Ensemble Learning Targeted Maximum Likelihood Estimation for Stata Users

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https://github.com/migariane/SUGML

2022 Spanish Stata Conference

October 20, 2022

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Causal Inference Tutorial

Link to the tutorial

https://onlinelibrary.wiley.com/doi/10.1002/sim.9234?af=R

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https://github.com/migariane/TutorialComputationalCausalInferenceEstimators

Notation and definitions

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Syntax eltmle Stata command

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Stata Implementation: overall structure

```
capture program drop eltmle
program define eltmle
         syntax varlist(min=3) [if] [pw] [, tmle tmlebgam tmleglsrf bal]
         version 13.2
         foreach v of var * {
         qui drop if missing(`v')
          }
         qui export delimited using "fulldata.csv", nolabel replace
         marksample touse
         local var `varlist' if `touse'
         tokenize `var'
         local yvar = "`1'"
         global flag = cond(`yvar'<=1,1,0)
         qui sum `yvar'
         global b = `r(max)'
         global a = `r(min)'
         qui replace `yvar' = (`yvar' - `r(min)') / (`r(max)' - `r(min)') if `yvar'>1
         local dir `c(pwd)'
         cd "`dir'"
         tempfile data
         qui save "`data'.dta", replace
         qui export delimited `var' using "data.csv", nolabel replace

         if "`tmlebgam'" == "" & "`tmleglsrf'" == "" & "`bal'" == ""{
                tmle `varlist'
                }
         else if "`tmle'" == "tmle" & "`bal'" == "bal" {
                tmlebal `varlist'
                }
         else if "`tmlebgam'" == "tmlebgam" & "`bal'" == "bal" {
                tmlebgambal `varlist'
                }
         else if "`tmleglsrf'" == "tmleglsrf" & "`bal'" == "bal" {
                tmleglsrfbal `varlist'
                }
         else if "`tmlebgam'" == "tmlebgam" {
                tmlebgam `varlist'
                }
         else if "`tmleglsrf'" == "tmleglsrf" {
                tmleglsrf `varlist'
                }
```

Stata Implementation: R code for calling the SL

```
program tmle
// Write R Code dependencies: foreign Surperlearner
set more off
qui: file close _all
qui: file open rcode using SLS.R, write replace
qui: file write rcode ///
        `"set.seed(123)"' _newline ///
        `"list.of.packages <- c("foreign","SuperLearner")"' _newline ///
        `"new.packages <- list.of.packages[!(list.of.packages %in% installed.packages()[,"Package"])]"' _newline ///
        `"if(length(new.packages)) install.packages(new.packages, repos='http://cran.us.r-project.org')"' _newline ///
        `"library(SuperLearner)"' _newline ///
        `"library(foreign)"' _newline ///
        `"data <- read.csv("data.csv", sep=",")"' _newline ///
        `"attach(data)"' _newline ///
        `"SL.library <- c("SL.glm","SL.step","SL.glm.interaction")"' _newline ///
        `"n <- nrow(data)"' _newline ///
        `"nvar <- dim(data)[[2]]"' _newline ///
        `"Y <- data[,1]"' _newline ///
        `"A <- data[,2]"' _newline ///
        `"X <- data[,2:nvar]"' _newline ///
        `"W <- data[,3:nvar]"' _newline ///
        `"X1 <- X0 <- X"' _newline ///
        `"X1[,1] <- 1"' _newline ///
        `"X0[,1] <- 0"' _newline ///
        `"newdata <- rbind(X,X1,X0)"' _newline ///
        `"Q <- try(SuperLearner(Y = data[,1] ,X = X, SL.library=SL.library, family=binomial(), newX=newdata, method="met
        `"Q <- as.data.frame(Q[[4]])"' _newline ///
        `"QAW <- Q[1:n,]"' _newline ///
        `"Q1W <- Q[((n+1):(2*n)),]"' _newline ///
        `"Q0W <- Q[((2*n+1):(3*n)),]"' _newline ///
        `"g <- suppressWarnings(SuperLearner(Y = data[,2], X = W, SL.library = SL.library, family = binomial(), method =
        `"ps <- g[[4]]"' _newline ///
        `"ps[ps<0.025] <- 0.025"' _newline ///
        `"ps[ps>0.975] <- 0.975"' _newline ///
        `"data <- cbind(data,QAW,Q1W,Q0W,ps,Y,A)"' _newline ///
        `"write.dta(data, "data2.dta")"'
qui: file close rcode
```

