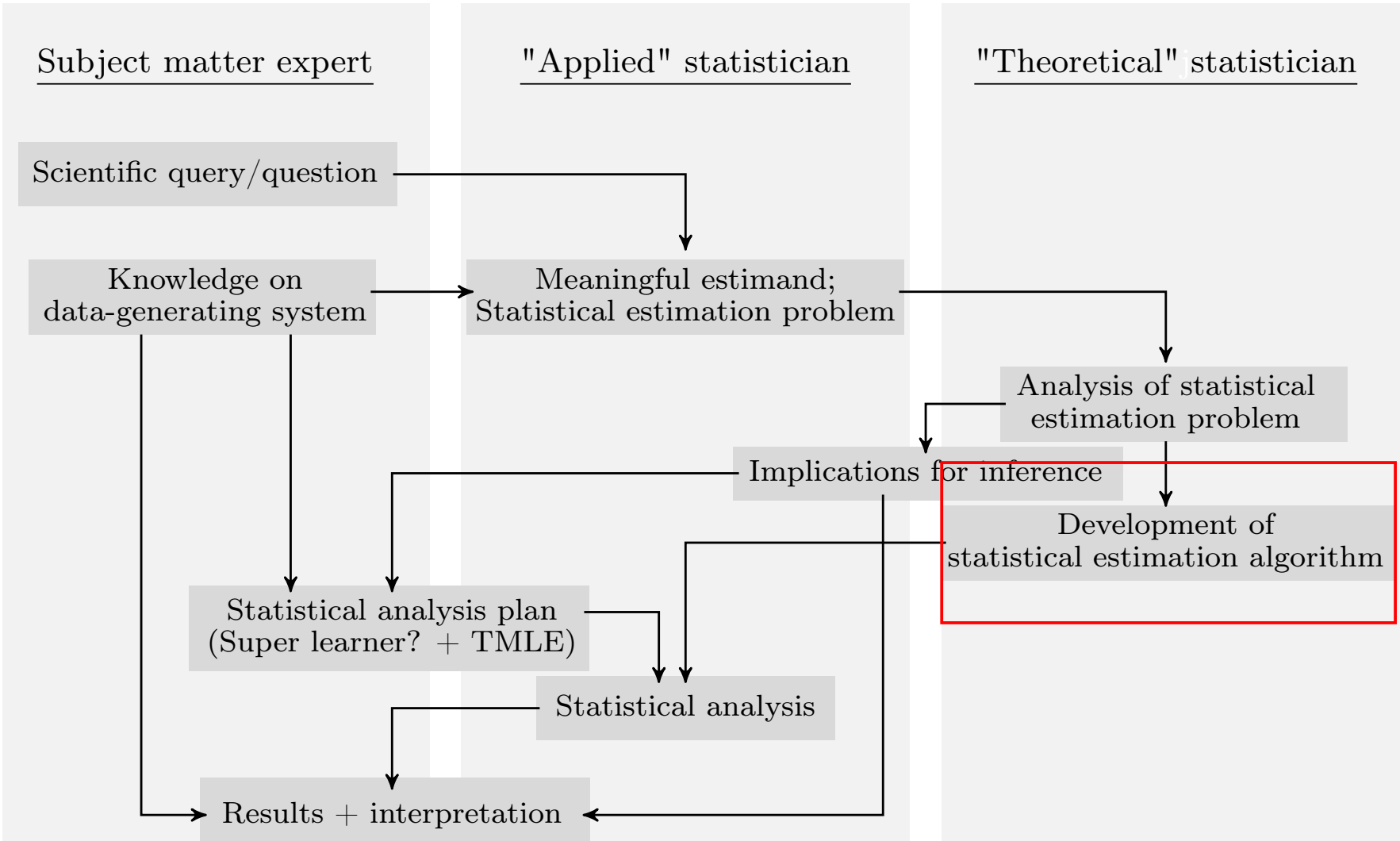
Day 2, Lecture 1

Targeted Minimum Loss-based Estimation (TMLE)

Targeted Minimum Loss-based Estimation (TMLE)



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, and TMLE as a practical estimation method.

After lunch (13 – 15): Time-varying treatments and outcomes.

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 $\Psi : \mathcal{M} \to \mathbb{R}$ (and a particular statistical model $\mathcal{M}$),

we have seen that —

Conditions (asymptotic linearity and efficiency)

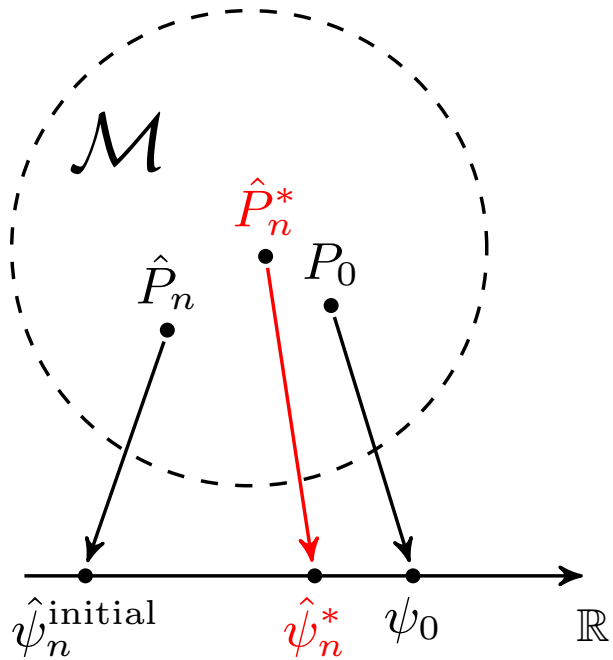
(C1) Solve the efficient influence curve equation: $\mathbb{P}_n \phi^*(\hat{P}_n) = o_P(n^{-1/2})$

