

Lecture 9  
Non-compliance in randomized  
experiments,  
instrumental variables  
Part I

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# 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<br>$Z_i$ | Vitamin<br>Supplements<br>$W_i^{\text{obs}}$ | Survival<br>$Y_i^{\text{obs}}$ | Number of Units<br>( $N = 23,682$ ) |
|---------------------|--|--------------------------------|-------------------------------------|
| 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<br>$Z_i$ | Vitamin<br>Supplements<br>$W_i^{\text{obs}}$ | Survival<br>$Y_i^{\text{obs}}$ | Number of Units<br>( $N = 23,682$ ) |
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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

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

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

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

- 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)
    - Always – takers (at)  $(W_i(0), W_i(1)) = (1, 1)$
    - never – takers (nt)  $(W_i(0), W_i(1)) = (0, 0)$
    - Defiers (df)  $(W_i(0), W_i(1)) = (1, 0)$
- Principal stratification depends on latent states (potential outcomes) of units!!

|          |   | $W_i(1)$ |    |
|----------|---|----------|----|
|          |   | 0        | 1  |
| $W_i(0)$ | 0 | nt       | co |
|          | 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 $W_i^{\text{obs}}$ | 0 | nt/co            | nt |
|   | 1 | –                | co |

- In general

|                    |   | $Z_i$ |       |
|--------------------|---|-------|-------|
|                    |   | 0     | 1     |
| $W_i^{\text{obs}}$ | 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  $ITT_{W,c}, ITT_{W,a}, ITT_{W,n}, ITT_{W,d}$

$$ITT_{W,c} = 1, ITT_{W,a} = 0, ITT_{W,n} = 0, ITT_{W,d} = -1$$

- For the primary outcome  $ITT_c, ITT_a, ITT_n, ITT_d$

- For the ITT effect on treatment received

$$ITT_W = \sum_{i=1}^N ITT_{W,i} = \pi_c ITT_{W,c} + \pi_a ITT_{W,a} + \pi_n ITT_{W,n} + \pi_d ITT_{W,d} = \pi_c - \pi_d$$

- For the ITT effect on primary outcome

$$ITT_Y = \sum_{i=1}^N ITT_{Y,i} = \pi_c ITT_c + \pi_a ITT_a + \pi_n ITT_n + \pi_d ITT_d$$

# 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

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

$\text{ITT}_c$  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  $ITT_W = \pi_c$  and  $ITT_Y = \pi_c ITT_c + \pi_a ITT_a + \pi_n ITT_n + \pi_d ITT_d = \pi_c ITT_c$
- IV estimand:  $ITT_c$  Complier average treatment effect (CATE)

$$CATE = ITT_c = \frac{ITT_Y}{ITT_W}$$

- **We can identify  $ITT_Y$  and  $ITT_W$ , so  $ITT_c$  is also identifiable**
- $CATE \neq ATE$  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:
  - $ITT_W = \pi_c - \pi_d > 0$  if  $\pi_d = 0$ , so if we can reject the null that  $ITT_W \geq 0$ , 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:

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

CATE estimate:

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

|              |        |
|--------------|--------|
| 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

| Assignment<br>$Z_i$ | Vitamin<br>Supplements<br>$W_i^{obs}$ | Survival<br>$Y_i^{obs}$ | Number of Units<br>( $N = 23,682$ ) |
|---------------------|---------------------------------------|-------------------------|-------------------------------------|
| 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                                |

# Uncertainty of the CATE estimator

- Method-of-moment estimator:  $\hat{t}^{iv} = \frac{\widehat{ITT}_Y}{\widehat{ITT}_W}$
- How to estimate the variance of  $\hat{t}^{iv}$ ?
  - 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  $\hat{t}^{iv}$  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

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

# 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,  $\widehat{ITT}_W = ITT_W + O\left(\frac{1}{\sqrt{N}}\right)$  thus (Slutsky's theorem):

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

- Then as  $ITT_c = \frac{ITT_Y}{ITT_W}$

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

- Same formula as before

# Estimate the covariance

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

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

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

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

- We have

$$\begin{aligned} \bar{W}_1^{obs} - \bar{W}_0^{obs} &= \frac{1}{N_1} \sum_{i=1}^N Z_i W_i(1) - \frac{1}{N_0} \sum_{i=1}^N (1 - Z_i) W_i(0) \\ \bar{Y}_1^{obs} - \bar{Y}_0^{obs} &= \frac{1}{N_1} \sum_{i=1}^N Z_i Y_i(1) - \frac{1}{N_0} \sum_{i=1}^N (1 - Z_i) Y_i(0) \end{aligned}$$

- 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)

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

# 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:  $\left[ \hat{\tau}^{iv} - 1.96\sqrt{\widehat{V}(\hat{\tau}^{iv})}, \hat{\tau}^{iv} + 1.96\sqrt{\widehat{V}(\hat{\tau}^{iv})} \right]$

- Under one-sided compliance

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

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

CATE estimate:

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

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