

Lecture 9

Non-compliance in randomized experiments, instrumental variables

Part I



Outline

- Non-compliance in randomized experiment
 - Principal stratification
 - The monotonicity and exclusion restriction assumptions
 - CATE estimand and the moment-based estimator
 - Uncertainty quantification of the moment-based estimator
- Textbook Chapters: Imbens and Rubin Chapters 23.1-23.7, 23.9 & 24.1-24.5, Peng Chapter 21.1-21.2

Ideal randomized experiment

- We have for now only considered an **ideal** randomized experiment
 - No loss to follow-up
 - Full adherence to the assigned treatment over the duration of the study
 - ex. most severely ill individuals in the control group tend to seek a heart outside of the study.
 - No measurement errors
 - ex. The PCR tests of COVID-19 may introduce false signals (depending on virus loading) when evaluating the causal effect of vaccine
 - A single version of treatment: different dosage of a drug
 - Double-blind assignment
 - in real life, both patients and doctors are aware of the received treatment

The Sommer-Zeger vitamin A supplement data

- Sommer and Zeger study the effect of vitamin A supplements on infant mortality in Indonesia
- The vitamin supplements were randomly assigned to villages, but some of the individuals in villages assigned to the treatment group failed to receive them.
- None of the individuals assigned to the control group received the supplements
- $N = 23,682$ infants
- Outcome: binary variable indicating survival of an infant
- $W_i^{\text{obs}} \in \{0,1\}$ whether the infant receives the vitamin supplement or not
- $Z_i \in \{0,1\}$ whether the infant is assigned to the treatment group or not
- We ignore the fact that treatment assignment is at the village level (clustered randomized experiment) and consider the experiment as from a completely randomized experiment

The Sommer-Zeger vitamin A supplement data

- In principle, 8 different possible values of the triple $(Z_i, W_i^{\text{obs}}, Y_i^{\text{obs}})$
- Non-compliance: $Z_i \neq W_i^{\text{obs}}$

Assignment Z_i	Vitamin Supplements W_i^{obs}	Survival Y_i^{obs}	Number of Units ($N = 23,682$)
0	0	0	74
0	0	1	11,514
1	0	0	34
1	0	1	2385
1	1	0	12
1	1	1	9663

Three types of traditional analyses

Method	Estimate	Calculation	Row Comparison
ITT	0.0026	$= \frac{2385 + 9663}{12 + 9663 + 34 + 2385} - \frac{11514}{74 + 11514}$	3, 4, 5, & 6 vs. 1 & 2
As-treated	0.0065	$= \frac{9663}{12 + 9663} - \frac{11514 + 2385}{74 + 11514 + 34 + 2385}$	5 & 6 vs. 1, 2, 3, & 4
Per-protocol	0.0052	$= \frac{9663}{12 + 9663} - \frac{11514}{74 + 11514}$	5 & 6 vs. 1 & 2

Assignment Z_i	Vitamin Supplements W_i^{obs}	Survival Y_i^{obs}	Number of Units ($N = 23,682$)
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- **Intention-to-Treat (ITT) analysis:**
control assigned v.s. treatment assigned
- **As-treated analysis:**
control received v.s. treatment received
- **Per-protocol analysis:**
control received within control assigned v.s. treatment received within treatment assigned

Non-compliance in randomized experiments

- In practice, randomized experiments are often not ideal
- Often, for ethical and logistical reasons, we cannot force all experimental units to follow the randomized treatment assignment
 - some in the treatment group refuse to take the treatment
 - some in the control group manage to receive the treatment
- Intention-to-Treat (ITT) analysis: causal effect of treatment assignment
 - ITT effect can be estimated without bias
 - ITT analysis does not yield the treatment effect
- As-treated analysis
 - comparison of the treated and untreated subjects (based on treatment received)
 - no benefit of randomization, can suffer from selection bias
- **Can we provide a better estimate?**