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

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)

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

- The role of the targeting step (Step 2):
  - Gain double robustness in consistency.
  - Easier to achieve asymptotic lineariy (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** $\mathscr{L}(f)(O)$ measuring the distance between an estimator f and the observed outcome Y, e.g., the negative log-likelihood:

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

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

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

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

Targeted Minimum Loss-based Estimation (TMLE)

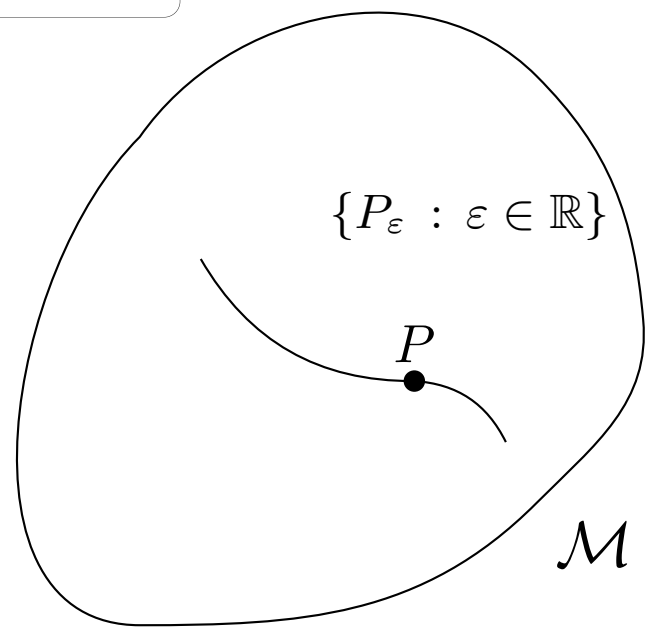
This is all about constructing a good estimator for the conditional expectation f;

- 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)

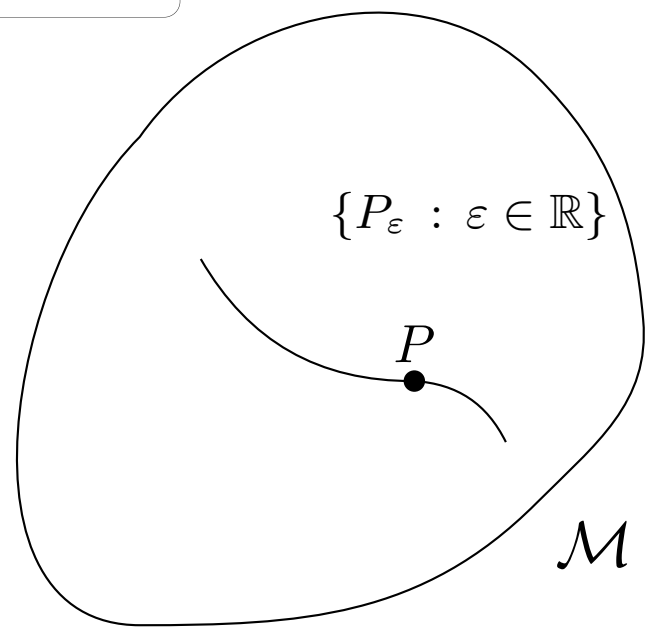
Step 2: We can minimize along a loss function in a certain way *that results in a good estimator for the target*.



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

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*.

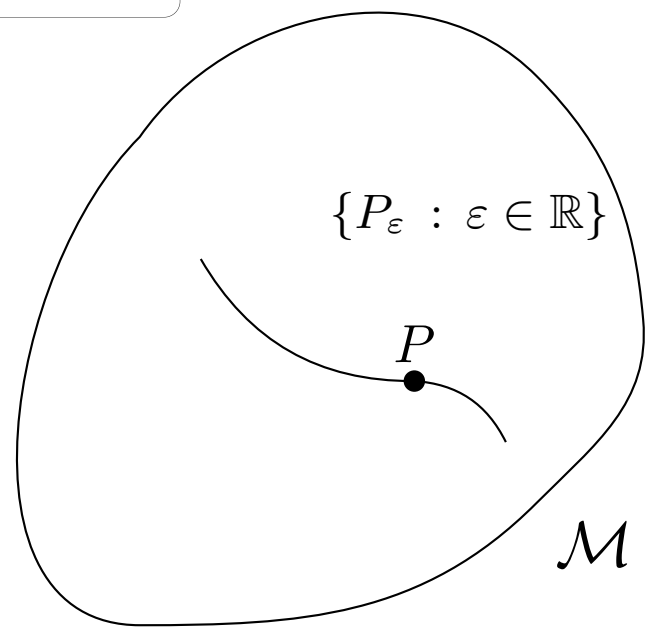


Loss function $\mathscr{L}(f)(O)$ + clever choice of a **parametric submodel** $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$.

