

# Targeted Bayesian Learning for Causal Inference: The Best of Both Worlds?

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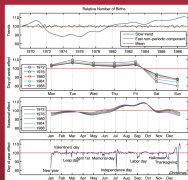
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# My background

- Framing: science as a social process (Kuhn, 1962)
  - Statistical cultures (Breiman, 2001) and causal inference cultures (Bonvini et al., 2021).
- PhD at UMass Amherst with Leontine Alkema – Bayesian modeling
- Doctoral and postdoc work with Antoine Chambaz (Université Paris Cité) – mathematical statistics, causal inference, non-parametric theory
- Current postdoc work with Iván Díaz (NYU Grossman School of Medicine)

## Bayesian Data Analysis

Third Edition



Andrew Gelman, John B. Carlin, Hal S. Stern,  
David B. Dunson, Aki Vehtari, and Donald B. Rubin

Springer Series in Statistics

Mark J. van der Laan  
Sherri Rose

## Targeted Learning

Causal Inference for Observational  
and Experimental Data

Springer

# Takeaways

- Targeted Maximum Likelihood Estimation (TMLE): frequentist method for estimating smooth finite-dimensional parameters in non-parametric models (van der Laan and Rose, 2011)
- Bayesian TMLE: (pseudo) Bayesian analogue of TMLE. (Díaz Muñoz et al., 2011).
- *This talk*: Bayesian TMLE + hierarchical modeling for estimating group-specific treatment effects.

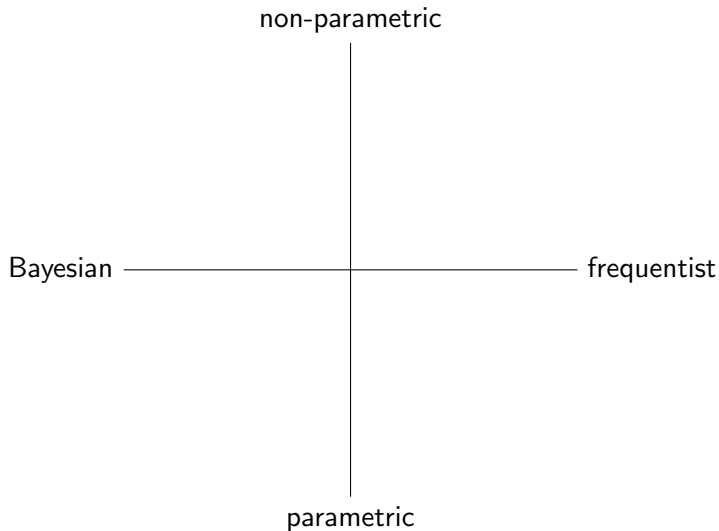
# Average Treatment Effect

- Suppose we observe  $n$  i.i.d. draws  $O_1, \dots, O_n$  of a variable  $O = (X, A, Y) \sim P_0$ .
  - $X$ : vector of covariates.
  - $A$ : binary treatment indicator.
  - $Y$ : binary outcome.
- We assume that  $P_0$  falls in the non-parametric model  $\mathcal{M}$ .
- For any  $P \in \mathcal{M}$ , define the *Average Treatment Effect* functional as

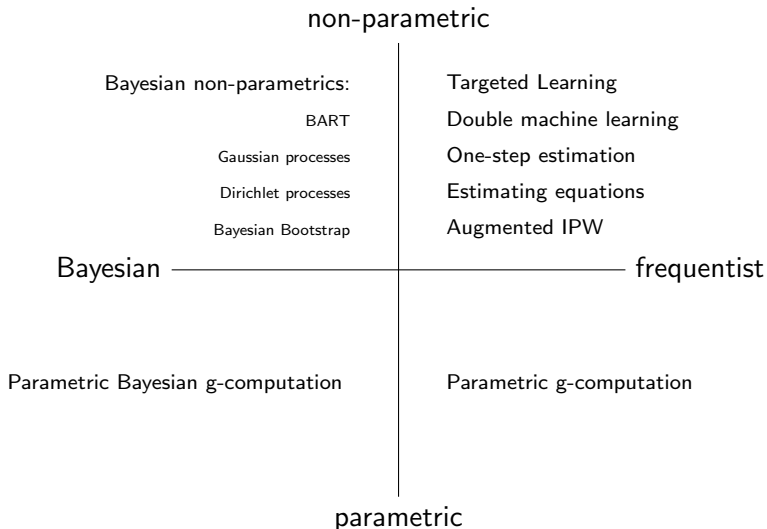
$$\psi(P) = E_P[E_P[Y|A=1, X] - E_P[Y|A=0, X]].$$

