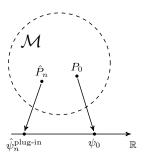
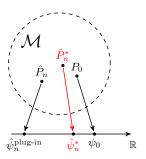
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we should focus estimation on our target  $\psi_0$  =  $\Psi(P_0)$  specifically



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Key (technical) concepts we cannot avoid talking about:

- \* asympotically linear estimation
- \* efficient influence curve
- \* von Mises expansions
- \* second-order remainders

While TMLE can be applied without knowing about these concepts ...

- ... we cannot understand the purpose of TMLE without knowing a bit about the efficient influence curve.
- ... to understand what conditions are required for TMLE, we need to understand the second-order remainder.

#### Important notation:<sup>1</sup>

 $\triangleright$  For a function  $h: \mathcal{O} \to \mathbb{R}$  and distribution P

$$Ph = \mathbb{E}_{P}[h(O)] = \int hdP = \int_{\mathcal{O}} h(o)dP(o)$$

where  $\mathcal{O} = \mathbb{R}^d \times \{0,1\} \times \{0,1\}$  is the sample space of O = (X,A,Y).

 $\triangleright$  For the empirical measure  $\mathbb{P}_n$  of the sample  $O_1, \ldots, O_n$ :

$$\mathbb{P}_n h = \int h d\mathbb{P}_n = \frac{1}{n} \sum_{i=1}^n h(O_i);$$

note: the right-hand-side is really just the empirical average.

$$\triangleright X_n = o_P(1)$$
 means that  $X_n \stackrel{P}{\rightarrow} 0$ ;  $X_n = o_P(n^{-1/2})$  means that  $n^{1/2}X_n \stackrel{P}{\rightarrow} 0$ .

<sup>&</sup>lt;sup>1</sup>van der Vaart, A. W. (2000). Asymptotic statistics (Vol. 3). Cambridge university press.

A very desirable property —

 $<sup>^{2}</sup>o_{P}(1)$  denotes a sequence which is converges to zero in probability.

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#### A very desirable property —

An estimator  $\hat{\psi}_n$  is  $\sqrt{n}$ -consistent and asymptotically linear with influence function  $\phi(P_0)(O)$  if <sup>2</sup>

$$\sqrt{n}(\hat{\psi}_n - \psi_0) = \sqrt{n} \mathbb{P}_n \phi(P_0) + o_P(1),$$

where  $\mathbb{E}_{P_0}[\phi(P_0)(O)] = 0$  and  $\mathbb{E}_{P_0}[\{\phi(P_0)(O)\}^2] < \infty$ .

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**Simple example:** Estimator for the mean  $\psi_0 = \mathbb{E}[X]$ :

$$\hat{\psi}_{n,0} = \frac{1}{n} \sum_{i=1}^{n} X_i$$

Then

$$\sqrt{n}(\hat{\psi}_n - \psi_0) = \sqrt{n} \frac{1}{n} \sum_{i=1}^n \underbrace{(X_i - \psi_0)}_{=\phi(P_0)(O_i)} = \sqrt{n} \mathbb{P}_n \phi(P_0)$$

 $\hat{\psi}_{\it n,0}$  is linear and thus asymptotically linear.

**Simple example:** Estimator for the mean  $\psi_0 = \mathbb{E}[X]$ :

$$\hat{\psi}_{n,1} = \frac{1}{n} \sum_{i=1}^{n} X_i + \frac{1}{n}$$

Then

$$\sqrt{n}(\hat{\psi}_{n} - \psi_{0}) = \sqrt{n} \frac{1}{n} \sum_{i=1}^{n} \underbrace{(X_{i} - \psi_{0})}_{=\phi(P_{0})(O_{i})} + \frac{\sqrt{n}}{n} = \sqrt{n} \mathbb{P}_{n} \phi(P_{0}) + \underbrace{\frac{1}{\sqrt{n}}}_{=o(1)}$$

 $\hat{\psi}_{\textit{n},1}$  is asymptotically linear.