Setup of the framework

- Treatment assignment (randomized encouragement): $Z_i \in \{0,1\}$
- Potential treatment variables: $(W_i(0), W_i(1))$
 - $W_i(z) = 1$: would receive the treatment if $Z_i = z$
 - $W_i(z) = 0$: would not receive the treatment if $Z_i = z$
- Observed treatment received: $W_i^{\text{obs}} = W_i(Z_i)$
- In the non-compliance setting, there are two “treatment”: assignment to treatment and receipt of treatment
- Potential outcomes: $Y_i(z, w)$ potential outcome if unit is assigned to z and receive w
- Observed outcome: $Y_i^{\text{obs}} = Y_i(Z_i, W_i(Z_i))$
- We can also write the potential outcomes as $Y_i(z) = Y_i(z, W_i(z))$

Underlying assumptions

- No interference assumption for $W_i(z)$ and $Y_i(z, w)$
- Randomization of the treatment assignment
$$(Y_i(0,0), Y_i(0,1), Y_i(1,0), Y_i(1,1), W_i(0), W_i(1)) \perp Z_i$$
- We don't have
$$(Y_i(0,0), Y_i(0,1), Y_i(1,0), Y_i(1,1)) \perp W_i^{\text{obs}}$$
or
$$(Y_i(0,0), Y_i(0,1), Y_i(1,0), Y_i(1,1)) \perp W_i^{\text{obs}} | Z_i$$
We don't know why some units comply and some units don't
- Compliance can not be controlled by randomized experiment

Intention-to-treat (ITT) effects

- ITT effect on the receipt of treatment level

$$\text{ITT}_{W,i} = W_i(1) - W_i(0) \quad \text{ITT}_W = \frac{1}{N} \sum_{i=1}^N \text{ITT}_{W,i} = \frac{1}{N} \sum_{i=1}^N (W_i(1) - W_i(0))$$

- ITT effect on the outcome of primary interest

$$\text{ITT}_{Y,i} = Y_i(1, W_i(1)) - Y_i(0, W_i(0))$$

$$\text{ITT}_Y = \frac{1}{N} \sum_{i=1}^N \text{ITT}_{Y,i} = \frac{1}{N} \sum_{i=1}^N (Y_i(1, W_i(1)) - Y_i(0, W_i(0)))$$

Statistical analysis of ITT effects

- Statistical analyses of these effects follow exactly the same procedures as before

$$\widehat{\text{ITT}_W} = \bar{W}_1^{\text{obs}} - \bar{W}_0^{\text{obs}} \quad \widehat{\mathbb{V}}(\widehat{\text{ITT}_W}) = \frac{s_{W,0}^2}{N_0} + \frac{s_{W,1}^2}{N_1}$$

$$s_{W,z}^2 = \sum_{i: W_i^{\text{obs}}=z} \frac{(W_i^{\text{obs}} - \bar{W}_z^{\text{obs}})^2}{N_z - 1} = \frac{N_z}{N_z - 1} \bar{W}_z^{\text{obs}}(1 - \bar{W}_z^{\text{obs}})$$

$$\widehat{\text{ITT}_Y} = \bar{Y}_1^{\text{obs}} - \bar{Y}_0^{\text{obs}} \quad \widehat{\mathbb{V}}(\widehat{\text{ITT}_Y}) = \frac{s_{Y,1}^2}{N_1} + \frac{s_{Y,0}^2}{N_0}$$

- We can also use regression analyses
- Drawback is that it estimates 'programmatic effectiveness' instead of '**biologic efficacy**'

Principal stratification

- Stratify individuals based on their compliance status
- Four principal strata
 - Compliers (co) $(W_i(0), W_i(1)) = (0,1)$
 - Non-compliers (nc) $\begin{cases} \text{Always - takers (at)} & (W_i(0), W_i(1)) = (1, 1) \\ \text{never - takers (nt)} & (W_i(0), W_i(1)) = (0, 0) \\ \text{Defiers (df)} & (W_i(0), W_i(1)) = (1, 0) \end{cases}$
 - Principal stratification depends on latent states (potential outcomes) of units!!