- Notation:
  - Marginal law of  $X$ :  $Q_P(X) = dP(X)$ .
  - Propensity score:  $g_P(A, X) = P(A|X)$ .
  - Outcome model:  $\mu_P(A, X) = E_P[Y|A, X]$ .

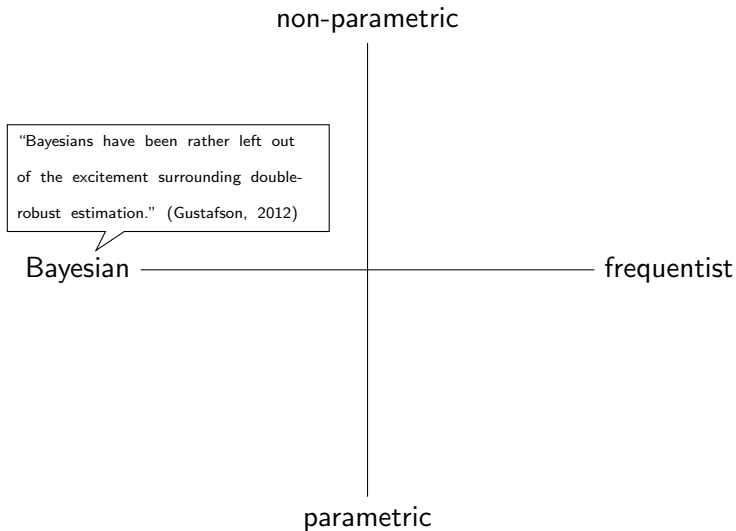
# A crude taxonomy



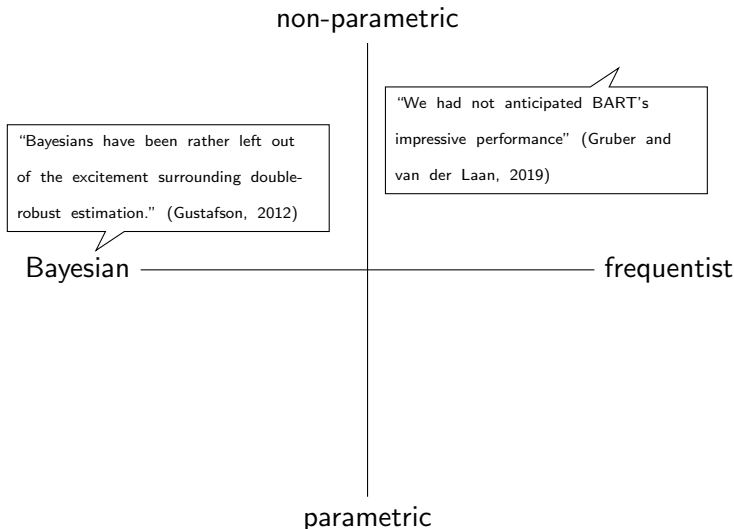
# A crude taxonomy



# A crude taxonomy

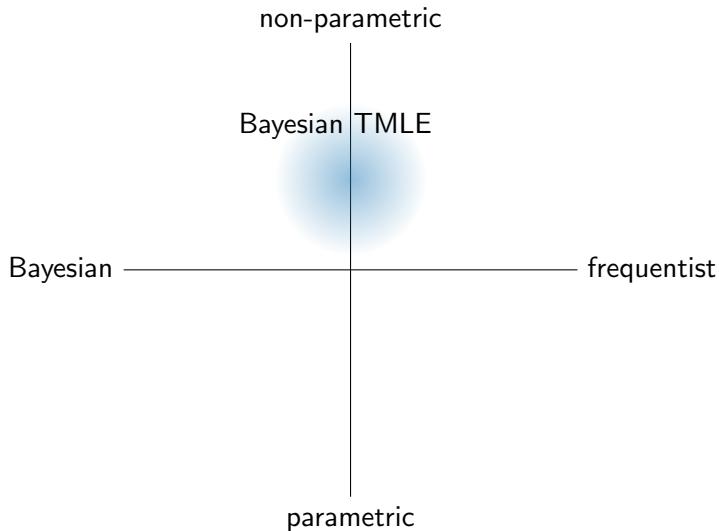


# A crude taxonomy

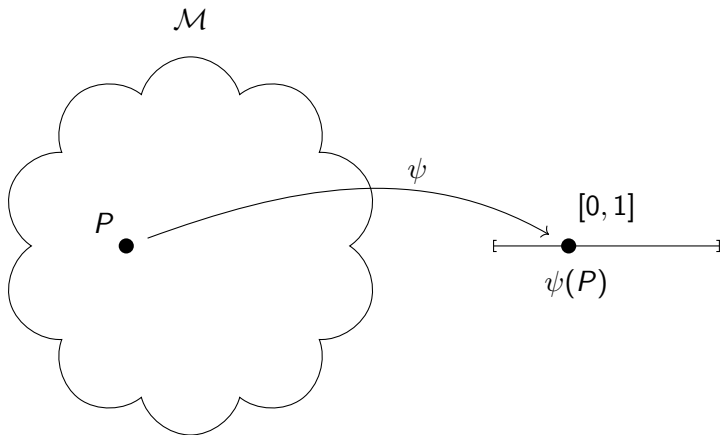




# A crude taxonomy



# Target parameter



(Warning: infinite dimensional space visualized in two dimensions!)

# Frequentist estimation of the ATE

- Any regular estimator  $\hat{\psi}_n$  of  $\psi(P_0)$  satisfies

$$\hat{\psi}_n = \psi(P_0) + \frac{1}{n} \sum_{i=1}^n \text{IF}(P_0)(O_i) + o_p(n^{-1/2}),$$

where  $\text{IF}(P_0) : \mathcal{O} \rightarrow \mathbb{R}$  is called an *influence function* of  $\psi$  at  $P_0$ .

- The influence function with the smallest variance is called the *efficient influence function* (EIF).