Stata Implementation: Batch file executing R

```
qui: file close rcode

// Write bacth file to find R.exe path and R version
set more off
qui: file close _all
qui: file open bat using setup.bat, write replace
qui: file write bat ///
`"@echo off"' _newline ///
`"SET PATHROOT=C:\Program Files\R\"' _newline ///
`"echo Locating path of R..."' _newline ///
`"echo."' _newline ///
`"if not exist "%PATHROOT%" goto:NO_R"' _newline ///
`"for /f "delims=" %%r in (' dir /b "%PATHROOT%R*" ') do ("' _newline ///
        `"echo Found %%r"' _newline ///
        `"echo shell "%PATHROOT%%%r\bin\x64\R.exe" CMD BATCH SLS.R > runr.do"' _newline ///
        `"echo All set!"' _newline ///
        `"goto:DONE"' _newline ///
`")"' _newline ///
`":NO_R"' _newline ///
`"echo R is not installed in your system."' _newline ///
`"echo."' _newline ///
`"echo Download it from https://cran.r-project.org/bin/windows/base/"' _newline ///
`"echo Install it and re-run this script"' _newline ///
`":DONE"' _newline ///
`"echo."' _newline ///
`"pause"'
qui: file close bat

//Run batch
shell setup.bat
//Run R
do runr.do

// Read Revised Data Back to Stata
clear
quietly: use "data2.dta", clear

// Q to logit scale
gen logQAW = log(QAW / (1 - QAW))
gen logQ1W = log(Q1W / (1 - Q1W))
gen logQ0W = log(Q0W / (1 - Q0W))

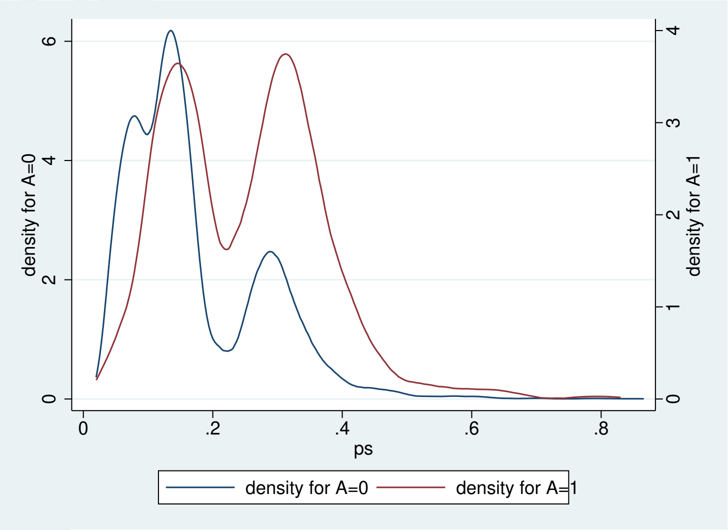
// Clever covariate HAW
```

Output for continuous outcome

```
.use http://www.stata-press.com/data/r14/cattaneo2.dta
.eltmle bweight mbsmoke mage medu prenatal mmarried, tmle
    Variable |        Obs        Mean    Std. dev.       Min        Max
-------------+---------------------------------------------------------
        POM1 |      4,642     2832.69     74.9141   2550.819   2968.504
        POM0 |      4,642    3062.695    91.22898   2844.977   3177.975
          ps |      4,642    .1861267    .1106222   .0377472   .8479414
--------------------------------
TMLE: Average Treatment Effect
--------------------------------
ATE:      | -230.0
SE:       |   24.5
P-value:  | 0.0000
95%CI:    | -277.9, -182.1
--------------------------------
-----------------------------
TMLE: Causal Risk Ratio (CRR)
-----------------------------
CRR: 0.93; 95%CI:(0.91, 0.94)
-----------------------------
-------------------------------
TMLE: Marginal Odds Ratio (MOR)
-------------------------------
MOR: 0.83; 95%CI:(0.80, 0.87)
-------------------------------
```