**Simple example:** Estimator for the mean  $\psi_0 = \mathbb{E}[X]$ :

$$\hat{\psi}_{n,2} = \frac{1}{n} \sum_{i=1}^{n} X_i + \frac{1}{n^{1/2 + 0.1}}$$

Then

$$\sqrt{n} (\hat{\psi}_n - \psi_0) = \sqrt{n} \frac{1}{n} \sum_{i=1}^n \underbrace{(X_i - \psi_0)}_{=\phi(P_0)(O_i)} + \frac{\sqrt{n}}{n^{1/2 + 0.1}} = \sqrt{n} \mathbb{P}_n \phi(P_0) + \underbrace{\frac{1}{n^{0.1}}}_{=o(1)}$$

 $\hat{\psi}_{\textit{n},2}$  is asymptotically linear.

**Simple example:** Estimator for the mean  $\psi_0 = \mathbb{E}[X]$ :

$$\hat{\psi}_{n,3} = \frac{1}{n} \sum_{i=1}^{n} X_i + \frac{1}{n^{1/2 - 0.1}}$$

Then

$$\sqrt{n}(\hat{\psi}_n - \psi_0) = \sqrt{n} \frac{1}{n} \sum_{i=1}^n \underbrace{(X_i - \psi_0)}_{=\phi(P_0)(O_i)} + \frac{\sqrt{n}}{n^{1/2 - 0.1}} = \sqrt{n} \mathbb{P}_n \phi(P_0) + \underbrace{n^{0.1}}_{\to \infty}$$

 $\hat{\psi}_{\textit{n},3}$  is  $\mathbf{not}$  asymptotically linear.

An estimator  $\hat{\psi}_n$  has rate of convergence  $r_n \to \infty$  if <sup>3</sup>

$$r_n(\hat{\psi}_n - \psi_0) = O_P(1)$$
, i.e.,  $\hat{\psi}_n - \psi_0 = O_P(1/r_n)$ .

The convergence rate  $r_n$  tells us how fast  $\hat{\psi}_n$  centers around  $\psi_0$ , with the difference  $\hat{\psi}_n - \psi_0$  behaving like  $1/r_n$ .

- One wants negligible bias such as to obtain reliable confidence intervals for  $\psi_0$ .
- ▶ The bias of an asymptotically linear estimator converges to zero at a rate faster than  $1/\sqrt{n}$ .

Data-adaptive machine learning estimators rarely achieve this rate.

 $<sup>^3</sup>O_P(1)$  denotes a sequence which is bounded in probability.

$$\sqrt{n}\hat{\psi}_{n,1} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{\stackrel{P}{\rightarrow}\psi_{0}} + \underbrace{\frac{\sqrt{n}}{n}}_{\stackrel{}{\rightarrow}0}, \quad \text{i.e.,} \quad \sqrt{n}(\hat{\psi}_{n,1} - \psi_{0}) = o_{P}(1).$$

$$\sqrt{n}\hat{\psi}_{n,2} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{P_{o}} + \underbrace{\frac{\sqrt{n}}{n^{1/2+0.1}}}_{\to 0}, \text{ i.e., } \sqrt{n}(\hat{\psi}_{n,3} - \psi_{0}) = o_{P}(1).$$

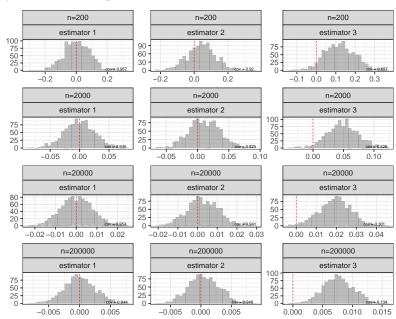
$$\sqrt{n}\hat{\psi}_{n,3} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{P} + \underbrace{\frac{\sqrt{n}}{n^{1/2-0.1}}}_{\to \infty}, \quad \text{i.e.,} \quad \sqrt{n}(\hat{\psi}_{n,3} - \psi_{0}) \stackrel{P}{\to} \infty.$$

$$\sqrt{n}\hat{\psi}_{n,1} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{P \to \psi_{0}} + \underbrace{\frac{\sqrt{n}}{n}}_{N}, \quad \text{i.e.,} \quad \sqrt{n}(\hat{\psi}_{n,1} - \psi_{0}) = o_{P}(1).$$