- The non-parametric efficiency bound for estimating  $\psi(P_0)$  is given by the variance of the efficient influence function:  $\text{Var}_{P_0}(\text{EIF}(P_0)(O))$ .
- A typical goal for frequentists is to propose an estimator that achieves the above efficiency bound.
- Classical references for semi-parametric efficiency theory: Bickel et al. (1993); van der Vaart and Wellner (1996). Excellent and accessible review: Kennedy (2023)

# Efficient influence function of the ATE

- Efficient influence function for the ATE,  $\text{EIF}(P)$ :

$$O \mapsto \frac{2A-1}{g_P(A, X)} (Y - \mu_P(A, X)) + \mu_P(1, X) - \mu_P(0, X) - \psi(P).$$

- The non-parametric efficiency bound for estimating  $\psi(P_0)$ :

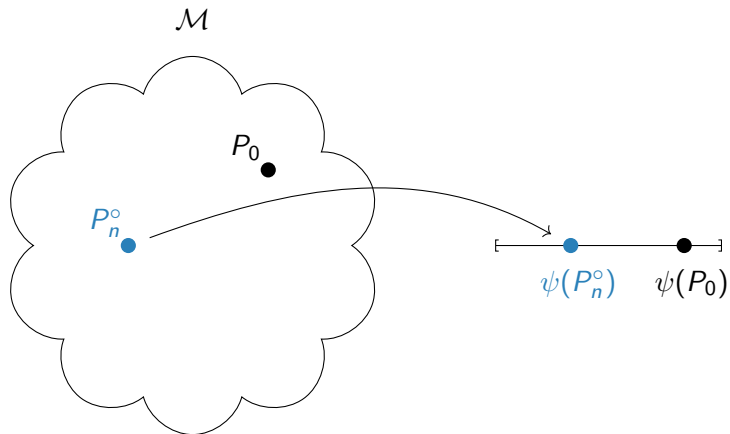
$$E_{P_0} \left[ \frac{\text{Var}_{P_0}(Y|A, X)}{g_{P_0}(A, X)^2} + (\mu_{P_0}(1, X) - \mu_{P_0}(0, X))^2 \right].$$

