# Causal Clustering: A new approach to analysis of treatment effect heterogeneity

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#### Motivation

Causal Clustering Adaptation to three widely-used clustering algorithms Efficient k-means causal clustering Application Application

# Motivation

# Average Treatment Effect

We begin with considering data structure

$$Z = (X, A, Y) \sim \mathbb{P}$$

where we have covariates  $X \in \mathbb{R}^d$ , treatment  $A \in \{0, 1\}$ , and outcome  $Y \in \mathbb{R}$ .

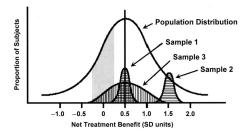
 $Y^a$ : potential outcome under treatment *a*.

The population-level average treatment effect (ATE) is defined by

$$\mathbb{E}_{\mathbb{P}}(Y^1 - Y^0). \tag{1}$$

# Heterogeneity in treatment effects

In many cases, we have a non-random variability in direction/magnitude of treatment effects



In this case, the standard ATE does not help to find an optimal policy.

Figure: Kravitz et al. 2004

# Heterogeneity in treatment effects

Identifying treatment effect heterogeneity and corresponding subgroups are of great importance

- cancer treatment [Zhang et al. 2017]
- efficacy of social programs [Imai and Ratkovic 2013]

# Previous approaches

Conditional average treatment effects (CATE):

$$\tau(X) = \mathbb{E}_{\mathbb{P}}[Y^1 - Y^0 \mid X] \tag{2}$$

Goal: find subgroups whose units have similar CATE

Previous attempts:

- simple parametric regression [e.g. Imai and Ratkovic 2013, Robins 1991]
- recursive partitioning via tree-based methods [e.g. Athey and Imbens 2015, Doove 2014]
- other supervised-learning [e.g. Kunzel 2017, van der Laan and Luedtke 2014]

# Limitations

- parametric restrictions
- not directly expandable to outcome-wide study [e.g. VanderWeele et al 2017, 2016, Li et al 2016] or multiple treatments [e.g. Lopez et al 2017]
- some drawbacks of the widely-used recursive partitioning methods
  - inefficient when lots of leafs have same effects
  - perform not very well for continuous variables [e.g. Lee et al 2017]
  - trade-off between reducing noise and decreasing bias

# **Causal Clustering**

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# Setup & Assumptions

Consider i.i.d samples from data structure  $Z = (X, A, Y) \sim \mathbb{P}$ , where

$$\mathcal{X} \in \mathbb{R}^d, \quad \mathcal{A} = \{0, 1, ..., p-1\}, \quad \mathcal{Y} \in \mathbb{R}.$$

Causal & Boundedness assumptions: for  $\forall a \in \mathcal{A}$ 

- (A1) (consistency)  $Y = \sum_{a} \mathbb{1}\{A = a\}Y^{a}$
- (A2) (no unmeasured confounding)  $A \perp Y^a \mid X$
- (A3) (positivity)  $\mathbb{P}(A = a \mid X)$  is bounded away from 0 a.s.
- (A4)  $\mathbb{E}[Y^a|X]$  is globally bounded  $\forall a$ .

All the pairwise CATE's are identified under (A1)-(A3).

### Representation map

#### Definition (Representation map) We define a map $\Phi : \mathcal{X} \to \mathbb{R}^p$ by

$$\Phi(X) = \left( \mathbb{E}[Y^0 \mid X], \dots, \mathbb{E}[Y^{p-1} \mid X] \right).$$
(3)

Let  $\mu_a \equiv \mathbb{E}[Y \mid X, A = a]$ . Under (A1)-(A3),  $\Phi(X)$  can be

constructed by estimating  $\mu_a$  for a = 0, ..., p - 1.

# Representation map: implication

On the image of  $\Phi$ ,

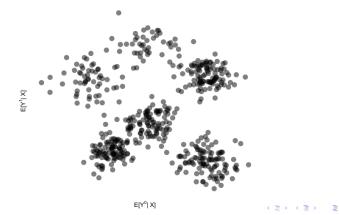
- ► a point whose coordinates are mostly the same ⇒ no treatments bring any visible effect
- for two unites i, j,

$$\Phi(X_i) \cong \Phi(X_j) \Rightarrow au_{a,0}(X_i) \cong au_{a,0}(X_j) ext{ for } orall a \in \mathcal{A}$$

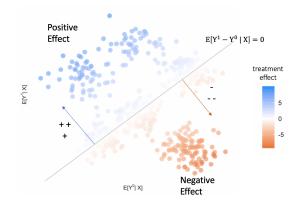
where  $\tau_{a,0}(X) = \mathbb{E}[Y^a - Y^0 | X]$ : i.e., the effect of receiving treatment *a* over placebo (a=0).