$$\sqrt{n}\hat{\psi}_{n,2} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{P_{n,i}} + \underbrace{\frac{\sqrt{n}}{\frac{n^{1/2+0.1}}{n}}}_{\to 0}, \text{ i.e., } \sqrt{n}(\hat{\psi}_{n,3} - \psi_{0}) = o_{P}(1).$$

$$\sqrt{n}\hat{\psi}_{n,3} = \sqrt{n}\underbrace{\frac{1}{n}\sum_{i=1}^{n}X_{i}}_{} + \underbrace{\frac{\sqrt{n}}{\underbrace{n^{1/2-0.1}}}}_{\to \infty}, \quad \text{i.e.,} \quad \sqrt{n}(\hat{\psi}_{n,3} - \psi_{0}) \overset{P}{\to} \infty.$$

[The remainder term that determines the asymptotic bias the estimator].



A quick run-through of the theoretical basis for targeted nonparametric inference

The decomposition that guides the construction of TMLE.

A key component in constructing a  $\sqrt{n}$ -consistent and asymptotically linear estimator, even when using machine learning estimation, is the so-called the efficient influence function (also known as the canonical gradient).

#### The von Mises expansion:

Suppose the functional (the target parameter)  $\Psi:\mathcal{M}\to\mathbb{R}$  is sufficiently smooth (as a map from distributions to the real line), in the sense that it admits a certain distributional Taylor expansion

$$\Psi(P) - \Psi(P') = \int \phi(P)(o)d(P - P')(o) + R_2(P, P'), \qquad (1)$$

for distributions  $P, P' \in \mathcal{M}$  for a function  $\phi$  satisfying  $P\phi(P) = 0$  (mean zero) and  $P\phi(P)^2 < \infty$  (finite variance).

Intuitively, the von Mises expansion is just a distributional analogue of a Taylor expansion, with the function  $\phi(P)$  acting as a usual derivative term; it describes how the functional  $\Psi$  changes locally when the distribution changes from P to P'.

When the model  $\mathcal{M}$  is assumed properly nonparametric, there exists \*one\* function  $\phi(P)$ . This is called the efficient influence curve; we also denote it  $\phi^*(P)$ .<sup>4</sup>

The efficient influence curve in nonparametric models indicates how to construct asymptotically linear (and efficient) estimators.

<sup>&</sup>lt;sup>4</sup>This may be confusing here, but it is useful in restricted (semi)parametric models, where multiple  $\phi$ 's can satisfy (1). For these situations we by the way have that  $P_0\phi(P_0)^2 \ge P_0\phi^*(P_0)^2$ .

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The efficient influence curve in nonparametric models indicates how to construct asymptotically linear (and efficient) estimators.

Also note that the efficient curve has many names (influence function, pathwise derivative, Neyman orthogonal score, canonical gradient).

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## Goal: $\sqrt{n}$ -consistency and asymptotically linearity

An estimator  $\hat{\psi}_n$  is  $\sqrt{n}$ -consistent and asymptotically linear with influence function  $\phi(P_0)(O)$  if

$$\sqrt{n}(\hat{\psi}_n - \psi_0) = \sqrt{n} \, \mathbb{P}_n \phi(P_0) + o_P(1),$$

where  $\mathbb{E}_{P_0}[\phi(P_0)(O)] = 0$  and  $\mathbb{E}_{P_0}[\{\phi(P_0)(O)\}^2] < \infty$ .

Then CLT + Slutsky implies:

$$\hat{\psi}_n \stackrel{as}{\sim} N(\Psi(P_0), \operatorname{Var}(\phi(P_0))/n).$$

The estimator behaves asymptotically as an average of the influence function.<sup>5</sup>

<sup>&</sup>lt;sup>5</sup>One may also note that the efficient influence curve characterizes the estimator with the smallest variance.

