Causal Inference Methods and Case Studies

STAT24630

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Lecture 6

Topic: Regression for complete randomized experiment

- Using regression with no covariates

- Using regression with covariates adjustments

- Using regression with covariates adjustments and interactions

- The LRC-CPPT cholesterol data example

Linear regression and causality

- Linear regression:

$$\mathbb{E}(Y_i | \boldsymbol{X}_i) = f(\boldsymbol{X}_i) = \alpha + \boldsymbol{\beta}^T \boldsymbol{X}_i$$

- Question:
  - When can we interpret the coefficient(s) as causal effect?
  - How can we do correct inference if we take into account the randomization procedure of treatment assignments?

- Benefit of using linear regression in randomized experiments
  - Provides a straightforward and familiar way to incorporate covariates
  - More accurate estimator if covariates are predictive of potential outcomes

- Some critiques
  - In complete randomized experiments, covariates are not confounders
  - Why do we want to assume a linear model if we don't need to?

    "Experiments should be analyzed as experiments, not as observational studies"

    ---- David A. Freedman, 2006

The LRC-CPPT cholesterol data

- An experiment to evaluate the effect of the drug cholestyramine on reducing cholesterol levels
- $N = 337$ patients are completely randomized
- **Pre-treatment covariates:** two cholesterol measurements before and after a suggestion of low-cholesterol diet, both measurements taken prior to the random assignment
  - Does chol2 − chol1 reflect the average causal effect of suggestion? Not necessarily
  - cholp = 0.25 chol1 + 0.75 chol2

Table 7.1. *Summary Statistics for PRC-CPPT Cholesterol Data*

	Variable	Control ($N_c = 172$)		Treatment ($N_t = 165$)			
		Average	Sample (S.D.)	Average	Sample (S.D.)	Min	Max
Pre-treatment	chol1	297.1	(23.1)	297.0	(20.4)	247.0	442.0
	chol2	289.2	(24.1)	287.4	(21.4)	224.0	435.0
	cholp	291.2	(23.2)	289.9	(20.4)	233.0	436.8
Post-treatment	cholf	282.7	(24.9)	256.5	(26.2)	167.0	427.0
	chold	−8.5	(10.8)	−33.4	(21.3)	−113.3	29.5
	comp	74.5	(21.0)	59.9	(24.4)	0	101.0

The LRC-CPPT cholesterol data

- An experiment to evaluate the effect of the drug cholestyramine on reducing cholesterol levels
- $N = 337$ patients are completely randomized
- **Post-treatment outcomes:**
  - cholf: post-treatment average cholesterol level
  - chold = cholf − cholp
  - comp: compliance rate, the percentage of individuals follow the treatment assignment

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The LRC-CPPT cholesterol data

- Can we evaluate the drug effect by simply look at whether chold is positive or negative?
  - No! The before-after comparison is NOT necessarily causal
  - Even for the control group, chold is significantly negative

- The patient's post-treatment cholesterol should be highly correlated with his/her pre-treatment cholesterol level
- How do we evaluate the causal effect after "adjusting for the pre-treatment cholesterol"?

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What does "adjust for" exactly mean here?

The LRC-CPPT cholesterol data

A bit explanation about compliance
- If we compare between control and treatment group, we are evaluating the causal effect of "being assigned", not the causal effect of actually taking the drug
- Compliance lower in the treatment group possibly due to the side effect of the drug
- Can we just throw away individuals who do not follow the treatment and estimate the causal effect of taking the drug based on the rest individuals? No
- Will discuss more about compliance in later lectures

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Linear regression with no covariates

- Neyman's approach

$$\hat{\tau}^{\text{dif}} = \overline{Y}_t^{\text{obs}} - \overline{Y}_c^{\text{obs}}$$

$$\overline{Y}_c^{\text{obs}} = \frac{1}{N_c} \sum_{i:W_i=0} Y_i^{\text{obs}} \quad \text{and} \quad \overline{Y}_t^{\text{obs}} = \frac{1}{N_t} \sum_{i:W_i=1} Y_i^{\text{obs}}$$