Output for continuous outcome and balance option

.eltmle bweight mbsmoke mage medu prenatal mmarried, tmle **bal**



Simulations comparing Stata ELTMLE vs R-TMLE

```
. mean psi aipw slaipw tmle
  Mean estimation
  Number of obs    =  1,000
  -------------------------
               |    Mean
  -------------+-----------
          True |    .173
          aipw |    .170
        slaipw |    .170
    Stata-tmle |    .170
  -------------------------
        R-TMLE |    .170
  -------------------------
```

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ONLINE open free tutorial

Link to the tutorial

https://migariane.github.io/TMLE.nb.html

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Stata Implementation: source code

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https://github.com/migariane/eltmle

Stata installation and step by step commented syntax

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Stata installation and step by step commented syntax

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github install migariane/eltmle
which eltmle
viewsource eltmle.ado
```

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One sample simulation: TMLE reduces bias

https://github.com/migariane/SUGML

eltmle

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Statistics in Medicine tutorial: TMLE

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- Keep original data and allow options to get some causal inference computed data and scalars.

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Thank YOU

THANK YOU FOR YOUR TIME

Background: Potential Outcomes framework

Rubin and Heckman

- This framework was developed first by statisticians (Rubin, 1983) and econometricians (Heckman, 1978) as a new approach for the estimation of **causal effects** from observational data.
- We will keep separate the **causal framework** (a conceptual issue briefly introduce here) and the **"how to estimate causal effects"** (an statistical issue also introduced here)

Causal effects with OBSERVATIONAL data

ASSUMPTIONS for Identification

- Rosebaum & Rubin, 1983: **The Ignorable Treatment Assignment** (A.K.A Ignorability, Unconfoundeness or Conditional Mean Independence).