An estimator  $\hat{\psi}_n$  is asymptotically linear if,

$$\sqrt{n}(\hat{\psi}_n - \Psi(P_0)) = \sqrt{n} \mathbb{P}_n \phi^*(P_0) + o_P(1). \quad (*)$$

$$\Psi(\hat{P}_{n}^{*}) - \Psi(P_{0}) = (\hat{P}_{n}^{*} - P_{0})\phi^{*}(\hat{P}_{n}^{*}) + R_{2}(\hat{P}_{n}^{*}, P_{0})$$

$$(*3)$$

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$$\Psi(\hat{P}_n^*) - \Psi(P_0) = (\hat{P}_n^* - P_0)\phi^*(\hat{P}_n^*) + R_2(\hat{P}_n^*, P_0)$$
$$= -P_0\phi^*(\hat{P}_n^*) + R_2(P_0, \hat{P}_n^*)$$

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An estimator  $\hat{\psi}_n$  is asymptotically linear if,  $\sqrt{n}(\hat{\psi}_n - \Psi(P_0)) = \sqrt{n} \, \mathbb{P}_n \phi^*(P_0) + o_P(1). \quad (*)$ 

Evaluating the von Mises expansion in an estimator  $\hat{P}_n^*$  and the true data-generating  $P_0$ :

$$\Psi(\hat{P}_{n}^{*}) - \Psi(P_{0}) = (\hat{P}_{n}^{*} - P_{0})\phi^{*}(\hat{P}_{n}^{*}) + R_{2}(\hat{P}_{n}^{*}, P_{0})$$

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$$+ R_{2}(\hat{P}_{n}^{*}, P_{0})$$

$$- \mathbb{P}_{n}\phi^{*}(\hat{P}_{n}^{*})$$
(\*3)

i.e., need (\*1)–(\*3) to be  $o_P(n^{-1/2})$ .

An estimator 
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$$\sqrt{n}(\hat{\psi}_n - \Psi(P_0)) = \sqrt{n} \, \mathbb{P}_n \phi^*(P_0) + o_P(1). \quad (*)$$

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+ (\mathbb{P}_{n} - P_{0})(\phi^{*}(\hat{P}_{n}^{*}) - \phi^{*}(P_{0})) (*1) 
+ R_{2}(\hat{P}_{n}^{*}, P_{0}) (*2) 
- \mathbb{P}_{n}\phi^{*}(\hat{P}_{n}^{*}) (*3)$$

- (\*1) is an empirical process term.
- (\*2) second-order bias term.
- (\*3) is called the efficient influence curve equation.

- ... about the empirical process term (\*1):
  - 1. can be handled by empirical process theory, if  $(\phi^*(P): P \in \mathcal{M})$  is assumed Donsker.<sup>6</sup>
  - 2. otherwise can handled by extra sample splitting.

<sup>&</sup>lt;sup>6</sup>Lemma 19.24 of van der Vaart, A. W. (2000): Asymptotic statistics yields then that  $(\mathbb{P}_n - P_0)(\phi^*(\hat{P}_n) - \phi^*(P_0)) = o_P(n^{-1/2})$ .

Side note: Usually, we will assume the Donsker class condition.

- this is a way of nonparametrically characterizing the complexity of nuisance parameters.
- classes of functions that are Donsker: Indicator functions, bounded monotone functions, Lipschitz parametric functions, smooth functions, . . .

Donsker classes also include traditional parametric functions.

We will not discuss this further. For a nice intro see Sections 4.2 and 4.3 of Kennedy, E. H. (2016): Semiparametric theory and empirical processes in causal inference.

# Estimator expansion

That is it.

# Estimator expansion

#### That is it.

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

### Construction of estimators

$$\Psi(\hat{P}_{n}) - \Psi(P_{0}) = \mathbb{P}_{n}\phi^{*}(P_{0}) + o_{P}(n^{-1/2}) + R(\hat{P}_{n}, P_{0}) - \mathbb{P}_{n}\phi^{*}(\hat{P}_{n})$$

For a given target parameter  $\Psi : \mathcal{M} \to \mathbb{R}$ , we need to

- 1. Know the efficient influence curve, so that we can solve the efficient influence curve equation.
- 2. Analyze the remainder  $R(P, P_0) := \Psi(P) \Psi(P_0) + P_0 \phi^*(P)$ .

NB: These are solely properties of the estimation problem, but also tell us how to construct estimators such as TMLE.