			$W_i(1)$	
			0	1
		0	nt	co
$W_i(0)$	1		df	at

Principal stratification

- Can not decide which principal strata each unit belong to simply based on the observed data
 - **one-sided compliance**: control group can never receive the treatment, but treatment group may not follow the assignment

		Assignment Z_i	
		0	1
Receipt of treatment W_i^{obs}	0	nt/co	nt
	1	—	co

- In general

		Z_i	
		0	1
W_i^{obs}	0	nt/co	nt/df
	1	at/df	at/co

ITT effect decomposition

- Denote the proportion of individuals that fall into each strata as $\pi_c, \pi_a, \pi_n, \pi_d$
 - For one-sided compliance data, $\pi_a = \pi_d = 0$
- Define the average ITT effect for each strata
 - For the treatment received $\text{ITT}_{W,c}, \text{ITT}_{W,a}, \text{ITT}_{W,n}, \text{ITT}_{W,d}$
 $\text{ITT}_{W,c} = 1, \text{ITT}_{W,a} = 0, \text{ITT}_{W,n} = 0, \text{ITT}_{W,d} = -1$

- For the primary outcome $\text{ITT}_c, \text{ITT}_a, \text{ITT}_n, \text{ITT}_d$

- For the ITT effect on treatment received

$$\text{ITT}_W = \sum_{i=1}^N \text{ITT}_{W,i} = \pi_c \text{ITT}_{W,c} + \pi_a \text{ITT}_{W,a} + \pi_n \text{ITT}_{W,n} + \pi_d \text{ITT}_{W,d} = \pi_c - \pi_d$$

- For the ITT effect on primary outcome

$$\text{ITT}_Y = \sum_{i=1}^N \text{ITT}_{Y,i} = \pi_c \text{ITT}_c + \pi_a \text{ITT}_a + \pi_n \text{ITT}_n + \pi_d \text{ITT}_d$$

Instrumental variables (IV)

Assumptions for Z_i being a valid IV:

- Randomization: $Z_i \in \{0,1\}$ are randomized
- Monotonicity: no defiers $\pi_d = 0$ or $W_i(0) \leq W_i(1)$ for all i
- Exclusion restriction: instrument affects the outcome only through treatment

$$Y_i(1, w) = Y_i(0, w)$$

- For always takers

$$\text{ITT}_{Y,i} = Y_i(1, W_i(1)) - Y_i(0, W_i(0)) = Y_i(1,1) - Y_i(0,1) = 0$$

so $\text{ITT}_a = 0$

- For never takers

$$\text{ITT}_{Y,i} = Y_i(1, W_i(1)) - Y_i(0, W_i(0)) = Y_i(1,0) - Y_i(0,0) = 0$$

so $\text{ITT}_n = 0$

- For compliers

$$\text{ITT}_{Y,i} = Y_i(1, W_i(1)) - Y_i(0, W_i(0)) = Y_i(1,1) - Y_i(0,0)$$

ITT_c is the average ``biological efficacy'' of the treatment on compliers

- Relevance: $\pi_c > 0$

Instrumental variables

Assumptions of Z_i being a valid IV :

- Randomization: $Z_i \in \{0,1\}$ are randomized
- Monotonicity: no defiers $\pi_d = 0$ or $W_i(0) \leq W_i(1)$ for all i
- Exclusion restriction: instrument affects the outcome only through treatment

$$Y_i(1, w) = Y_i(0, w)$$

- Relevance: $\pi_c > 0$
- Then $\text{ITT}_W = \pi_c$ and $\text{ITT}_Y = \pi_c \text{ITT}_c + \pi_a \text{ITT}_a + \pi_n \text{ITT}_n + \pi_d \text{ITT}_d = \pi_c \text{ITT}_c$
- IV estimand: ITT_c Complier average treatment effect (CATE)

$$\text{CATE} = \text{ITT}_c = \frac{\text{ITT}_Y}{\text{ITT}_W}$$

- We can identify ITT_Y and ITT_W , so ITT_c is also identifiable
- $\text{CATE} \neq \text{ATE}$ unless ATE for noncompliers equals CATE