- **POSITIVITY**.
- **SUTVA**.

Causal effect with OBSERVATIONAL data

IGNORABILITY

$$(Y_i(1), Y_i(0)) \perp A_i \mid W_i$$

POSITIVITY

POSITIVITY: $P(A = a \mid W) > 0$ for all a, W

SUTVA

- We have assumed that there is only on version of the treatment (**consistency**) **Y(1)** if **A = 1** and **Y(0)** if **A = 0**.
- The assignment to the treatment to one unit doesn't affect the outcome of another unit (**no interference**) or **IID** random variables.
- The model used to estimate the assignment probability has to **be correctly specified**.

Causal effect

Potential Outcomes

We only observe:

$$Y_i(1) = Y_i(A = 1) \text{ and } Y_i(0) = Y_i(A = 0)$$

However we would like to know what would have happened if:

Treated $Y_i(1)$ would have been non-treated $Y_i(A = 0) = Y_i(0)$.

Controls $Y_i(0)$ would have been treated $\mathbf{Y_i(A = 1) = Y_i(1)}$.

Identifiability

- How we can identify the effect of the potential outcomes $\mathbf{Y}^a$ if they are not observed?
- How we can estimate the expected difference between the potential outcomes **E[Y(1) - Y(0)]**, namely the **ATE**.

G-Formula for the **identification** of the ATE with observational data

$$E(Y^a) = \sum_y E(Y^a \mid W = w)P(W = w)$$
$$= \sum_y E(Y^a \mid A = a, W = w)P(W = w) \text{ by consistency}$$
$$= \sum_y E(Y = y \mid A = a, W = w)P(W = w) \text{ by ignorability}$$

The **ATE**=

$$\sum_{\mathbf{w}} \left[\sum_{\mathbf{y}} \mathbf{P(Y = y \mid A = 1, W = w)} - \sum_{\mathbf{y}} \mathbf{P(Y = y \mid A = 0, W = w)} \right] \mathbf{P(W = w)}$$

$$P(W = w) = \sum_{y,a} P(W = w, A = a, Y = y)$$

G-Formula, (Robins, 1986)

G-Formula for the identification of the ATE with observational data

The **ATE**=

$$\sum_{\mathbf{w}} \left[\sum_{\mathbf{y}} \mathbf{P}(\mathbf{Y} = \mathbf{y} \mid \mathbf{A} = \mathbf{1}, \mathbf{W} = \mathbf{w}) - \sum_{\mathbf{y}} \mathbf{P}(\mathbf{Y} = \mathbf{y} \mid \mathbf{A} = \mathbf{0}, \mathbf{W} = \mathbf{w}) \right] \mathbf{P}(\mathbf{W} = \mathbf{w})$$

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G-Formula

- The sums is generic notation. In reality, likely involves sums and integrals (we are just integrating out the W's).