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

$\Rightarrow$ 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 $\hat{\varepsilon}_n$ that minimizes the loss.

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

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

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

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

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

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

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

- kth updated estimator $\hat{P}_n^k$
- Minimizer $\hat{\varepsilon}_{n,k}$ of $\varepsilon \mapsto \mathbb{P}_n \mathscr{L}(\hat{P}_{n,\varepsilon}^k)$
- Update: $\hat{P}_n^{k+1} := \hat{P}_{\hat{\varepsilon}_{n,k}}^k$

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

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

- kth updated estimator $\hat{P}_n^k$
- Minimizer $\hat{\varepsilon}_{n,k}$ of $\varepsilon \mapsto \mathbb{P}_n \mathscr{L}(\hat{P}_{n,\varepsilon}^k)$
- Update: $\hat{P}_n^{k+1} := \hat{P}_{\hat{\varepsilon}_{n,k}}^k$

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

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

The targeting step (Step 2)

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

(i) A parametric submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, P) \mapsto \mathscr{L}(P)(O)$

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

- kth updated estimator $\hat{P}_n^k$
- Minimizer $\hat{\varepsilon}_{n,k}$ of $\varepsilon \mapsto \mathbb{P}_n \mathscr{L}(\hat{P}_{n,\varepsilon}^k)$
- Update: $\hat{P}_n^{k+1} := \hat{P}_{\hat{\varepsilon}_{n,k}}^k$

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

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

The targeting step (Step 2)

For example, consider the one-dimensional submodel

$$dP_\varepsilon = (1 + \varepsilon\phi^*(P))dP,$$

which fulfills for the log-likelihood loss $\mathscr{L}(P) = -\log dP$ that

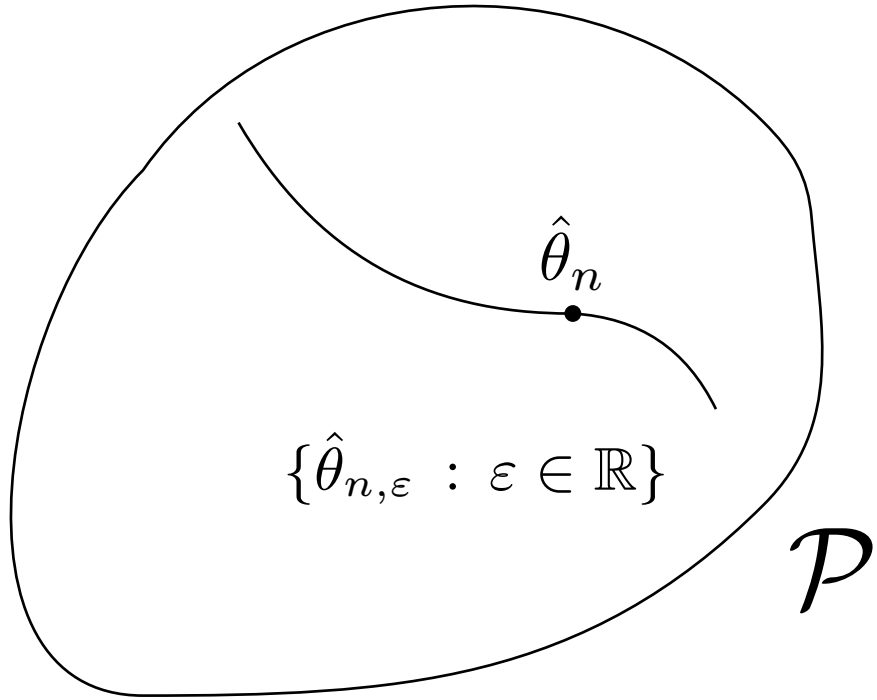
$$\left.\frac{d}{d\varepsilon}\right|_{\varepsilon=0} \mathscr{L}(P_\varepsilon) = \phi^*(P).$$

The value $\hat{\varepsilon}_n$ which minimizes the loss maximizes the likelihood, i.e.,

$$\hat{\varepsilon}_{n,k} = \operatorname*{argmin}_\varepsilon \mathbb{P}_n \mathscr{L}(\hat{P}^k_{n,\varepsilon})$$

is just a good-old MLE.

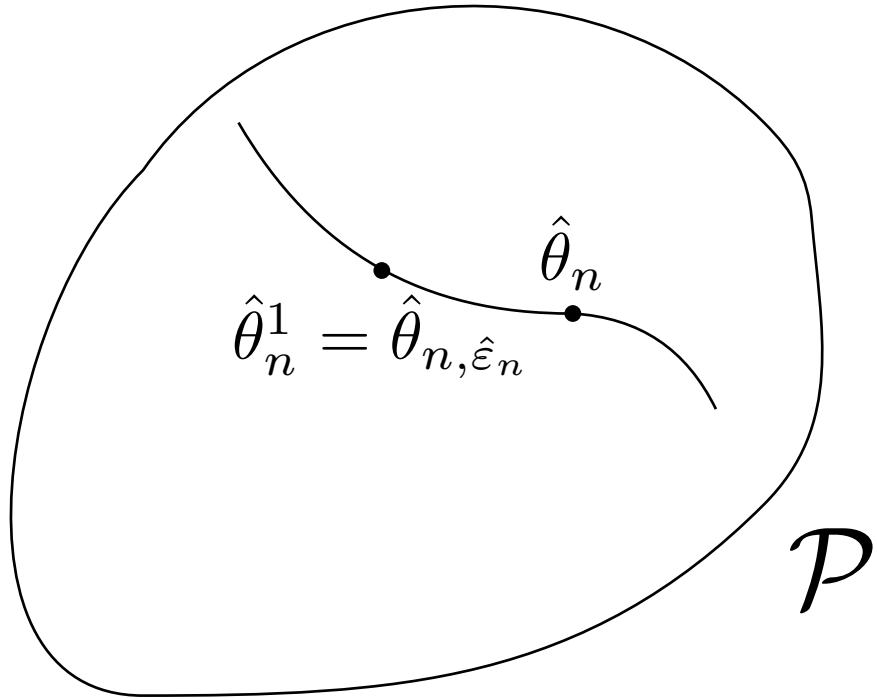
The targeting step (Step 2)