- An alternative way to get $\hat{\tau}^{\text{dif}}$ is by linear regression

$$(\hat{\alpha}, \hat{\beta}) = \arg\min_{(a,b)} \sum_{i=1}^{n} (Y_i - a - bZ_i)^2$$

- It is easy to show that $\hat{\beta} = \hat{\tau}^{\text{dif}}$

- However, if we use lm to compute $\text{var}(\hat{\beta})$, the variance estimator is different from $\frac{s_c^2}{N_c} + \frac{s_t^2}{N_t}$

Linear regression with no covariates

- A causal interpretation of the linear regression model

- Linear model on the potential outcomes
$$Y_i(w) = \alpha + \tau_i w + \varepsilon_i^* = \alpha + \tau w + \varepsilon_i(w)$$
where $\mathbb{E}(\varepsilon_i^*) = 0$ and $\varepsilon_i(w) = \varepsilon_i^* + (\tau_i - \tau)w$

- Assume that there is a super-population and the potential outcomes are random (i.i.d. samples)

- Notice that the observed outcomes $Y_i = W_i Y_i(1) + (1 - W_i)Y_i(0)$ are not i.i.d. samples under complete randomization

- For binary treatment:
$$Y_i(0) = \alpha + \varepsilon_i^*, Y_i(1) = Y_i(0) + \tau_i$$

- Define PATE: $\tau = \mathbb{E}(\tau_i) = \mathbb{E}\big(Y_i(1) - Y_i(0)\big)$
- $\alpha = \mathbb{E}\big(Y_i(0)\big)$ and $\mathbb{E}\big(\varepsilon_i(w)\big) = 0$

Linear regression with no covariates

- Causal model on the potential outcomes

$$Y_i(w) = \alpha + \tau_i w + \varepsilon_i^* = \alpha + \tau w + \varepsilon_i(w)$$

where $\mathbb{E}(\varepsilon_i^*) = 0$ and $\varepsilon_i(w) = \varepsilon_i^* + (\tau_i - \tau)w$

  - If the treatment is binary ($w = 0,1$), then the above model essentially has no assumption on $Y_i(0)$ and $Y_i(1)$
  - If the treatment is continuous, the model assumes a linear but heterogenous causal effect on each individual

  - How to estimate τ from observed data?
  - When does the above model imply the linear regression model on observed data?

$$Y_i^{\text{obs}} = \alpha + \tau W_i + \varepsilon_i$$

Linear regression with no covariates

$$Y_i(w) = \alpha + \tau_i w + \varepsilon_i^* = \alpha + \tau w + \varepsilon_i(w)$$

We assume the following identification conditions

- Randomization of the treatment:

$$(\boldsymbol{Y}(0), \boldsymbol{Y}(1)) \perp \boldsymbol{W}$$

  - Satisfied in complete randomized experiments
  - Then, $\mathbb{E}\big(Y_i(w)\big) = \mathbb{E}\big(Y_i^{\mathrm{obs}}|W_i = w\big) = \alpha + \tau w$ Regression model for the observed Y_i^{obs}

  - So this implies a regression model $Y_i^{\mathrm{obs}} = \alpha + \tau W_i + \varepsilon_i$ and $\varepsilon_i = \varepsilon_i(W_i)$
  - In the regression model, we treat assignment vectors as fixed

- Random sampling of the units
  - $(\varepsilon_i(0), \varepsilon_i(1))$ are independent across i
  - This implies that ε_i in the linear regression model are independent as W_i are treated as fixed (the regression model is conditional on W_i)

Least square estimator

$$(\hat{\tau}^{\text{ols}}, \hat{\alpha}^{\text{ols}}) = \arg\min_{\tau,\alpha} \sum_{i=1}^{N} \left(Y_i^{\text{obs}} - \alpha - \tau \cdot W_i \right)^2 ,$$

with solutions

$$\hat{\tau}^{\text{ols}} = \frac{\sum_{i=1}^{N} \left(W_i - \overline{W} \right) \cdot \left(Y_i^{\text{obs}} - \overline{Y}^{\text{obs}} \right)}{\sum_{i=1}^{N} \left(W_i - \overline{W} \right)^2}, \quad \text{and} \quad \hat{\alpha}^{\text{ols}} = \overline{Y}^{\text{obs}} - \hat{\tau}^{\text{ols}} \cdot \overline{W},$$

where

$$\overline{Y}^{\text{obs}} = \frac{1}{N} \sum_{i=1}^{N} Y_i^{\text{obs}} \quad \text{and} \quad \overline{W} = \frac{1}{N} \sum_{i=1}^{N} W_i = \frac{N_t}{N}.$$