# Example: ATE estimation

# 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:

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

# EXAMPLE: Average treatment effect (ATE)

1. The efficient influence function:

$$\phi^{*}(P)(O) = \tilde{\phi}^{*}(f,\pi)(O)$$

$$= \left(\frac{A}{\pi(A \mid X)} - \frac{1 - A}{\pi(A \mid X)}\right) (Y - f(A,X)) + f(1,X) - f(0,X) - \Psi(P)$$

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2. The remainder:

$$\begin{split} R(P,P_0) &= \tilde{R}(f,\pi,f_0,\pi_0) \\ &= \int_{\mathbb{R}^d} \sum_{a=0,1} (2a-1) \frac{\pi_0(a\mid x) - \pi(a\mid x)}{\pi(a\mid x)} \big( f_0(a,x) - f(a,x) \big) d\mu_{0,X}(x) \end{split}$$

$$f(A,X) = \mathbb{E}_{P}[Y \mid A,X], \ \pi(A \mid X) = P(A = a \mid X)$$
  
$$f_{0}(A,X) = \mathbb{E}_{P_{0}}[Y \mid A,X], \ \pi_{0}(A \mid X) = P(A = a \mid X)$$

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

2. Deriving the remainder for the ATE:

$$R(P, P_{0}) = \mathbb{E}_{P}[f(1, X) - f(0, X)] - \mathbb{E}_{P_{0}}[f_{0}(1, X) - f_{0}(0, X)]$$

$$+ \mathbb{E}_{P_{0}}\left[\left(\frac{A}{\pi(A \mid X)} - \frac{1 - A}{\pi(A \mid X)}\right)(Y - f(A, X))\right]$$

$$+ \mathbb{E}_{P_{0}}[f(1, X) - f(0, X)] - \Psi(P)$$

$$\stackrel{*}{=} \int_{\mathbb{R}^{d}} \sum_{a=0,1} (2a - 1)\left(\frac{\pi_{0}(a \mid x)}{\pi(a \mid x)} - 1\right)(f_{0}(a, x) - f(a, x))d\mu_{0, X}(x)$$

$$= \int_{\mathbb{R}^{d}} \sum_{a=0,1} (2a - 1)\frac{\pi_{0}(a \mid x) - \pi(a \mid x)}{\pi(a \mid x)}(f_{0}(a, x) - f(a, x))d\mu_{0, X}(x)$$

the equality marked by \* is detailed on the next slide.

We used that:

$$\mathbb{E}_{P_{0}}\left[\left(\frac{A}{\pi(A\mid X)} - \frac{1-A}{\pi(A\mid X)}\right)(Y - f(A, X))\right]$$

$$= \mathbb{E}_{P_{0}}\left[\frac{2A - 1}{\pi(A\mid X)}(Y - f(A, X))\right]$$

$$= \mathbb{E}_{P_{0}}\left[\mathbb{E}_{P_{0}}\left[\frac{2A - 1}{\pi(A\mid X)}(Y - f(A, X))\middle|A, X\right]\right]$$

$$= \mathbb{E}_{P_{0}}\left[\frac{2A - 1}{\pi(A\mid X)}(f_{0}(A, X) - f(A, X))\right]$$

$$= \int_{\mathbb{R}^{d}} \sum_{a=0,1} \frac{2a - 1}{\pi(a\mid x)}(f_{0}(a, x) - f(a, x))\pi_{0}(a\mid x)d\mu_{0, X}(x)$$

$$= \int_{\mathbb{R}^{d}} \sum_{a=0,1} (2a - 1)\frac{\pi_{0}(a\mid x)}{\pi(a\mid x)}(f_{0}(a, x) - f(a, x))d\mu_{0, X}(x)$$

The remainder determines the asymptotic bias.