Then the TMLE algorithm is really just a series of MLE problems.

At each step, the empirical log-likelihood is increased relative to the previous step (this is exactly how ε is chosen), and, if there is no increase in the empirical log-likelihood, then $\varepsilon \approx 0$, and the algorithm has converged.

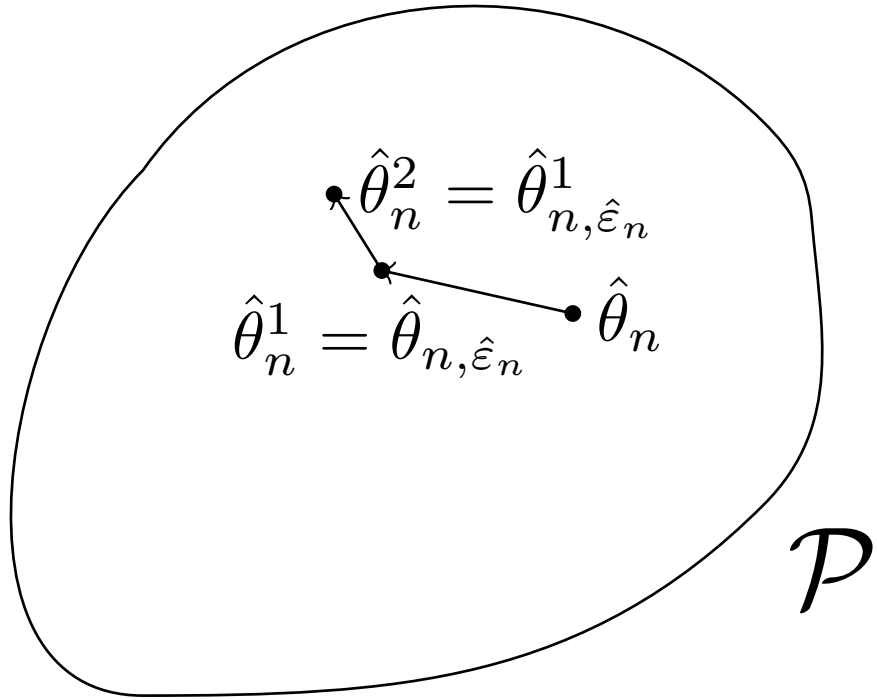
The targeting step (Step 2)



Then the TMLE algorithm is really just a series of MLE problems.

At each step, the empirical log-likelihood is increased relative to the previous step (this is exactly how ε is chosen), and, if there is no increase in the empirical log-likelihood, then $\varepsilon \approx 0$, and the algorithm has converged.

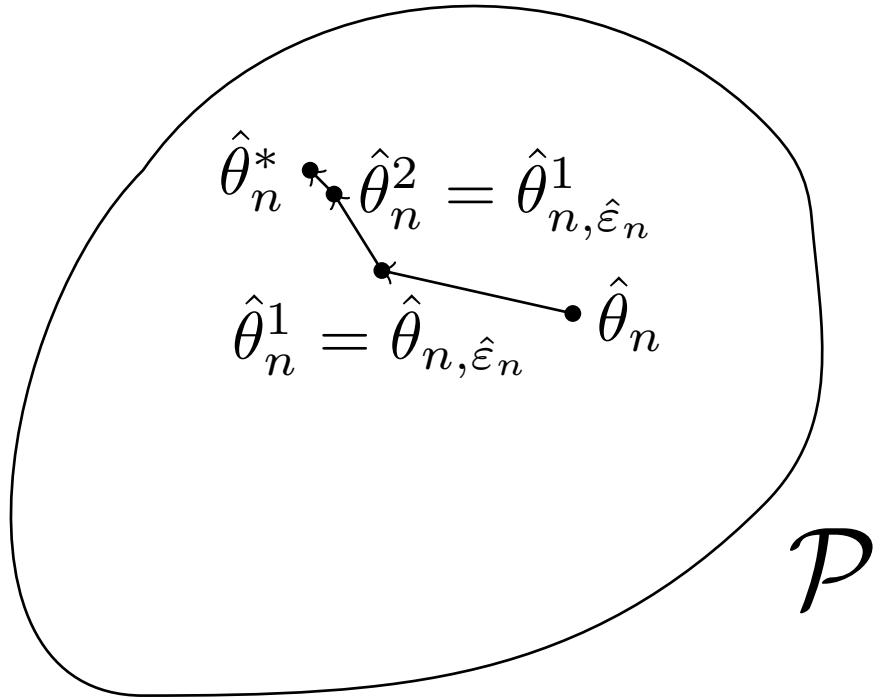
The targeting step (Step 2)



Then the TMLE algorithm is really just a series of MLE problems.