The monotonicity assumption

- **Monotonicity:** no defiers $\pi_d = 0$ or $W_i(0) \leq W_i(1)$ for all i
- Defiers are individuals who never follow treatment assignment no matter what treatment assignment is
- For one-sided compliance data, monotonicity is always satisfied
- Check the monotonicity assumption in general:
 - $\text{ITT}_W = \pi_c - \pi_d > 0$ if $\pi_d = 0$, so if we can reject the null that $\text{ITT}_W \geq 0$, then monotonicity assumption must fail
 - Otherwise, the monotonicity assumption is not testable
 - Need to decide whether the monotonicity assumption is reasonable or not based on domain knowledge

The exclusion restriction assumption

- **Exclusion restriction:** instrument affects the outcome only through treatment
$$Y_i(1, w) = Y_i(0, w)$$
- Double-blinding in experiments guarantees exclusion restriction
- The assumption in general is not testable, and need subject-matter knowledge to judge
- The subject-matter knowledge needed is often more subtle than that required to evaluate SUTVA

Moment-based IV estimator

- Causal estimand assuming a super population

$$\text{CATE} = \frac{\text{ITT}_Y}{\text{ITT}_W} = \frac{\mathbb{E}(Y_i(1) - Y_i(0))}{\mathbb{E}(W_i(1) - W_i(0))}$$

- Method-of-moment estimator:

$$\hat{\tau}^{iv} = \frac{\widehat{\text{ITT}}_Y}{\widehat{\text{ITT}}_W}$$

Simplification under one-sided compliance:

- As $W_i(0) \equiv 0$, we have

$$\widehat{\text{ITT}}_W = \bar{W}_1^{\text{obs}} - \bar{W}_0^{\text{obs}} = \bar{W}_1^{\text{obs}}$$

proportions of units who follow the assignment in the treated group

Result in Sommer-Zeger Vitamin Supplement data

ITT Estimates:

- $N_1 = 12 + 9663 + 34 + 2385 = 12094, N_0 = 74 + 11514 = 11588$
- $\widehat{\text{ITT}}_W = \bar{W}_1^{\text{obs}} = \frac{12+9663}{N_1} = 0.8$
- $\widehat{\text{ITT}}_Y = \frac{2385+9663}{N_1} - \frac{11514}{N_0} = 0.0026$

CATE estimate:

- $\hat{\tau}^{iv} = \frac{0.0026}{0.8} = 0.0032$

ITT	0.0026
As-treated	0.0065
Per-protocol	0.0052

- ITT estimate is biased down
- The as-protocol or as-treated estimates are possibly biased up

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Uncertainty of the CATE estimator

- Method-of-moment estimator: $\hat{\tau}^{iv} = \frac{\widehat{ITT}_Y}{\widehat{ITT}_W}$
- How to estimate the variance of $\hat{\tau}^{iv}$?
 - Estimation of \widehat{ITT}_Y and \widehat{ITT}_W are correlated because they use the same dataset
- When the number of units N is large
 - \widehat{ITT}_Y and \widehat{ITT}_W are close to the true values ITT_Y and ITT_W

$$\widehat{ITT}_Y = ITT_Y + O\left(\frac{1}{\sqrt{N}}\right), \quad \widehat{ITT}_W = ITT_W + O\left(\frac{1}{\sqrt{N}}\right)$$