# Illustrating example

Consider samples projected through the representation map, where  $\mathcal{A} = \{0, 1\}$  and  $\mathbb{E}[Y^1 - Y^0] = 0$ .

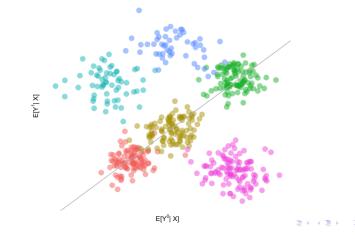


# Illustrating example



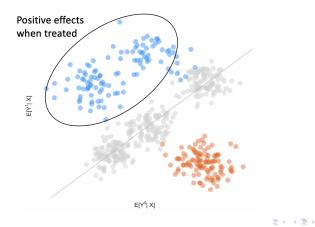
# Illustrating example

It would be worth analyzing each *cluster* separately (e.g. k-means),



# Illustrating example

or based on the distance from  $\mathbb{E}[Y^1 - Y^0 \mid X] = 0$  line.



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Causal Clustering: the idea

Analysis of treatment effect heterogeneity:

- need to ascertain a subgroup that shows similar responses towards given treatments (in terms of CATE)
- $\Rightarrow$  Perform **cluster analysis** on the **image of**  $\Phi$ .

# Adaptation to three widely-used clustering algorithms

# Main result I

Challenges

 every coordinate μ<sub>a</sub> = E[Y<sup>a</sup>|X] in Φ is a random function that needs to be estimated

#### Our result

We show that for three widely-used clustering algorithms (k-means, hierarchical, density), the additional cost comes out to be the cost of estimating μ<sub>a</sub>'s (as a linearly additive error).

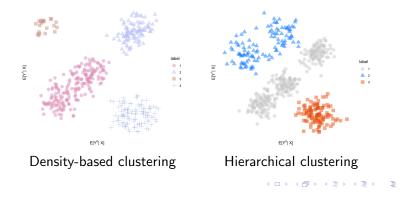
## k-means causal clustering

 $\widehat{C}$ : sample splitting  $\rightarrow$  plug-in  $\rightarrow$  empirical risk minimizer Theorem (Error bound for k-means causal clustering) Under the same conditions of Linder et al (1994), there exists an N such that for every n > N

$$\mathbb{E} \left| R(\widehat{C}) - R(C^*) \right| \\ \leq 64 \underbrace{B^2 \sqrt{\frac{k(d+1)\log n}{n}}}_{Linder \ et \ al \ (1994)} + \underbrace{4\sqrt{2}B \sum_{a \in \mathcal{A}} \|\widehat{\mu}_a - \mu_a\|}_{additional \ cost}.$$

# Hierarchical & (level-set) Density clustering

We also verify *Hierarchical* and *Density* causal clustering can be done at the additional error/risk of  $O(\sum_{a} \|\widehat{\mu}_{a} - \mu_{a}\|)$ 



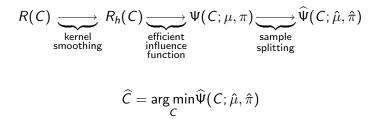
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# Efficient k-means causal clustering

# Nonparametric condition on nuisance parameters

- ► Cost of ∑<sub>a</sub> ||µ<sub>a</sub> µ<sub>a</sub>|| seems expensive; to attain n<sup>-1/2</sup> rates overall, we need to estimate each µ<sub>a</sub> at n<sup>-1/2</sup> rate which is infeasible in nonparametric modeling
- We may want to utilize information about treatment process (i.e., propensity score)

# Semiparametric approach



We will focus on k-means causal clustering

# Main result II: Efficient k-means causal clustering

#### Theorem (Error bound)

Under the margin condition (Levrard 2015, 2018) and other weak conditions, if

$$R(\widehat{C}) - R(C^*) = O_{\mathbb{P}}\left(\frac{1}{\sqrt{n}}\right).$$

Sufficient condition: now  $\mu, \pi$  can be estimated at  $n^{-1/4}$  rates.