At each step, the empirical log-likelihood is increased relative to the previous step (this is exactly how ε is chosen), and, if there is no increase in the empirical log-likelihood, then $\varepsilon \approx 0$, and the algorithm has converged.

The targeting step (Step 2)



Then the TMLE algorithm is really just a series of MLE problems.

At each step, the empirical log-likelihood is increased relative to the previous step (this is exactly how ε is chosen), and, if there is no increase in the empirical log-likelihood, then $\varepsilon \approx 0$, and the algorithm has converged.

The targeting step (Step 2)

SMALL EXERCISE: As a very simple example, consider $\Psi(P) = \mathbb{E}_P[Y]$ with efficient influence curve $\phi^*(P)(O) = Y - \Psi(P)$.

Let p denote the density of P with respect to an appropriate dominating measure, and define the one-dimensional submodel

$$dP_\varepsilon = (1 + \varepsilon\phi^*(P))dP.$$

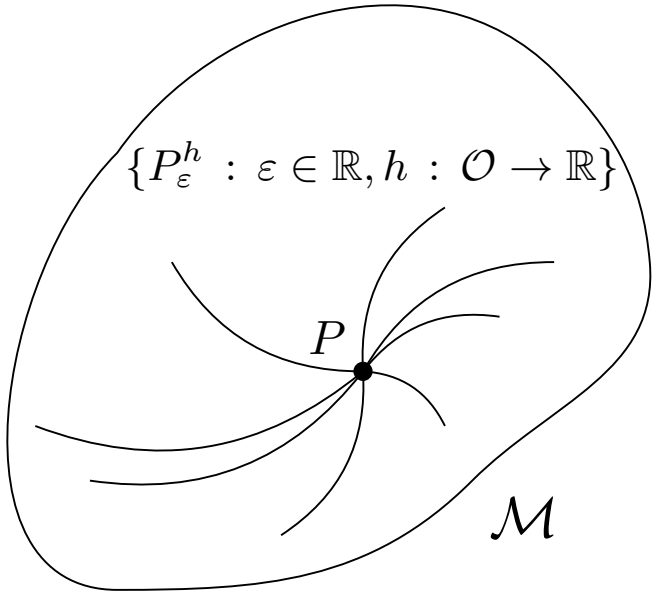
Let $\mathscr{L}(P)(O) = -\log dP(O)$ denote the log-likelihood loss.

Show that:

1. $\frac{d}{d\varepsilon}\big|_{\varepsilon=0}\mathscr{L}(P_\varepsilon) = \phi^*(P)$.
2. Using the estimator $\hat{P}_n = \mathbb{P}_n$, write up the estimate the estimator for the target parameter $\hat{\psi}_n = \Psi(\hat{P}_n)$.
3. Argue that $\hat{P}_n = \mathbb{P}_n$ already maximizes the likelihood, so that $\hat{\varepsilon}_{n,1} = 0$ in the first iteration of the targeting step.

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:

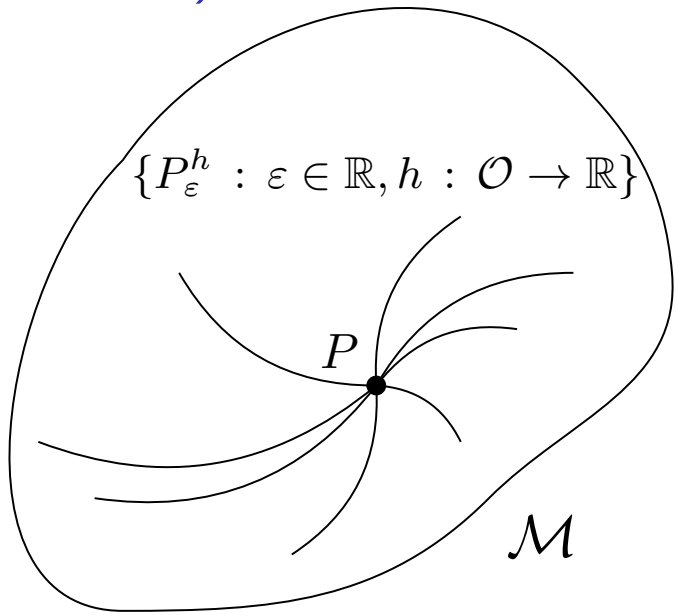
- define pathwise differentiability:[1]

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

- derive a nonparametric lower bound on the variance.