# Plug-in estimation

- Suppose we have an initial estimate  $P_n^\circ = \{\mu_n^\circ, Q_n^\circ\}$  of the parts of  $P_0$  relevant to  $\psi$ .
  - Covariate distribution  $Q_n^\circ$ : empirical distribution.
  - Outcome model  $\mu_n^\circ$ : logistic regression, machine learning algorithms, ...
- Form a plug-in estimator of  $\psi$ :

$$\begin{aligned}\hat{\psi}^{\text{plug-in}} &= \psi(P_n^\circ) \\ &= \frac{1}{n} \sum_{i=1}^n \mu_n^\circ(1, X_i) - \mu_n^\circ(0, X_i).\end{aligned}$$

# Plug-in estimation



# Analysis of plug-in estimator

- Apply expansion of the ATE (von Mises, 1947):

$$\psi(P_n^\circ) = \psi(P_0) + \frac{1}{n} \sum_{i=1}^n \text{IF}(P_n^\circ)(O_i) + R(P_n^\circ, P_0).$$

- Problems with plug-in estimator:
  - First-order bias term  $\frac{1}{n} \sum_{i=1}^n \text{IF}(P_n^\circ)(O_i)$  not necessarily zero.
  - Second-order remainder term  $R(P_n^\circ, P_0)$  doesn't necessarily converge to zero, or does so too slowly.

# Targeted Learning

- Many different ways to form unbiased and asymptotically efficient estimators of parameters like the ATE
  - e.g. double machine learning, one-step estimation, estimating equations, augmented IPW
- Frequentist analysis typically proceeds by showing how they make the first-order bias term disappear, and under which conditions the second-order remainder term is  $o_p(n^{-1/2})$ .
- We focus on *Targeted Maximum Likelihood Estimation* (TMLE) (van der Laan and Rubin, 2006; van der Laan and Rose, 2011).



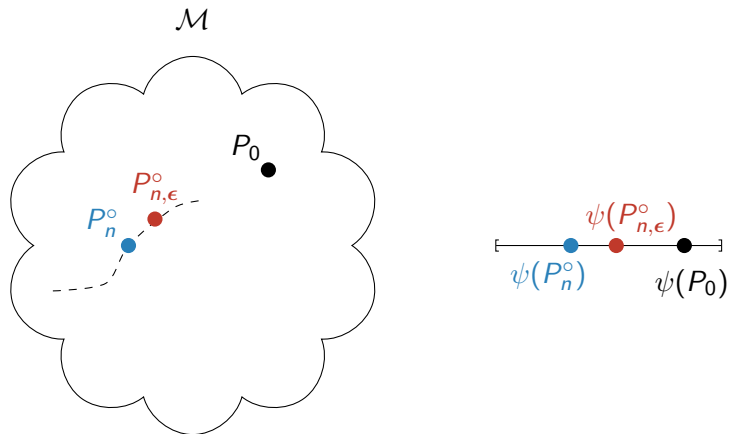
# Targeted Maximum Likelihood Estimation

- Key idea: carefully *fluctuate* the initial estimate  $P_n^\circ$  in order that the first-order bias term becomes zero.
- More specifically, plug-in estimator of the form

$$\hat{\psi}^{\text{TMLE}} = \psi(P_{n, \epsilon_n^*}^\circ)$$

with  $\{P_{n, \epsilon}^\circ : \epsilon \in \mathbb{R}\} \subset \mathcal{M}$  a well-chosen *fluctuation* of  $P_n^\circ$ , and  $\epsilon_n^*$  chosen by maximum-likelihood with respect to a carefully chosen likelihood  $\mathcal{L}$ .