For the ATE, the remainder has a really nice structure!

$$R(P, P_0) = \tilde{R}(f, \pi, f_0, \pi_0)$$

$$= \int_{\mathbb{R}^d} \sum_{a=0,1} (2a-1) \frac{\pi_0(a \mid x) - \pi(a \mid x)}{\pi(a \mid x)} (f_0(a, x) - f(a, x)) d\mu_{0,X}(x)$$

A "double robust" structure, which has some important implications.

$$|R(P, P_0)| = |\tilde{R}(f, \pi, f_0, \pi_0)|$$

$$\leq \sum_{a=0}^{\infty} \int_{\mathbb{R}^d} \frac{|\pi_0(a \mid x) - \pi(a \mid x)|}{\pi(a \mid x)} |f_0(a, x) - f(a, x)| d\mu_{0, X}(x)$$

$$|R(P, P_{0})| = |\tilde{R}(f, \pi, f_{0}, \pi_{0})|$$

$$\leq \sum_{a=0,1} \int_{\mathbb{R}^{d}} \frac{|\pi_{0}(a \mid x) - \pi(a \mid x)|}{\pi(a \mid x)} |f_{0}(a, x) - f(a, x)| d\mu_{0, X}(x)$$

$$\stackrel{*}{\leq} \sum_{a=0,1} \frac{1}{\pi(a \mid x)} \sqrt{\int_{\mathbb{R}^{d}} \left\{ \pi_{0}(a \mid x) - \pi(a \mid x) \right\}^{2} d\mu_{0, X}(x)}$$

$$\times \sqrt{\int_{\mathbb{R}^{d}} \left\{ f_{0}(a, x) - f(a, x) \right\}^{2} d\mu_{0, X}(x)}$$

$$|R(P, P_{0})| = |\tilde{R}(f, \pi, f_{0}, \pi_{0})|$$

$$\leq \sum_{a=0,1} \int_{\mathbb{R}^{d}} \frac{|\pi_{0}(a \mid x) - \pi(a \mid x)|}{\pi(a \mid x)} |f_{0}(a, x) - f(a, x)| d\mu_{0, X}(x)$$

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$$\times \sqrt{\int_{\mathbb{R}^{d}} \left\{ f_{0}(a, x) - f(a, x) \right\}^{2} d\mu_{0, X}(x)}$$

Thus, if  $\pi(a|X) > \delta > 0$  a.s., then:

$$|\tilde{R}(\hat{f}_{n}^{*}, \hat{\pi}_{n}, f_{0}, \pi_{0})| \leq \sum_{a=0.1} \delta^{-1} \|\pi_{0}(a \mid \cdot) - \hat{\pi}_{n}(a \mid \cdot)\|_{\mu_{0}} \|f_{0}(a \mid \cdot) - \hat{f}_{n}(a \mid \cdot)\|_{\mu_{0}}$$

# What does this imply for estimation?

### Double robustness in consistency

$$\begin{split} |\tilde{R}(\hat{f}_{n}^{*},\hat{\pi}_{n},f_{0},\pi_{0})| &\leq \sum_{a=0,1} \delta^{-1} \underbrace{\|\pi_{0}(a\mid\cdot) - \hat{\pi}_{n}(a\mid\cdot)\|_{\mu_{0}}}_{o_{P}(1), \text{ or }} \underbrace{\|f_{0}(a\mid\cdot) - \hat{f}_{n}^{*}(a\mid\cdot)\|_{\mu_{0}}}_{o_{P}(1)} \end{split}$$
 then  $\tilde{\Psi}(\hat{f}_{n}^{*}) - \tilde{\Psi}(f_{0}) = o_{P}(1)$ .

### Asymptotic linearity (easier to establish due to double robust structure)

$$\begin{split} |\tilde{R}(\hat{f}_n^*,\hat{\pi}_n,f_0,\pi_0)| &\leq \sum_{a=0,1} \delta^{-1} \underbrace{\|\pi_0(a\,|\,\cdot) - \hat{\pi}_n(a\,|\,\cdot)\|_{\mu_0}}_{=o_P(n^{-1/4})} \underbrace{\|f_0(a\,|\,\cdot) - \hat{f}_n^*(a\,|\,\cdot)\|_{\mu_0}}_{=o_P(n^{-1/4})} \end{split}$$
 i.e., 
$$\tilde{R}(\hat{f}_n^*,\hat{\pi}_n,f_0,\pi_0) = o_P(n^{-1/2}).$$

I.e., bias is converging at fast enough rate for reliable confidence intervals.

Side note: Showing the double robustness in consistency . . .

Say we have estimators  $(\hat{f}_n^*, \hat{\pi}_n)$ ;

- converging to  $(f, \pi)$
- solving the efficient influence curve equation.