# Efficient k-means causal clustering

#### Theorem (Asymptotic normality)

Under the stronger version of the margin condition along with the other proper assumptions, we have

$$\sqrt{n}(\widehat{C}-C^*) \rightsquigarrow N\left(0,\Sigma'_{C^*,\eta}\right)$$

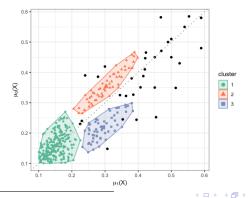
where  $\eta = (\pi, \mu)$  and  $\Sigma'_{\mathcal{C}^*, \eta}$  is kp imes kp covariance matrix.

► Our estimate of C satisfies √n-consistent, asymptotic normality property, under weak NP conditions.

# Application

# Application: the EAGeR aspirin data<sup>1</sup>

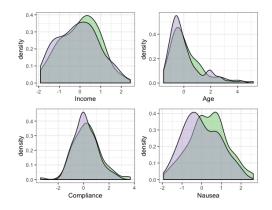
Goal: study the effect of aspirin on pregnancy loss  $A \in \{0, 1\}$ : low-dose aspirin,  $Y \in \mathbb{R}$ : indicator of pregnancy loss,  $X \in \mathbb{R}^d$ : pretreatment covariates  $\Rightarrow \widehat{\mathbb{E}}[Y^1 - Y^0] \cong 0$ 



<sup>1</sup>https://www.nichd.nih.gov/about/org/diphr/officebranch/eb/effects-aspirin

## Application: aspirin data

seems 'Nausea' drives the difference



# Conclusion

- Causal Clustering: a new framework for the analysis of treatment effect heterogeneity by leveraging tools in clustering analysis
  - pursue an intuitive way of ascertaining subgroups with similar treatment effects based on *unsupervised* method
- show that three widely-used clustering methods can be successfully adopted into our framework
- develop efficient k-means causal clustering algorithm that attains fast convergence rates/asymptotic normality even when incorporating flexible machine learning methods

# End of Talk

Thank you

# Appendix

Appendix

Margin condition (Levrard 2015, 2018)

#### Definition (Margin condition)

Let us define  $p(t) \coloneqq \sup_{C \in \mathcal{M}^*} \mathbb{P}(W \in N_C(t))$ . We assume that there exists a fixed  $\kappa > 0$  such that for all  $0 \le t \le \kappa$ 

$$p(t) \lesssim t^{lpha}$$

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for some  $\alpha > 0$ .

# hierarchical clustering

#### Theorem (Balcan et al (2014))

Suppose each  $\widehat{\mu}_a$  is estimated in the separate sample set  $D^n$  and let similarity function K (induced from Euclidean distance d) satisfy the  $(\alpha, \nu)$ -good neighborhood property for the clustering problem (S, I). Then under the additional set of assumptions (A1)-(A4), we have robust hierarchical clustering (Balcan et al, 2014) on  $(\widehat{S}, I)$  with a pruning that have error at most  $\nu + \xi + \delta$ with respect to the true target clustering on (S, I) with probability at least  $1 - \delta$ , where  $\xi = O(\sum_{a \in \mathcal{A}} \|\widehat{\mu}_a - \mu_a\|_{\infty})$ .

# (level-set) density clustering

Theorem (Rinaldo et al (2010), Kim et al (2018)) Suppose that  $L_{h,t}$  is stable and let  $H(\cdot, \cdot)$  be the Hausdorff distance between two sets. Suppose each  $\hat{\mu}_a$  is estimated in the separate sample set  $D^n$ , and suppose Assumptions (A1)-(A6). Let  $\{h_n\}_{n \in \mathbb{N}} \subset (0, h_0)$  be satisfying

$$\limsup_n \frac{(\log(1/h_n))_+}{nh_n^2} < \infty.$$

Then,

$$H(\widehat{L}_t, L_{h,t}) = O_P\left(\sqrt{\frac{(\log(1/h_n))_+}{nh_n^2}} + \frac{1}{h_n^3}\min\left\{\sum_a \|\widehat{\mu}_a - \mu_a\|_1, h_n\right\}\right)$$