# Targeted Maximum Likelihood Estimation



# TMLE: details for the ATE

- Fluctuation submodel:

$$\begin{aligned}\text{logit} \left\{ \mu_{n,\epsilon}^{\circ}(A, X) \right\} &= \text{logit} \left\{ \mu_n^{\circ}(A, X) + \frac{2A - 1}{g_P(A, X)} \epsilon \right\}, \\ Q_{n,\epsilon}^{\circ}(X) &\propto Q_n^{\circ}(X) \exp \left\{ \mu_n^{\circ}(1, X) - \mu_n^{\circ}(0, X) - \psi(P_n^{\circ}) \right\}.\end{aligned}$$

- Log-likelihood:

$$\begin{aligned}\mathcal{L}(O|\epsilon) &= Y \log(\mu_{n,\epsilon}^{\circ}(A, X)) \\ &\quad + (1 - Y) \log(1 - \mu_{n,\epsilon}^{\circ}(A, X)) + \log Q_{n,\epsilon}^{\circ}(X).\end{aligned}$$

# TMLE: details for the ATE

- Key property of log-likelihood and fluctuation submodel:

$$\text{EIF}(P) \in \text{span} \left\{ \left. \frac{d}{d\epsilon} \mathcal{L}(\cdot | \epsilon) \right|_{\epsilon=0} \right\}$$

- Estimate  $\epsilon_n^*$  be maximizing  $\epsilon \mapsto \mathcal{L}(O_1, \dots, O_n | \epsilon)$ .
- Form a new plug-in estimator as

$$\hat{\psi}^{\text{TMLE}} = \psi(P_{n, \epsilon_n^*}^\circ)$$

- It can then be shown that

$$\frac{1}{n} \sum_{i=1}^n \text{EIF}(P_{n, \epsilon_n^*}^\circ)(O_i) \approx 0,$$

i.e. the bias term of the expansion is zero.

# Frequentist properties of TMLE

- Double-robust consistency: remarkably,  $\hat{\psi}^{\text{TMLE}}$  is consistent as long as *either*  $\mu_n^\circ$  or  $g_n^\circ$  consistently estimate  $\mu_{P_0}$  or  $g_{P_0}$ .
- Asymptotically normal and efficient so long as
  - Nuisance estimation rates:  
 $\|\mu_n^\circ - \mu_{P_0}\| \times \|g_n^\circ - g_{P_0}\| = o_p(n^{-1/2})$ .
  - Nuisance estimators are not too complex (e.g. fall in Donsker class). Note such assumptions can be obviated through the use of cross-fitting (Zheng and van der Laan, 2011).

# Bayesian TMLE

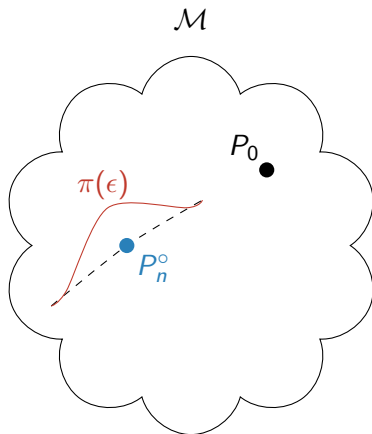
- Idea: in Bayesian TMLE, apply Bayesian inference to derive a (pseudo) posterior distribution for  $\epsilon$ :

$$\pi(\epsilon | O_1, \dots, O_n, P_n^\circ) \propto \prod_{i=1}^n \mathcal{L}(O_i | \epsilon) \pi(\epsilon),$$

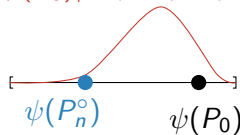
where  $\pi(\epsilon)$  is a prior on  $\epsilon$ .