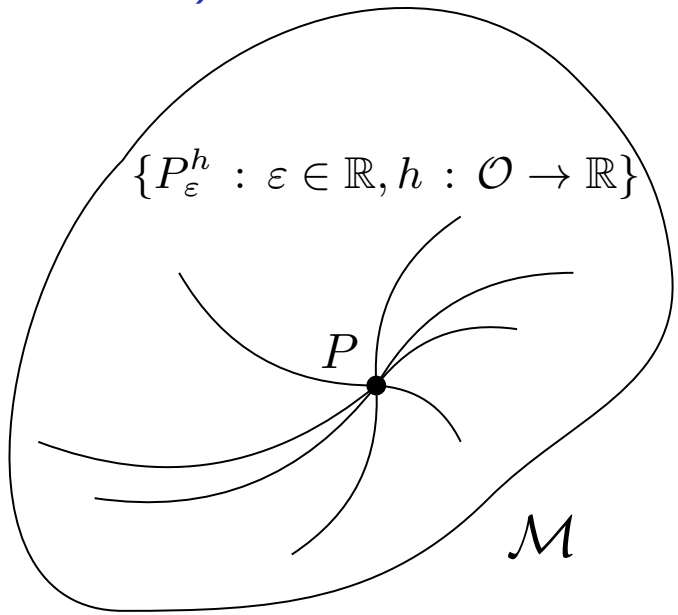
[1] (1) should hold across any smooth submodel $\{P_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$.

The targeting step (Step 2) *ASIDE*



- Index submodel by its score function: $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}, h : \mathcal{O} \to \mathbb{R}\}$.
  - i.e., $\frac{d}{d\varepsilon}\big|_{\varepsilon=0} \log dP_\varepsilon^h(o) = h(o)$.
- 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 $\mathcal{M}$:

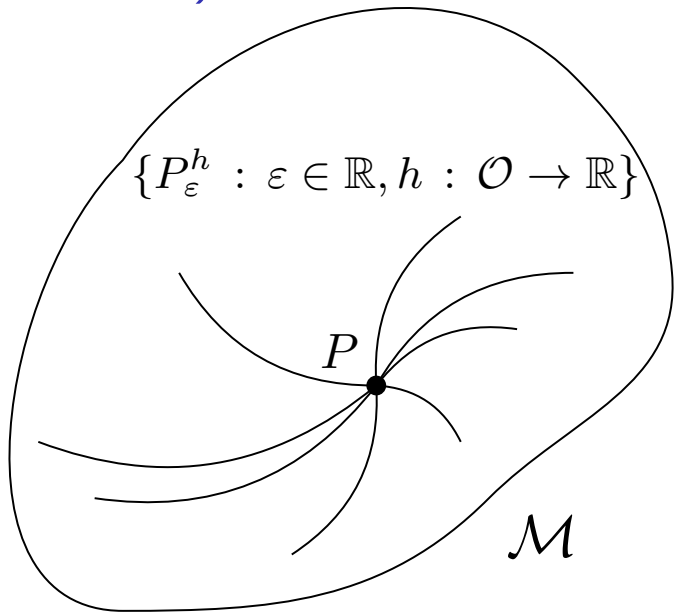
The targeting step (Step 2) *ASIDE*



- Index submodel by its score function: $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}, h : \mathcal{O} \to \mathbb{R}\}$.
  - i.e., $\frac{d}{d\varepsilon}\big|_{\varepsilon=0} \log dP_\varepsilon^h(o) = h(o)$.
- 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 $\mathcal{M}$:

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

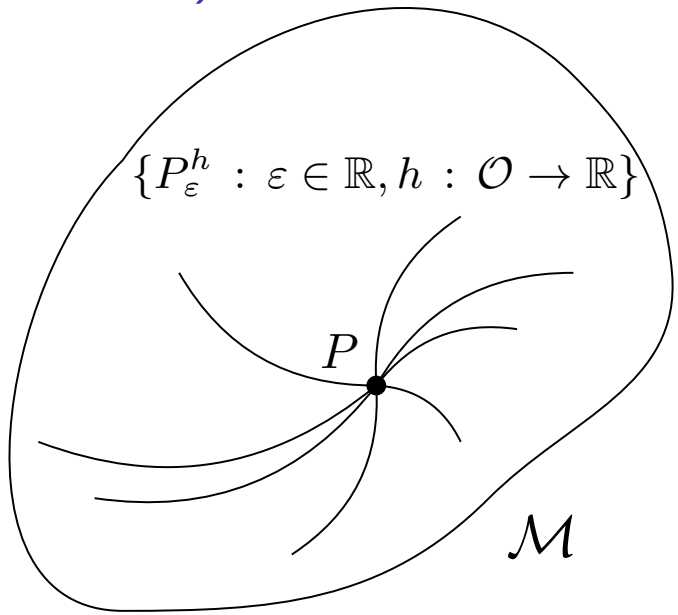
The targeting step (Step 2) *ASIDE*



- Index submodel by its score function: $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}, h : \mathcal{O} \to \mathbb{R}\}$.
  - i.e., $\frac{d}{d\varepsilon}\big|_{\varepsilon=0} \log dP_\varepsilon^h(o) = h(o)$.
- 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 $\mathcal{M}$:

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

The targeting step (Step 2) *ASIDE*



- Index submodel by its score function: $\{P_\varepsilon^h : \varepsilon \in \mathbb{R}, h : \mathcal{O} \to \mathbb{R}\}$.
  - i.e., $\frac{d}{d\varepsilon}\big|_{\varepsilon=0} \log dP_\varepsilon^h(o) = h(o)$.
- 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 $\mathcal{M}$:

$$\frac{(\frac{d}{d\varepsilon}\big|_{\varepsilon=0}\Psi(P_\varepsilon^h))^2}{Ph^2} \overset{\text{PD}}{=} \frac{(P\phi^*(P)h)^2}{Ph^2} \overset{\text{CS}}{\leq} P\{\phi^*(P)\}^2 \qquad (*)$$

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 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)

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:

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

[a] With (C2) depending on how well we do for the initial estimation step.