- Perform Taylor expansion of $\hat{\tau}^{iv}$ at ITT_Y and ITT_W :

$$\frac{\widehat{ITT}_Y}{\widehat{ITT}_W} = \frac{ITT_Y}{ITT_W} + \frac{1}{ITT_W}(\widehat{ITT}_Y - ITT_Y) - \frac{ITT_Y}{ITT_W^2}(\widehat{ITT}_W - ITT_W) + O\left(\frac{1}{N}\right)$$

- Then

$$V(\hat{\tau}^{iv}) \approx \frac{1}{ITT_W^4} \{ ITT_W^2 V(\widehat{ITT}_Y) + ITT_Y^2 V(\widehat{ITT}_W) - 2ITT_Y ITT_W \text{Cov}(\widehat{ITT}_W, \widehat{ITT}_Y) \}$$

Uncertainty of the CATE estimator

- Another equivalent way to get the formula of $\mathbb{V}(\hat{\tau}^{iv})$ (see Section 21.2.2 of Peng's book)

- When N is large, $\widehat{\text{ITT}}_W = \text{ITT}_W + O\left(\frac{1}{\sqrt{N}}\right)$ thus (Slutsky's theorem):

$$\hat{\tau}^{iv} - \text{ITT}_c = \frac{\widehat{\text{ITT}}_Y - \text{ITT}_c \widehat{\text{ITT}}_W}{\widehat{\text{ITT}}_W} \approx \frac{\widehat{\text{ITT}}_Y - \text{ITT}_c \widehat{\text{ITT}}_W}{\text{ITT}_W}$$

- Then as $\text{ITT}_c = \frac{\text{ITT}_Y}{\text{ITT}_W}$

$$\begin{aligned}\mathbb{V}(\hat{\tau}^{iv} - \text{ITT}_c) &\approx \frac{\mathbb{V}(\widehat{\text{ITT}}_Y - \text{ITT}_c \widehat{\text{ITT}}_W)}{\text{ITT}_W^2} = \mathbb{V}(\widehat{\text{ITT}}_Y) + \text{ITT}_c^2 \mathbb{V}(\widehat{\text{ITT}}_W) - 2\text{ITT}_c \text{Cov}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) \\ &= \frac{1}{\text{ITT}_W^4} \{ \text{ITT}_W^2 \mathbb{V}(\widehat{\text{ITT}}_Y) + \text{ITT}_Y^2 \mathbb{V}(\widehat{\text{ITT}}_W) - 2\text{ITT}_Y \text{ITT}_W \text{Cov}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) \}\end{aligned}$$

- Same formula as before

Estimate the covariance

- Plug-in estimator of $\mathbb{V}(\hat{\tau}^{iv})$:

$$\widehat{\mathbb{V}}(\hat{\tau}^{iv}) \approx \frac{1}{\widehat{\text{ITT}}_W^4} \{ \widehat{\text{ITT}}_W^2 \widehat{\mathbb{V}}(\widehat{\text{ITT}}_Y) + \widehat{\text{ITT}}_Y^2 \widehat{\mathbb{V}}(\widehat{\text{ITT}}_W) - 2\widehat{\text{ITT}}_Y \widehat{\text{ITT}}_W \widehat{\text{Cov}}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) \}$$

- The covariance between $\widehat{\text{ITT}}_Y$ and $\widehat{\text{ITT}}_W$:

$$\text{Cov}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) = \text{Cov}(\bar{W}_1^{\text{obs}} - \bar{W}_0^{\text{obs}}, \bar{Y}_1^{\text{obs}} - \bar{Y}_0^{\text{obs}})$$

- We have

$$\bar{W}_1^{\text{obs}} - \bar{W}_0^{\text{obs}} = \frac{1}{N_1} \sum_{i=1}^N Z_i W_i(1) - \frac{1}{N_0} \sum_{i=1}^N (1 - Z_i) W_i(0)$$

$$\bar{Y}_1^{\text{obs}} - \bar{Y}_0^{\text{obs}} = \frac{1}{N_1} \sum_{i=1}^N Z_i Y_i(1) - \frac{1}{N_0} \sum_{i=1}^N (1 - Z_i) Y_i(0)$$