- A posterior distribution for  $\psi$  can then be formed via the mapping  $\psi(P_{n,\epsilon}^\circ)$ .
- Bernstein von-Mises type results suggest posterior converges to normal distribution centered on efficient estimator with variance given by the non-parametric efficiency bound, and is double robust.
- Bayesian TMLE has been developed for a few parameters: ATE, class proportions in unlabeled data, parameter of marginal structural models (Díaz Muñoz et al., 2011; Díaz et al., 2020; Susmann and Chambaz, 2023).

# Bayesian TMLE



$$\pi(\psi(P_0) | O_1, \dots, O_n, P_n^o)$$



# Bayesian TMLE in Stan

```
1= data {
2  int<lower=0> N;
3  array[N] int<lower=0, upper=1> y;
4  vector[N] Qbar;
5  vector[N] Qbar0;
6  vector[N] Qbar1;
7
8  vector[N] H1;
9  vector[N] H1_0;
10 vector[N] H1_1;
11
12 vector[N] H2;
13 }
14= transformed data {
15 vector[N] Qw = rep_vector(1.0 / N, N);
16 }
17= parameters {
18 real epsilon;
19 }
20= transformed parameters {
21 vector[N] Qbar_fluctuated_logit = logit(Qbar) + epsilon * H1;
22 vector[N] Qw_fluctuated = exp(epsilon .* H2) .* Qw;
23 Qw_fluctuated = Qw_fluctuated / sum(Qw_fluctuated);
24
25 vector[N] Qbar0_fluctuated = inv_logit(logit(Qbar0) + epsilon * H1_0);
26 vector[N] Qbar1_fluctuated = inv_logit(logit(Qbar1) + epsilon * H1_1);
27
28 real<lower=-1, upper=1> psi = sum(Qw_fluctuated .* (Qbar1_fluctuated - Qbar0_fluctuated));
29
30 // Jacobian adjustment
31 vector[N] dQbar = H1_1 .* Qbar1_fluctuated .* (1 - Qbar1_fluctuated)
32 - H1_0 .* Qbar0_fluctuated .* (1 - Qbar0_fluctuated);
33 vector[N] dQw = Qw_fluctuated .* (H2 - Qw .* H2 .* exp(epsilon .* H2) / sum(Qw .* exp(epsilon .* H2)));
34 real dpsl = sum(dQw .* (Qbar1_fluctuated - Qbar0_fluctuated) + Qw_fluctuated .* dQbar);
35 }
36= model {
37 // Jacobian adjustment
38 target += log(dpsl);
39
40 // Prior
41 psi ~ uniform(-1, 1);
42
43 // Likelihood
44 y ~ bernoulli_logit(Qbar_fluctuated_logit);
45 target += sum(log(Qw_fluctuated));
46 }
47
```



# Group Treatment Effects

- Suppose that instead of estimating a single Average Treatment Effect, we would like to estimate a set of *group-specific* treatment effects.
- Data structure is now  $O = (X, A, D, Y)$ , where
  - $X$ : vector of covariates.
  - $D \in \{1, \dots, G\}$ : indicator of group membership.
  - $A$ : binary treatment indicator.
  - $Y$ : binary outcome.
- For  $g \in \{1, \dots, G\}$ , define *group-specific treatment effect* as

$$\psi_g(P) = E_P[E_P[Y|A = 1, D, X] - E_P[Y|A = 0, D, X]|D = g].$$

- Note that the functional  $\psi_g$  has a causal interpretation under similar “standard causal assumptions” as the ATE.

# Partial pooling

- How should we estimate  $\psi_g(P_0)$ , especially in instances where there are many groups ( $G$  is large) or there are groups with few observations?
- For Bayesians, natural to think about *partial pooling* of group-specific treatment effects (Feller and Gelman, 2015).
- Place a hierarchical model on  $\psi_g(P_0)$ , for example:

$$\psi_g(P_0) \sim N(m, \sigma^2),$$

with appropriate hyperpriors on  $m, \sigma$ .

