Some notes on RACTs

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Spring 2008

Random assignment clinical trial

- New drugs that lower cholesterol
- Recruit N people with high cholesterol
  - ½ in treatment (receive active ingredient)
  - ½ in control (placebo)
- Measure cholesterol levels before the start of treatment
- Then again after a specified time

- Let Y_i be change in cholesterol levels for person i
- Z_i=1 if the person is assigned to a treatment group
- n people in the survey and n_i be person i
- $n_1 = \Sigma_i n_i$ (# in treatment)
- $n_o = \Sigma i(1-n_i)$ (# in control)

- $\bar{Y}_1 = \bar{Y} | z_i=1$
- $\bar{Y}_0 = \bar{Y} | z_i=0$
- Impact of experiment is
- $\Delta = \bar{Y}_1 - \bar{Y}_0$
- If drug is effective, we would expect $\Delta<0$
- Δ is called the 'Intention to treat'

- Consider regression model
- $y_i = \gamma_o + z_i \gamma_1 + v_i$

- Predicted value of Y when in treatment
- $\bar{Y}_1 = \gamma_o + \gamma_1$
- Pedicted value of Y when not in treatment
- $\bar{Y}_0 = \gamma_o$

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- Notice that
- $\bar{Y}_1 - \bar{Y}_0 = \gamma_o + \gamma_1 - \gamma_o = \gamma_1 = \Delta$

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Some questions to consider?

- What does the parameter Δ identify?
- Why are we confident that Δ is an unbiased estimate when it is generated from a random assignment clinical trial?

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Imperfect Compliance

- The assignment to a treatment group is random
- The hope is that the people in the trial will take their pills
- However, not everyone complies with the experiment – some will not take their pills
- What is the maker of the drugs ultimately interested in?

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- Let x_i be mg's of active ingredient ingested daily
- What is of interest is
- $y_i = \beta_0 + \beta_1 x_i + \varepsilon_i$
- Suppose we can measure compliance or x

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- Assignment into treatment will increase x
- $x_i = \alpha_0 + z_i\alpha_1 + \mu$
- What is α_1?

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Equation of interest?

- $y_i = \beta_0 + x_i\beta_1 + \varepsilon_i$
- The parameter of interest is β_1
- The units of measure are $\beta_1 = dy/dx$
- (what happens to outcomes when we change mg's of active ingredients)

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Measure of compliance?

- $x_i = \alpha_0 + z_i\alpha_1 + \mu$
- The parameter of interest from this model is α_1
- Its units of measure are dx/dz
- "first stage relationship"

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What is estimated?

- From RACT,
- $y_i = \gamma_o + z_i \gamma_1 + v_i$
- "Intention to treat" or sometimes called reduced-form
- What does this mean?

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- mg's of usage are a function of assignment into treatment
- x=g(z)
- Outcomes (Y) are a function of compliance
- y=g(x)
- But since x is a function of z
- y=g(x(z))

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- Therefore, in the equation
- $y_i = \gamma_o + z_i \gamma_1 + v_i$
- The units of measure on γ_1 are
- dY/dz but, implicitly this is a function of two things
- dy/dz = (dy/dx)(dx/dx)

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Put this all together

- Intention to treat
- $y_i = \gamma_o + z_i \gamma_1 + v_i$
- γ_1 = dy/dz=(dy/dx)(dx/dz)
- First stage
- $x_i = \alpha_0 + z_i\alpha_1 + \mu_i$
- α_1=(dx/dz)

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- Divide ITT by 1st stage
- $\gamma_1/\alpha_1 = (dy/dx)(dx/dz)/(dx/dz) = dy/dx$

- Recall the equation of interest
- $y_i = \beta_0 + x_i\beta_1 + \varepsilon_i$
- The units of measure are $\beta_1 = dy/dx$
- So the ratio γ_1/α_1 is an estimate of β_1

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What is β_1?