The targeting step (Step 2)

We can usually decompose the efficient influence curve into separate pieces:

$$\phi^*(P) = \phi_1^*(P) + \phi_2^*(P) + \cdots + \phi_J^*(P).$$

In practice we can construct a submodel

$$\{P_{\varepsilon_j}^j : \varepsilon_j \in \mathbb{R}\}$$

for each relevant component P^j of P (that the target parameter Ψ depends on), which for an accompagnying loss function $\mapsto \mathscr{L}_j(P^j)$ fulfills that

$$\left.\frac{d}{d\varepsilon_j}\right|_{\varepsilon_j=0} \mathscr{L}_j(P_{\varepsilon_j}^j) = \phi_j^*(P).$$

Note that each submodel $\{P_{\varepsilon_j}^j : \varepsilon_j \in \mathbb{R}\}$ and/or loss function $(O, P^j) \mapsto \mathscr{L}_j(P^j)(O)$ may depend on $P^{j'}$ for $j' \neq j$, as well as on other parts of the data-generating distribution.

The targeting step (Step 2)

If we bundle these together into one J-dimensional submodel in $\varepsilon = (\varepsilon_j)_{1 \le j \le J}$

$$P_{\varepsilon_1,\ldots,\varepsilon_J} = \{P^1_{\varepsilon_1}, \ldots, P^J_{\varepsilon_J} : \varepsilon_1, \ldots, \varepsilon_J \in \mathbb{R}\},$$

and define the combined loss function $\mathscr{L}(P) = \mathscr{L}_1(P^1) + \cdots \mathscr{L}_J(P^J)$, then

$$\left.\frac{d}{d\varepsilon_j}\right|_{\varepsilon=0} \mathscr{L}(P_{\varepsilon_1,\ldots,\varepsilon_J}) = \phi_j^*(P)$$

and if $\varepsilon_1 = \cdots = \varepsilon_J$, this is just the one-dimensional submodel with score equal to $\phi^*(P) = \phi_1^*(P) + \phi_2^*(P) + \cdots + \phi_J^*(P)$.

The targeting step (Step 2)

In the kth iteration of the targeting step, we replace optimization over ε with optimization over $\varepsilon_1, \ldots, \varepsilon_J$, where each $\hat{\varepsilon}_{j,n}^k$ is obtained by minimizing

$$\varepsilon_j \mapsto \mathbb{P}_n \mathscr{L}(\hat{P}^{k-1}_{n,\hat{\varepsilon}^k_{1,n},\ldots,\hat{\varepsilon}^k_{j-1,n},\varepsilon_j,0,\ldots,0}).$$

At convergence, $\hat{\varepsilon}_n^{k^*} = (\hat{\varepsilon}_j^{k^*})_{1 \leq j \leq J} \approx 0$, and $\hat{P}_n^{k^*}$ solves $\mathbb{P}_n \phi_j^*(\hat{P}_n^{k^*}) \approx 0$ for all j.

Targeting the average treatment effect (ATE)

Targeting the average treatment effect (ATE)

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:

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

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 $\Psi : \mathcal{M} \to \mathbb{R}$ as

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

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:

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

$$+ f(1,X) - f(0,X) - \tilde{\Psi}(f)$$

Targeting the average treatment effect (ATE)

EXAMPLE: Average treatment effect (ATE)

We need:

0. The efficient influence function:

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

Targeting the average treatment effect (ATE)

EXAMPLE: Average treatment effect (ATE)

We need:

0. The efficient influence function:

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

Further, we need:

(i) A parametric submodel $\{f_\varepsilon : \varepsilon \in \mathbb{R}\} \subset \mathcal{M}$

(ii) A loss function $(O, f) \mapsto \mathscr{L}(f)(O)$

such that

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

Targeting the average treatment effect (ATE)

(i) Log-likelihood loss function:

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

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

(ii) Logistic regression model:

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

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

Targeting the average treatment effect (ATE)

(i) Log-likelihood loss function:

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

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

(ii) Logistic regression model:

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

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

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

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

Targeting the average treatment effect (ATE)

(i) Log-likelihood loss function:

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

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

(ii) Logistic regression model:

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

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

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

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

Targeting the average treatment effect (ATE)

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

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

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

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

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

Then: $\mathbb{P}_n \dfrac{d}{d\varepsilon}\Big|_{\varepsilon=\hat{\varepsilon}_n} \mathscr{L}(\hat{f}_{n,\varepsilon}) = 0$, 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)

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

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

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

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:

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

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)