# Hierarchical models for Bayesian TMLE

- Bayesian TMLE for group-specific treatment effects: set up fluctuation model separately for each group, with fluctuation parameters  $\epsilon_g$ ,  $g = 1, \dots, G$ .
- Each  $\epsilon_g$  maps to a group-specific treatment effect via  $\psi_g(P_{n, \epsilon_g}^\circ)$ .
- Place a hierarchical model on the group-specific treatment effects in order to share information between groups:

$$\psi_g(P_{n, \epsilon_g}^\circ) \sim N(m, \sigma^2).$$

# Illustrative simulation study

- Data generating process:
  - For each group  $g = 1, \dots, G$ , draw a group-specific effect  $\lambda_g \sim \text{Uniform}(-0.5, 0.5)$ .
  - Observations are drawn from

$$W \sim N_5(0_5, I_5),$$

$$D|W \sim \text{Categorical}(\{1, \dots, G\}, \{1, 2, 1, \dots, \}),$$

$$A|D, W \sim \text{Bernoulli}(\text{logit}^{-1}(0.25 + 0.25W^{(1)} + 0.25W^{(2)})),$$

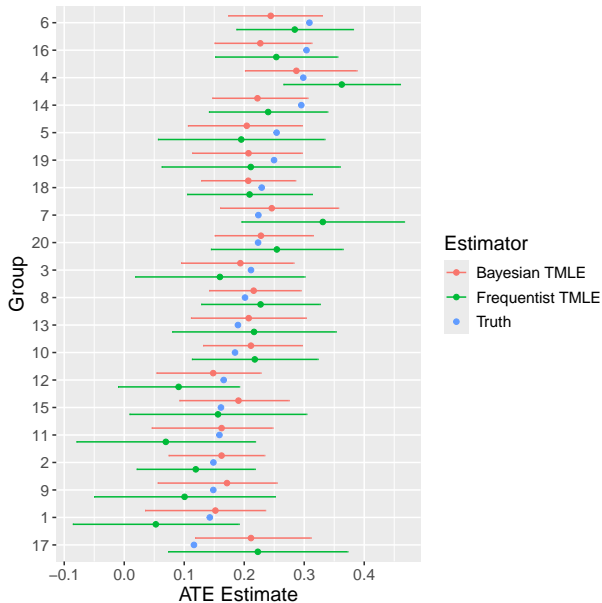
$$Y|W, D, A \sim \text{Bernoulli}(\text{logit}^{-1}(-0.25 + 0.5W^{(1)} + 0.25W^{(2)} + A + \lambda_D)).$$

- Form simulation datasets by drawing  $N = 2500, 5000, 10000$  observations 100 times from the above data generating process, with  $G = 20$  groups.

# Illustrative simulation study

- Estimate propensity score and outcome models using ensemble estimators.
  - SuperLearner with candidate algorithms `SL.mean`, `SL.knn`, `SL.glm`, `SL.glm.interaction`, `SL.glmnet`.
- Compare against frequentist TMLE run separately for each group.
- Code available on GitHub:  
[github.com/herbps10/bayes\\_tmle](https://github.com/herbps10/bayes_tmle).

# Simulation example



## Simulation results: mean error

N	Frequentist TMLE	Bayes hierarchical TMLE
<i>Both consistent</i>		
2500	-0.008	-0.011
5000	-0.003	-0.005
10000	-0.002	-0.003
<i>Propensity consistent, outcome inconsistent</i>		
2500	-0.025	-0.033
5000	-0.018	-0.025
10000	-0.013	-0.017
<i>Propensity inconsistent, outcome consistent</i>		
2500	-0.013	-0.013
5000	-0.007	-0.008
10000	-0.002	-0.002
<i>Both inconsistent</i>		
2500	-0.041	-0.041
5000	-0.040	-0.041
10000	-0.038	-0.038