Simple linear algebra shows that
$$\hat{\tau}^{\text{ols}} = \overline{Y}_t^{\text{obs}} - \overline{Y}_c^{\text{obs}} = \hat{\tau}^{\text{dif}}$$

- $\hat{\tau}^{\text{ols}}$ is unbiased for the estimation of τ
- How to estimate the variance of $\hat{\tau}^{\text{ols}}$?

Homoscedastic error assumption

Homoscedastic error assumption: $\mathbb{V}(\varepsilon_i(0)) = \mathbb{V}(\varepsilon_i(1)) = \sigma^2$

- Then $\mathbb{V}(Y_i^{\text{obs}}|W_i) = \varepsilon_i = \varepsilon_i(W_i)$ always has variance σ^2

- Notice that in general the homoscedastic error assumption on the observed data linear regression model is not true

- Under homoscedasticity, OLS estimates of the variance is

$$\hat{\sigma}_{Y|W}^2 = \frac{1}{N-2}\sum_{i=1}^{N}\hat{\varepsilon}_i^2 = \frac{1}{N-2}\sum_{i=1}^{N}\left(Y_i^{\text{obs}} - \hat{Y}_i^{\text{obs}}\right)^2,$$

where the estimated residual is $\hat{\varepsilon}_i = Y_i^{\text{obs}} - \hat{Y}_i^{\text{obs}}$, and the predicted value $\hat{Y}_i^{\text{obs}}$ is

$$\hat{Y}_i^{\text{obs}} = \begin{cases} \hat{\alpha}^{\text{ols}} & \text{if } W_i = 0, \\ \hat{\alpha}^{\text{ols}} + \hat{\tau}^{\text{ols}} & \text{if } W_i = 1. \end{cases}$$

Homoscedastic error assumption

Homoscedastic error assumption: $\mathbb{V}(\varepsilon_i(0)) = \mathbb{V}(\varepsilon_i(1)) = \sigma^2 = \mathbb{V}(Y_i^{\text{obs}}|W_i)$

- Then from OLS, estimate of the variance of $\hat{\tau}^{\text{ols}}$

$$\hat{\mathbb{V}}^{\text{homosk}} = \frac{\hat{\sigma}^2_{Y|W}}{\sum_{i=1}^{N}(W_i - \overline{W})^2}$$

- For binary treatment, one can show that

$$\hat{\mathbb{V}}^{\text{homosk}} \approx \frac{s_c^2}{N_t} + \frac{s_t^2}{N_c}$$

- This is not the same as the Neyman's approach variance $\frac{s_c^2}{N_c} + \frac{s_t^2}{N_t}$ even for large-sample size

Heteroscedastic errors

- If we don't want to assume $\mathbb{V}(\varepsilon_i(0)) = \mathbb{V}(\varepsilon_i(1))$, then the homoscedastic error assumption fails

- Robust variance estimation of $\hat{\tau}^{\text{ols}}$ allowing any heterogeneity of $\mathbb{V}(Y_i^{\text{obs}}|W_i)$ across i

$$\hat{\mathbb{V}}^{\text{hetero}} = \frac{\sum_{i=1}^{N} \hat{\varepsilon}_i^2 \cdot \left(W_i - \overline{W}\right)^2}{\left(\sum_{i=1}^{N} \left(W_i - \overline{W}\right)^2\right)^2}$$

- $\hat{\varepsilon}_i = Y_i^{\text{obs}} - \hat{\alpha} - \hat{\tau}W_i = Y_i^{\text{obs}} - \hat{Y}_i^{\text{obs}}$ are the residuals

- If we replace $\hat{\varepsilon}_i^2$ by $\hat{\sigma}_{Y|W}^2$, then we get back the OLS variance estimation of $\hat{\tau}^{\text{ols}}$

- This is also called the Sandwich estimator that is robust to the violation of the homoscedastic noise assumption in linear regression