- This measures the impact of x on y
- But, it is derived from those who 'comply' with the treatment
- Think of the world as having 2 groups
  - Compliers
  - Non-compliers
- The impact of z on x and z on y is determined by the compliers

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- Therefore β_1 measures the impact of 'treatment' on the 'treated'

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- In this case
- Y=birth weight in grams
- X=cigarettes per day
- Z=1 of treated, =0 otherwise

- What did treatment do to smoking?
- $x_i = \alpha_0 + z_i\alpha_1 + \mu_i$

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1st stage

- Because Z is dichotomous (1 and 0), this males it easy
- $\bar{X}_1$ = mean of X when treated (z_i =1)
  $=\alpha_0 + z_i\alpha_1 = \alpha_0 + \alpha_1$
- $\bar{X}_0$ = mean of X when not treated (z_i=0)
  $=\alpha_0 + z_i\alpha_1 = \alpha_0$
- $\bar{X}_1 - \bar{X}_0 = \alpha_1$

Table 2.—Smoking Characteristics of Control and Treatment Groups at Eighth Month of Pregnancy*

	Control Group	Treatment Group
% reporting smoking, cigarettes/day†		
N	395†	388§
0	20.0	43.0
1-5	12.7	19.1
6-10	22.0	16.2
11-20	31.4	17.8
≥20	13.9	3.9
Mean ± SD‖	12.8 ± 11.5	6.4 ± 8.7
Thiocyanate, μmole/L		
N	389	380
Mean ± SD¶	2,452 ± 1,228	2,094 ± 1,209

Z_i=0 $\bar{X}_0$=12.8 Z_i=1 $\bar{X}_1$=6.4

$\alpha_1 = \bar{X}_1 - \bar{X}_0 = 6.4 - 12.8 = -6.4$

Intention to treat

- $y_i = \gamma_o + z_i\,\gamma_1 + v_i$
- $\bar{Y}_1$ = mean of y when treated (z=1)
- $\gamma_o + z_i\,\gamma_1 = \gamma_o + \gamma_1$
- $\bar{Y}_0$ = mean of y when not treated (z=0)
- $\gamma_o + z_i\,\gamma_1 = \gamma_o$
- $\bar{Y}_1 - \bar{Y}_0 = \gamma_1$

$\bar{Y}_0$=3186 $\bar{Y}_1$=3278

Table 4.—Measurement of Status of Newborn*

	Control Group (N=438)		Treatment Group (N=429)		
	N	Mean ± SD	N	Mean ± SD	t
Primary factor					
Birth weight, g	438	3,186 ± 566	429	3,278 ± 627	2.28†
<2,500, %	438	6.9	429	6.8	...
<1,500, %	438	1.1	429	1.9	...
Other factors					
Birth length, cm	410	49.70 ± 4.16	406	50.30 ± 3.67	2.18†
Head circumference, cm	421	34.06 ± 2.44	413	34.14 ± 1.79	0.54
Apgar score (1 min)	430	8.01 ± 1.55	425	7.96 ± 1.65	0.49
<7, %	430	10.5	425	10.6	...
Apgar score (5 min)	431	9.00 ± 0.92	425	8.97 ± 1.09	0.45
<7, %	431	1.9	425	2.8	...
Gestational age, wk	436	39.09 ± 2.77	429	39.65 ± 2.77	0.22

*Includes only single, live births.
†P<.05 by Student's t test.

$\gamma_1 = \bar{Y}_1 - \bar{Y}_0 = 3278 - 3186 = -92$

Putting it all together

- $y_i = \beta_0 + x_i\beta_1 + \varepsilon_i$
- $\beta_1 = \gamma_1/\alpha_1 = -92/-6.4 = -14.4$
- Smoking an additional cigarette/day decreases the average birth weight by 14.4 grams

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- Average baby is about 3500 grams
  - 28.35 grams in an ounce
  - 3500 grams is 123.4 ounces or 7.7 lbs
- The difference between in weights for babies with non-smoking moms and pack a day smoking mon is

  (20)(-14.4) = -288 grams or -10.1 ounces

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For the next group of papers

- What is the reduced-form
- What is the intention to treat?
- What is the treatment on the treated?

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