## Simulation results: mean absolute error

N	Frequentist	TMLE	Bayes hierarchical	TMLE
<i>Both consistent</i>				
2500		0.073		0.047
5000		0.052		0.040
10000		0.037		0.030
<i>Propensity consistent, outcome inconsistent</i>				
2500		0.075		0.053
5000		0.054		0.043
10000		0.038		0.033
<i>Propensity inconsistent, outcome consistent</i>				
2500		0.072		0.046
5000		0.052		0.040
10000		0.036		0.031
<i>Both inconsistent</i>				
2500		0.080		0.056
5000		0.063		0.051
10000		0.048		0.044



## Simulation results: empirical coverage

N	Frequentist TMLE	Bayes hierarchical TMLE
<i>Both consistent</i>		
2500	92.37%	93.25%
5000	94.12%	92.32%
10000	93.81%	95.38%
<i>Propensity consistent, outcome inconsistent</i>		
2500	92.63%	90.88%
5000	93.97%	90.41%
10000	94.90%	93.85%
<i>Propensity inconsistent, outcome consistent</i>		
2500	93.45%	93.09%
5000	93.85%	91.77%
10000	95.00%	93.25%
<i>Both inconsistent</i>		
2500	91.70%	87.47%
5000	89.36%	82.45%
10000	83.57%	81.79%

# Bayesian TMLE: Best (or worst) of both worlds?

## Pros

- Good asymptotic frequentist properties.
- In practice, prior only needs to be placed on the parameter of interest (the group-specific treatment effects).
- Nuisance parameters can be estimated using any method, including flexible data-adaptive algorithms.
- Simulations suggest hierarchical modeling improves finite-sample performance for group-specific treatment effects.

## Cons

- Not strictly Bayesian; interpretation of posterior not clear in finite samples.
- May be example of “frequentist pursuit” (Robins et al., 2015).

# Discussion

- Bayesian TMLE: (pseudo) Bayesian method with applications in causal inference.
- To Bayesians, our proposal should be pretty obvious: use hierarchical modeling!
- Moral: bringing together ideas from separate “statistical cultures” combines advantages (and disadvantages) of both.
  - Exciting recent work combining Bayesian inference with concepts from non-parametric efficiency theory (Ray and Szabo, 2019; Ray and van der Vaart, 2020; Yiu et al., 2023; Breunig et al., 2024).

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## Appendix: Causal inference for the average treatment effect

- Separate task into two components: (1) definition and (2) estimation of causal effects (Díaz, 2019).
- Observe  $n$  i.i.d. draws  $O_1, \dots, O_n$  of a variable  $O = (X, A, Y) \sim P_0$ 
  - $X$ : vector of covariates
  - $A$ : binary treatment indicator
  - $Y$ : binary outcome
- Let  $Y(0)$  and  $Y(1)$  be the *potential outcomes* under treatment assignment  $A = 0$  and  $A = 1$ , respectively (Rubin, 1974).
- Define *Average Treatment Effect (ATE)*:

$$\Psi = E[Y(1) - Y(0)]$$

## Appendix: Identification

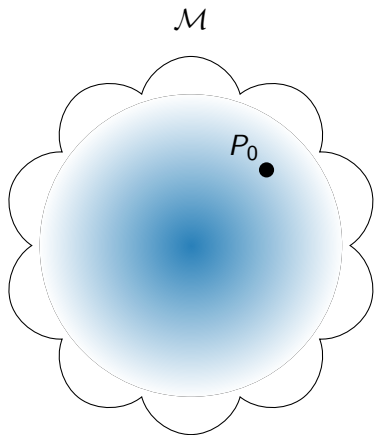
- Assume “Standard causal assumptions”:
  - Consistency:  $Y = Y(A)$ ,
  - Ignorability:  $Y(0), Y(1) \perp\!\!\!\perp A|X$ ,
  - Positivity (overlap):  $0 < P(A = 1|X) < 1$  for all  $X$ .
- g-computation identification result: (Robins, 1986):

$$\psi(P) = E_P [E_P[Y|A = 1, X] - E_P[Y | A = 0, X]] .$$

- We are now firmly in the realm of statistics. How shall we go about estimating  $\psi(P)$ ?



## Appendix: Bayesian non-parametrics



$$P(\psi(P_0) | O_1, \dots, O_n)$$