- As $\hat{\tau}$ is estimated from Y_i^{obs}, $\mathbb{E}(\hat{\varepsilon}_i^2) < \mathbb{V}(\varepsilon_i)$

- When sample size N is small, $\hat{\mathbb{V}}^{\text{hetero}}$ will underestimate the true variance of $\hat{\tau}^{\text{ols}}$

Heteroscedastic errors

- The HC2 adjustment

$$\widehat{\mathbb{V}}_{HC2}^{\text{hetero}} = \frac{\sum_{i=1}^{N}(\hat{\varepsilon}_i/\sqrt{1-h_{ii}})^2(W_i - \bar{W})^2}{\left(\sum_{i=1}^{N}(W_i - \bar{W})^2\right)^2}$$

  - h_{ii} is the leverage of unit i in the linear regression

  - If W_i is binary. $\widehat{\mathbb{V}}_{HC2}^{\text{hetero}} = \frac{s_c^2}{N_c} + \frac{s_t^2}{N_t}$

- This is the same variance estimator as from Neyman's approach, or our two-sample testing approach

Linear regression with covariates adjustment

To summarize the logic

- We build a (linear) model on the potential outcomes
- This model implies a linear regression model on the observed outcome if $(Y(0), Y(1)) \perp W$
- The coefficient on W_i in the linear regression model is the average causal effect (PATE)
- The linear regression model treat W as fixed so it works for any randomization assignment mechanism that satisfy $(Y(0), Y(1)) \perp W$
- Noise in the linear regression model are independent as long as potential outcomes are independent across units

- For statistical inference
  - The OLS estimator estimator is always unbiased
  - We can apply standard linear regression inference results if we assume $\mathbb{V}(\varepsilon_i(0)) = \mathbb{V}(\varepsilon_i(1))$
  - If $\mathbb{V}(\varepsilon_i(0)) \neq \mathbb{V}(\varepsilon_i(1))$, we need to use the robust variance estimator

Linear regression with covariates adjustment

- Regress $Y_i(0)$ on the pre-treatment covariates $\boldsymbol{X}_i$
$$Y_i(w) = \alpha + \tau_i w + \boldsymbol{\beta}^T \boldsymbol{X}_i + \varepsilon_i^* = \alpha + \tau w + \boldsymbol{\beta}^T \boldsymbol{X}_i + \varepsilon_i(w)$$
where $\mathbb{E}(\varepsilon_i^* | \boldsymbol{X}_i) = 0$ and $\varepsilon_i(w) = \varepsilon_i^* + (\tau_i - \tau)w$

  - We assume that $\mathbb{E}(Y_i(0) | \boldsymbol{X}_i) = \alpha + \boldsymbol{\beta}^T \boldsymbol{X}_i$
  - Individual-level causal effect is $\tau_i = Y_i(1) - Y_i(0)$
  - Assume CATE $\tau(\boldsymbol{x}) = \mathbb{E}(\tau_i | \boldsymbol{X}_i = \boldsymbol{x}) \equiv \tau = $ PATE constant across levels of $\boldsymbol{X}_i$
  - We can allow for heterogeneous causal effect but need $\mathbb{E}(\tau_i - \tau \mid \boldsymbol{X}_i) = 0$ (individual causal effects are independent from the pre-treatment covariates)
  - The above implies that $\mathbb{E}(\varepsilon_i(w) | \boldsymbol{X}_i) = 0$

  - The above also implies that $\mathbb{E}(Y_i(w) | \boldsymbol{X}_i) = \alpha + \tau w + \boldsymbol{\beta}^T \boldsymbol{X}_i$

When does the above model imply the linear regression model on observed data?
$$Y_i^{\text{obs}} = \alpha + \tau W_i + \boldsymbol{\beta}^T \boldsymbol{X}_i + \varepsilon_i$$

Linear regression with covariates adjustment

$$Y_i(w) = \alpha + \tau w + \boldsymbol{\beta}^T \boldsymbol{X}_i + \varepsilon_i(w)$$

We assume the following identification conditions

- (Conditional) randomization of the treatment:

$$\big(\boldsymbol{Y}(0), \boldsymbol{Y}(1)\big) \perp \boldsymbol{W} \mid \boldsymbol{X}$$