- Completely randomized experiment:

$$Z_i \perp (W_i(0), W_i(1), Y_i(1), Y_i(0))$$

- It can be shown that (condition on Z_i first)

$$\text{Cov}(\bar{W}_1^{\text{obs}} - \bar{W}_0^{\text{obs}}, \bar{Y}_1^{\text{obs}} - \bar{Y}_0^{\text{obs}}) = \frac{\text{Cov}(Y_i(1), W_i(1))}{N_1} + \frac{\text{Cov}(Y_i(0), W_i(0))}{N_0}$$

Estimate the covariance

- To estimate the covariance $\text{Cov}(Y_i(z), W_i(z))$ for $z = 0, 1$:

$$\widehat{\text{Cov}}(Y_i(z), W_i(z)) = \frac{1}{N_z - 1} \sum_{i:Z_i=z} (W_i^{\text{obs}} - \bar{W}_z^{\text{obs}})(Y_i^{\text{obs}} - \bar{Y}_z^{\text{obs}})$$

- So, the plug-in estimator is

$$\widehat{\text{Cov}}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) = \sum_{z=0}^1 \frac{\sum_{i:Z_i=z} (W_i^{\text{obs}} - \bar{W}_z^{\text{obs}})(Y_i^{\text{obs}} - \bar{Y}_z^{\text{obs}})}{N_z(N_z - 1)}$$

- 95% confidence interval of CATE: $[\hat{\tau}^{iv} - 1.96\sqrt{\hat{V}(\hat{\tau}^{iv})}, \hat{\tau}^{iv} + 1.96\sqrt{\hat{V}(\hat{\tau}^{iv})}]$

- Under one-sided compliance

- $\hat{V}(\widehat{\text{ITT}}_W) = \frac{s_{W,1}^2}{N_1} = \frac{\bar{W}_1^{\text{obs}}(1-\bar{W}_1^{\text{obs}})}{N_1-1}$ as $s_{W,0}^2 = 0$

- $\widehat{\text{Cov}}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) = \frac{\sum_{i:Z_i=1} (W_i^{\text{obs}} - \bar{W}_1^{\text{obs}})(Y_i^{\text{obs}} - \bar{Y}_1^{\text{obs}})}{N_1(N_1-1)}$

Result in Sommer-Zeger Vitamin Supplement data

ITT Estimates:

- $N_1 = 12094, N_0 = 11588$
- $\widehat{\text{ITT}}_W = \bar{W}_1^{\text{obs}} = \frac{12+9663}{N_1} = 0.8, \widehat{\text{V}}(\widehat{\text{ITT}}_W) = \frac{\bar{W}_1^{\text{obs}}(1-\bar{W}_1^{\text{obs}})}{N_1-1} = \frac{0.2*0.8}{12093} = 0.0036^2$
- $\widehat{\text{ITT}}_Y = \frac{2385+9663}{N_1} - \frac{11514}{N_0} = 0.0026, \widehat{\text{V}}(\widehat{\text{ITT}}_Y) = \sum_{z=0}^1 \frac{\bar{Y}_z^{\text{obs}}(1-\bar{Y}_z^{\text{obs}})}{N_z-1} = 0.0009^2$
- 95% CI of ITT_Y : (0.0008, 0.0044)

CATE estimate:

- $\widehat{\tau}^{iv} = \frac{0.0026}{0.8} = 0.0032$
- $\widehat{\text{Cov}}(\widehat{\text{ITT}}_W, \widehat{\text{ITT}}_Y) = -0.0000017$ (correlation -0.05)
- $\widehat{\text{V}}(\widehat{\tau}^{iv}) = 0.0012^2$
- 95% CI of CATE: (0.0010, 0.0055)

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