- The **g-formula** is a **generalization of standardization** and allow to estimate unbiased treatment effect estimates.

RA

Regression-adjustment

$$\widehat{ATE}_{RA} = N^{-1}\sum_{i=1}^{N}[E(Y_i \mid A = 1, W_i) - E(Y_i \mid A = 0, W_i)]$$

$$m_A(w_i) = E(Y_i \mid A_i = A, W_i)$$

$$\widehat{ATE}_{RA} = N^{-1}\sum_{i=1}^{N}[\hat{m}_1(w_i) - \hat{m}_0(w_i)]$$

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IPTW (Inverse probability treatment weighting)

Survey theory (Horvitz-Thompson)

$$\hat{P}_i = E(A_i \mid W_i) \text{ ; So , } \frac{\mathbf{1}}{\hat{\mathbf{p}}_\mathbf{i}} \text{ , if A = 1 and , } \frac{\mathbf{1}}{(\mathbf{1} - \hat{\mathbf{p}}_\mathbf{i})} \text{ , if A = 0}$$

over the total number of individuals

$$\widehat{ATE}_{IPTW} = N^{-1} \sum_{i=1}^{N} \frac{A_i Y_i}{\hat{p}_i} - N^{-1} \sum_{i=1}^{N} \frac{(1 - A_i) Y_i}{(1 - \hat{p}_i)}$$

AIPTW

AIPTW (Augmented Inverse probability treatment weighting)

Solving Estimating Equations

$$\widehat{ATE}_{AIPTW} =$$

$$N^{-1}\sum_{i=1}^{N}[(Y(1) \mid A_i = 1, W_i) - (Y(0) \mid A_i = 0, W_i)] +$$

$$N^{-1}\sum_{i=1}^{N}\left(\frac{(A_i = 1)}{P(A_i = 1 \mid W_i)} - \frac{(A_i = 0)}{P(A_i = 0 \mid W_i)}\right)[Y_i - E(Y \mid A_i, W_i)]$$

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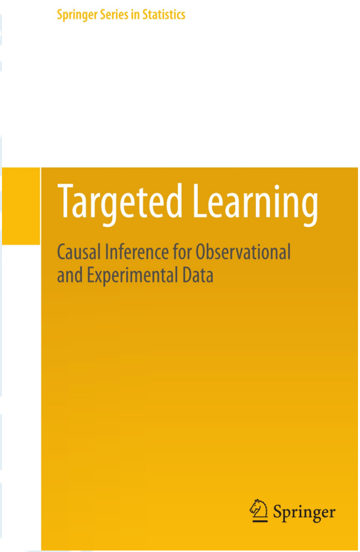
Targeted learning



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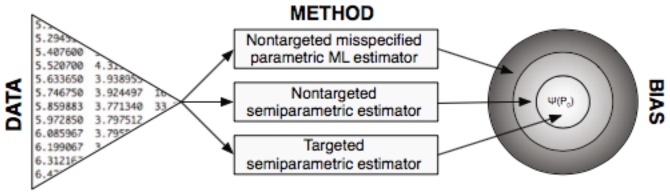
Why Targeted learning?



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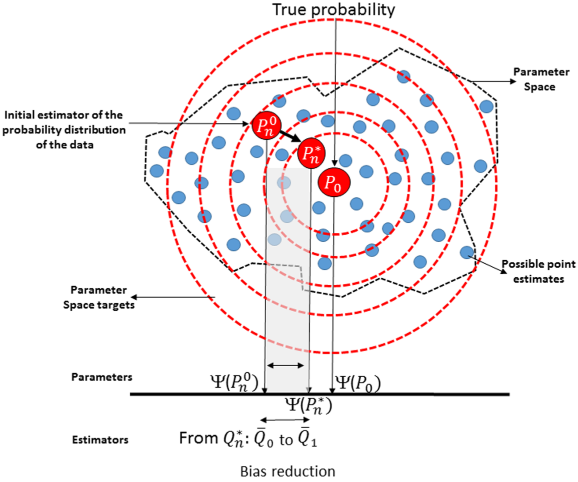
MC simulations: Luque-Fernandez et al, 2017 (in press, American Journal of Epidemiology)

	ATE		BIAS (%)		RMSE		95%CI coverage (%)	
	N=1,000	N=10,000	N=1,000	N=10,000	N=1,000	N=10,000	N=1,000	N=10,000
First scenario* (correctly specified models)								
True ATE	**-0.1813**							
Naïve	-0.2234	-0.2218	23.2	22.3	0.0575	0.0423	77	89
AIPTW	-0.1843	-0.1848	1.6	1.9	0.0534	0.0180	93	94
IPTW-RA	-0.1831	-0.1838	1.0	1.4	0.0500	0.0174	91	95
TMLE	-0.1832	-0.1821	1.0	**0.4**	0.0482	0.0158	**95**	**95**
Second scenario ** (misspecified models)								
True ATE	**-0.1172**							