  - Always satisfied in randomized experiments
  - $\mathbb{E}(Y_i(w)|\boldsymbol{X}_i = \boldsymbol{x}) = \mathbb{E}\big(Y_i^{\mathrm{obs}}|W_i = w, \boldsymbol{X}_i = \boldsymbol{x}\big) = \alpha + \tau w + \boldsymbol{\beta}^T \boldsymbol{X}_i$

    Regression model for the observed Y_i^{obs}

  - So this implies a regression model $Y_i^{\mathrm{obs}} = \alpha + \tau W_i + \boldsymbol{\beta}^T \boldsymbol{X}_i + \varepsilon_i$ and $\varepsilon_i = \varepsilon_i(W_i)$
  - Both $\boldsymbol{X}_i$ and W_i are treated as fixed

- Random sampling of the units
  - $(\varepsilon_i(0), \varepsilon_i(1))$ are independent across i
  - This implies that $\varepsilon_i = \varepsilon_i(W_i)$ are independent across units

OLS with covariates adjustment

$$(\hat{\alpha}^{\mathrm{ols}}, \hat{\tau}^{\mathrm{ols}}, \hat{\beta}^{\mathrm{ols}}) = \arg\min_{\alpha,\tau,\beta} \sum_{i=1}^{N} \left(Y_i^{\mathrm{obs}} - \alpha - \tau \cdot W_i - X_i \beta \right)^2$$

- The estimator $\hat{\tau}^{\mathrm{ols}}$ is unbiased for the causal estimand τ
- Even if the model is incorrect (either the violation of $\mathbb{E}(Y_i(0) \mid \boldsymbol{X}_i) = \alpha + \boldsymbol{\beta}^T \boldsymbol{X}_i$ or $\tau \equiv \mathbb{E}(\tau_i \mid \boldsymbol{X}_i = \boldsymbol{x})$), $\hat{\tau}^{\mathrm{ols}}$ still converges to the PATE $\mathbb{E}(\tau_i)$ under complete randomization

Efficiency gain from regression
- If the model is correct, we have

$$\mathbb{V}(\hat{\tau}^{\mathrm{ols}}) \approx \frac{\mathbb{E}\{\mathbb{V}(Y_i(1) \mid \boldsymbol{X}_i)\}}{N_t} + \frac{\mathbb{E}\{\mathbb{V}(Y_i(0) \mid \boldsymbol{X}_i)\}}{N_c} \leq \frac{\sigma_c^2}{N_c} + \frac{\sigma_t^2}{N_t}$$

  - If $\boldsymbol{X}_i$ is predictive of the (potential) outcomes, we have a more accurate estimator
- If the linear model is incorrect, the efficiency might be lost
  (Freedman 2008, *Adv. Appl. Math.*)

Estimate of the variance of $\hat{\tau}^{\text{ols}}$ with covariates adjustment

- Assume homoscedastic error assumption:

$$\mathbb{V}(\varepsilon_i(0)) = \mathbb{V}(\varepsilon_i(1)) = \sigma^2 = \mathbb{V}(Y_i^{\text{obs}}|W_i, \boldsymbol{X}_i)$$

We can follow standard linear regression inference and estimate variance of $\hat{\tau}^{\text{ols}}$ as

$$\hat{\mathbb{V}}_{\text{sp}}^{\text{homo}} = \frac{1}{N(N-1-\dim(X_i))} \cdot \frac{\sum_{i=1}^{N}\left(Y_i^{\text{obs}} - \hat{\alpha}^{\text{ols}} - \hat{\tau}^{\text{ols}} - X_i\hat{\beta}^{\text{ols}}\right)^2}{\overline{W} \cdot (1-\overline{W})}$$

- The robust variance estimator (Sandwich estimator) without assuming homoscedasticity

$$\hat{\mathbb{V}}_{\text{sp}}^{\text{hetero}} = \frac{1}{N(N-1-\dim(X_i))}$$

$$\cdot \frac{\sum_{i=1}^{N}(W_i - \overline{W})^2 \cdot \left(Y_i^{\text{obs}} - \hat{\alpha}^{\text{ols}} - \hat{\tau}^{\text{ols}} - X_i\hat{\beta}^{\text{ols}}\right)^2}{(\overline{W} \cdot (1-\overline{W}))^2}$$

Linear regression with covariates adjustment and interactions

What if the assumption $\tau \equiv \tau(x) = \mathbb{E}(\tau_i| \, X_i = x)$ constant across levels of X_i is incorrect?