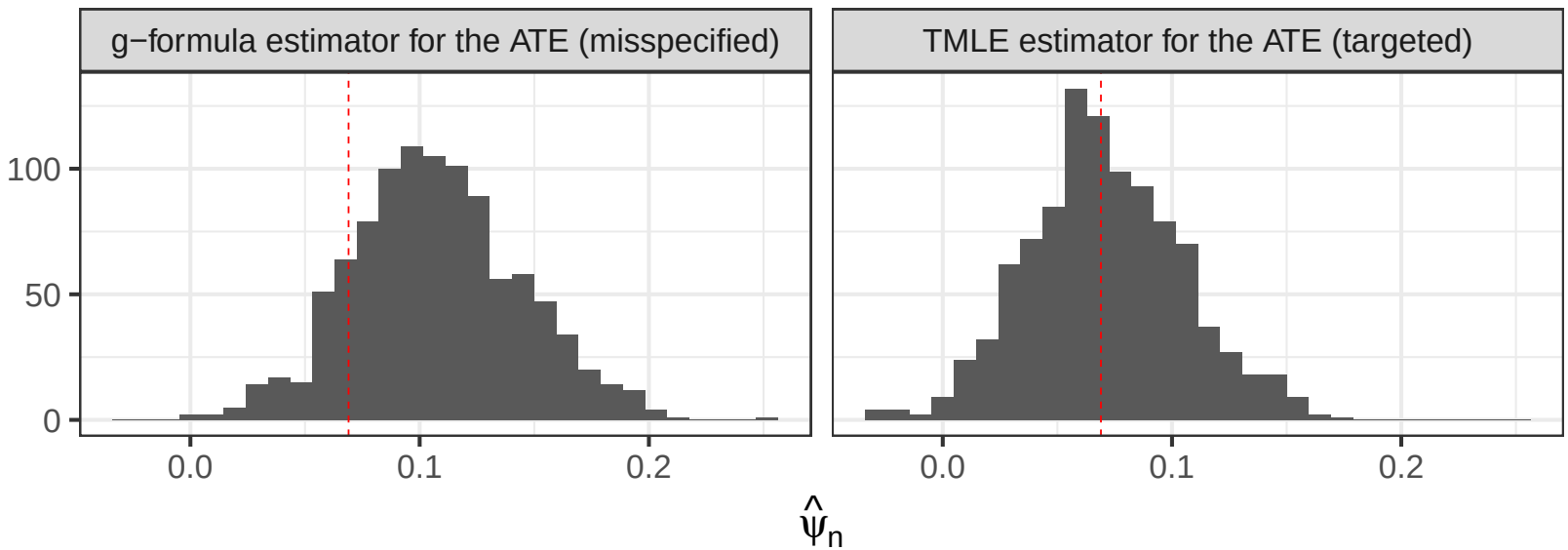
```
      id           X A Y      f.A1      f.A0 f.A1.tmle f.A0.tmle
  1:   1 -1.1991422 0 1 0.7655621 0.6713853 0.7488795 0.6755825
  2:   2  0.7408744 1 1 0.7396070 0.6399080 0.7349584 0.6504368
  3:   3  1.6675031 1 1 0.7265721 0.6244167 0.7228545 0.6481588
  4:   4 -0.8624022 0 1 0.7611886 0.6660214 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
```

```
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 $\log \mathrm{RR}$ and the $\log \mathrm{OR}$.

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: Inference for derived parameters

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: Inference for derived parameters

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: Inference for derived parameters

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 $\Psi_a(P) = \mathbb{E}_P[Y^a]$:

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

Comments for practical: Inference for derived parameters

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 $\Psi_a(P) = \mathbb{E}_P[Y^a]$:

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

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: Inference for derived parameters

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: Inference for derived parameters

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

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

and,

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

Comments for practical: Inference for derived parameters

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

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

and,

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

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

Comments for practical: Inference for derived parameters

Let $\phi^*(P)$ be the efficient influence function for a parameter $\psi = \Psi(P)$, and suppose an asymptotically linear estimator $\hat{\psi}_n$ with influence function ϕ_P is available, but interest is in the parameter $h \circ \Psi$ for a function h.

The delta method + some arguments ($\rightarrow$):

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

$$\phi^{h,*}(P) = h'(\psi)\phi^*(P).$$

I.e.:

$$\sqrt{n}(h(\hat{\psi}_n) - h(\psi)) \overset{wk}{\rightarrow} N(0, P_0\{h'(\psi)\phi_P\}^2).$$

Comments for practical: Inference for derived parameters

The targeted estimator $\hat{\psi}_n$ is, under conditions, asymptotically linear with influence function equal to the efficient influence curve,

$$\sqrt{n}\big(\hat{\psi}_n - \psi\big) = \sqrt{n}\,\mathbb{P}_n\phi^*(P) + o_P(1).$$

The delta method yields directly that

$$\sqrt{n}\big(h(\hat{\psi}_n) - h\circ\psi\big) = \sqrt{n}\,\mathbb{P}_n h'(\psi)\phi^*(P) + o_P(1).$$

General arguments for $\phi^{h,*}(P) = h'(\psi)\phi^*(P)$ being the efficient influence curve are provided in vdV Chapter 25.7. (We can make a simple argument because we work with the nonparametric model $\mathcal{P}$:

- any influence function of RAL estimator is a gradient,
- the canonical gradient (efficient influence curve) is the unique gradient,
- i.e., $\phi^{h,*}(P) = h'(\psi)\phi^*(P)$ is the efficient influence curve.)

Comments for practical: Inference for derived parameters

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 $\log \mathrm{RR}$ estimator and the $\log \mathrm{OR}$ estimator.

Practical 1: Implementing the targeting step

Practical Part 1 Implementing the targeting step.

Practical Part 2 Computing the variances of the ATE, the $\log \mathrm{RR}$ and the $\log \mathrm{OR}$.

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

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