Per definition,  $\tilde{R}(\hat{f}_n^*,\hat{\pi}_n,f_0,\pi_0) = \tilde{\Psi}(\hat{f}_n^*) - \tilde{\Psi}(f_0) + P_0\tilde{\phi}^*(\hat{f}_n^*,\hat{\pi}_n).$ 

i.e., 
$$\tilde{\Psi}(\hat{f}_n^*) - \tilde{\Psi}(f_0) = -P_0 \tilde{\phi}^* (\hat{f}_n^*, \hat{\pi}_n) + \tilde{R}(\hat{f}_n^*, \hat{\pi}_n, f_0, \pi_0)$$
$$= (\mathbb{P}_n - P_0) \phi^* (\hat{f}_n^*, \hat{\pi}_n) + \tilde{R}(\hat{f}_n^*, \hat{\pi}_n, f_0, \pi_0)$$

The first term is an empirical process term which equals  $(\mathbb{P}_n - P_0)\tilde{\phi}^*(f,\pi)$  plus an  $o_P(n^{-1/2})$ -term.

This then gives

$$\tilde{\Psi}(\hat{f}_n^*) - \tilde{\Psi}(f_0) = \underbrace{(\mathbb{P}_n - P_0)\tilde{\phi}^*(f, \pi)}_{\text{ILN applies}} + \tilde{R}(\hat{f}_n^*, \hat{\pi}_n, f_0, \pi_0) + o_P(n^{-1/2})$$

which yields that  $\tilde{\Psi}(\hat{f}_n^*) - \tilde{\Psi}(f_0) = o_P(1)$  if  $\tilde{R}(\hat{f}_n^*, \hat{\pi}_n, f_0, \pi_0) = o_P(1)$ .

# Analysis of a concrete estimation problem

# EXAMPLE: Average treatment effect (ATE)

1. The efficient influence function:

$$\phi^{*}(P)(O) = \tilde{\phi}^{*}(f,\pi)(O)$$

$$= \left(\frac{A}{\pi(A|X)} - \frac{1-A}{\pi(A|X)}\right) (Y - f(A,X)) + f(1,X) - f(0,X) - \Psi(P)$$

2. The remainder:

$$R(P, P_0) = \tilde{R}(f, \pi, f_0, \pi_0)$$

$$= \int_{\mathbb{R}^d} \sum_{a=0}^{\infty} (2a - 1) \frac{\pi_0(a \mid x) - \pi(a \mid x)}{\pi(a \mid x)} (f_0(a, x) - f(a, x)) d\mu_{0, X}(x)$$

Deriving these is done once for a given target parameter  $\Psi: \mathcal{M} \to \mathbb{R}$ .

# TMLE as an estimation procedure

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

#### TMLE is a two-step procedure:

- Step 1 Construct initial estimator  $\hat{P}_n$  for P such that  $R(\hat{P}_n, P_0) = o_P(n^{-1/2})$ .
- Step 2 Update the estimator  $\hat{P}_n \mapsto \hat{P}_n^*$  such that  $\hat{P}_n^*$  solves the efficient influence curve equation.<sup>7</sup>

<sup>&</sup>lt;sup>7</sup>TMLE and the estimating equation estimator both solve the efficient influence curve equation . . . that is why they have the same asymptotic (large-sample) properties.

# **TMLE**

- ▶ The role of the targeting step (Step 2):
  - Gaining double robustness in consistency.
  - Easier to get 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.

In this exercise we continue the simulation setting of Practical 1. Now we want to explore —  $\,$ 

- 1. Inference for estimators based on the efficient influence curve;
  - ► TMLE:
  - Estimating equation (EE) estimator;
- 2. Variance estimation and coverage of confidence intervals;
- 3. Small-sample properties, particularly under positivity violations.

This is described in detail in: day1-practical2.pdf.

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- there may be small-sample differences in performance (often argued in favor of TMLE);
- otherwise, the differences are not so important for the ATE estimation problem. BUT, for other problems (e.g., in survival analysis), the substitution property of TMLE may be crucial!
- also, the ideas of TMLE, and targeting, extend in various important (technical) directions, where estimating equations estimators do not.