- $Y_i(w) = \alpha + \tau_i w + \boldsymbol{\beta}^T X_i + \varepsilon_i^* = \alpha + \tau w + \boldsymbol{\beta}^T X_i + \varepsilon_i(w)$ where $\mathbb{E}(\varepsilon_i^*|X_i) = 0$ and $\varepsilon_i(w) = \varepsilon_i^* + (\tau_i - \tau)w$

- Assume CATE $\tau(x) = \mathbb{E}(\tau_i| \, X_i = x) = \tau + \boldsymbol{\gamma}^T(x - \overline{X})$
- τ is still the population average treatment effect
- Then $\mathbb{E}(\varepsilon_i(w)| \, X_i) = \boldsymbol{\gamma}^T(\, X_i - \overline{X})w$

- The above also implies that $\mathbb{E}(Y_i(w)| \, X_i) = \alpha + \tau w + \boldsymbol{\beta}^T X_i + \boldsymbol{\gamma}^T(\, X_i - \overline{X})w$

- When does the above model imply the linear regression model with interactions on observed data?

$$Y_i^{\text{obs}} = \alpha + \tau W_i + \boldsymbol{\beta}^T X_i + \boldsymbol{\gamma}^T(\, X_i - \overline{X})W_i + \varepsilon_i$$

- Same assumptions as before (slide 15)
- We can still use least square estimators

Results on the LRC-CPPT cholesterol data

- We estimate the PATE for both the post-treatment cholesterol level cholf and compliance
  - A considerable reduction of the variance of $\hat{\tau}^{\text{ols}}$ for cholf when we add the pre-treatment cholesterol levels in the regression
  - Our goal is always estimating PATE even after "covariates adjustment"
  - In randomized experiments satisfying $(Y(0), Y(1)) \perp W$, adjusting for covariates or not, our estimate of PATE is always valid, we only change the efficiency of our estimate

| Covariates | Effect of Assignment to Treatment on | | | |
| | Post-Cholesterol Level | | Compliance | |
	$\hat{\tau}$	$\widehat{(\text{s. e.})}$	$\hat{\tau}$	$\widehat{(\text{s. e.})}$
No covariates	−26.22	(3.93)	−14.64	(3.51)
cholp	−25.01	(2.60)	−14.68	(3.51)
chol1, chol2	−25.02	(2.59)	−14.95	(3.50)
chol1, chol2, interacted with W	−25.04	(2.56)	−14.94	(3.49)

Results on the LRC-CPPT cholesterol data

- We estimate the PATE for both the post-treatment cholesterol level cholf and compliance
  - A considerable reduction of the variance of $\hat{\tau}^{ols}$ for cholf when we add the pre-treatment cholesterol levels in the regression
  - Our goal is always estimating PATE even after "covariates adjustment"
  - In randomized experiments satisfying $(Y(0), Y(1)) \perp W$, adjusting for covariates or not, our estimate of PATE is always valid, we only change the efficiency of our estimate
  - Which variables are "significantly" contributing to the variance reduction of $\hat{\tau}^{ols}$ for cholf ?

Covariates	Model for Levels	
	Est	$\widehat{(s.\,e.\,)}$
Assignment	−25.04	(2.56)
Intercept	−3.28	(12.05)
chol1	0.98	(0.04)
chol2-chol1	0.61	(0.08)
chol1 × Assignment	−0.22	(0.09)
(chol2-chol1) × Assignment	0.07	(0.14)
R-squared	0.63	

Why do we use linear regression in randomized experiments?

- Covariate adjustment can be used to improve efficiency in randomized experiments
- Under various experimental designs, linear regression models are useful methods for this purpose

- Randomization of treatment assignment protects researchers from misspecification
  - independence between treatment and covariates
  - linear regression estimators are often consistent even when the model is incorrect