Naïve	-0.0127	-0.0121	89.2	89.7	0.1470	0.1100	0	0
BFit AIPTW	-0.1155	-0.0920	1.5	**11.7**	0.0928	0.0773	65	65
BFit IPTW-RA	-0.1268	-0.1192	8.2	**1.7**	0.0442	0.0305	52	73
TMLE	-0.1181	-0.1177	**0.8**	**0.4**	0.0281	0.0107	**93**	**95**

*First scenario : correctly specified models and near-positivity violation

**Second scenario: misspecification, near-positivity violation and adaptive model selection

TMLE ROAD MAP



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Targeted estimate of the ATE from $\Psi^{(0)}$ to $\Psi^{(1)}$: ($\widehat{\Psi}$)

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$$\mathbf{IC} = \left(\frac{(A_i = 1)}{P(A_i = 1 \mid W_i)} - \frac{(A_i = 0)}{P(A_i = 0 \mid W_i)} \right) [Y_i - E_1(Y \mid A_i, W_i)] + [E_1(Y(1) \mid A_i = 1, W_i) - E_1(Y(0) \mid A_i = 0, W_i)] - \psi$$

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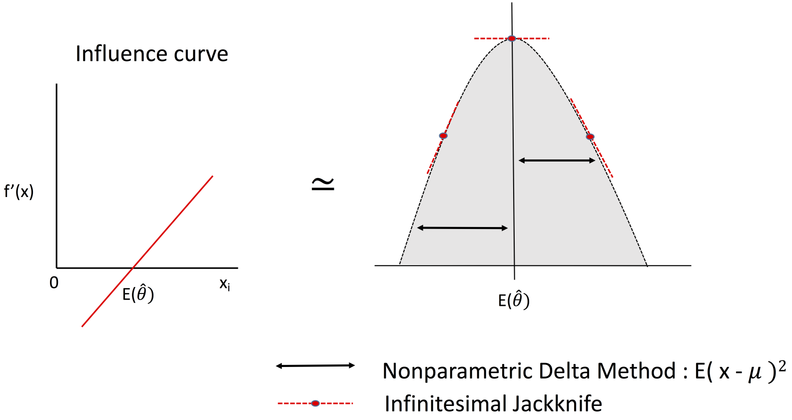
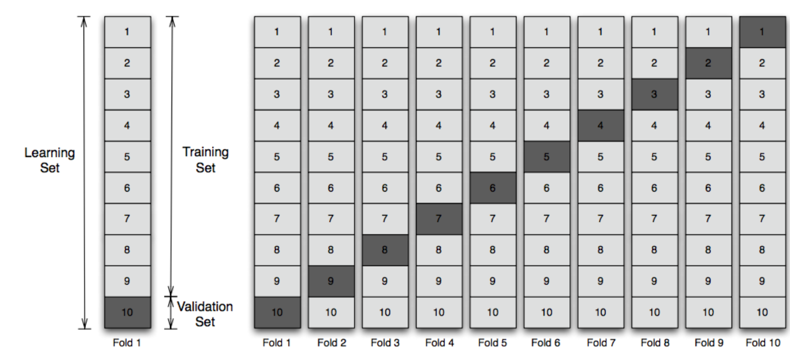
IC: Geometric interpretation



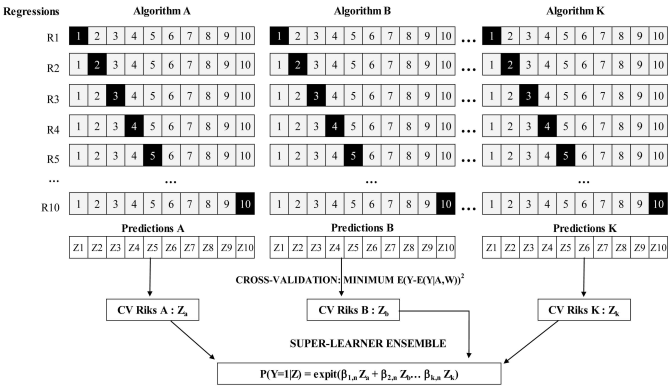
Estimate of the ψ Standard Error using the efficient Influence Curve.
Image credit: Miguel Angel Luque-Fernandez

Targeted learning



Source: Mark van der Laan and Sherri Rose. Targeted learning: causal inference for observational and experimental data. Springer Series in Statistics, 2011.

Super-Learner: Ensemble learning



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Asymptotically, the final weighted combination of algorithms (Super Learner) performs as well as or better than the best-fitting algorithm (van der Laan, 2007).

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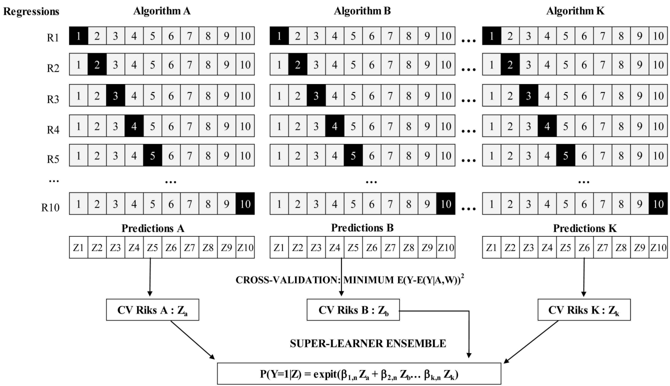

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M-ESTIMATORS: Semi-parametric and Empirical processes theory

An estimator is **asymptotically linear** with **influence function** φ **(IC)** if the estimator can be **approximate by an empirical average** in the sense that

$$(\hat{\theta} - \theta_0) = \frac{1}{n}\sum_{i=1}^{n}(IC) + Op(1/\sqrt{n})$$

(Bickel, 1997).

TMLE inference: Bickel (1993); Tsiatis (2007); Van der Laan (2011); Kennedy (2016)

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