

A Markov Compliance Behavior and Outcome Model for Causal Analysis in Longitudinal Studies

Xin Gao, Michael R. Elliott

Department of Biostatistics
University of Michigan

APHA 2009

Outline

- 1 Motivating Study
- 2 Markov Compliance Behaviors and Outcomes Model
- 3 Main Results
- 4 Conclusions

Motivating Study

- A longitudinal study enrolled 114 suicide attempters randomized to usual care or usual care + cognitive therapy.
- The Clinical outcome, Beck Depression Inventory (BDI), is a measurement of the severity of depression.
- BDI is recorded at the end of each of 4 follow-up periods (1, 3, 5, and 12 months).
- Objectives
 1. To assess the effect of current causal effect of cognitive therapy on the future compliance behavior
 2. To assess the causal effect of cognitive therapy

Motivating Study

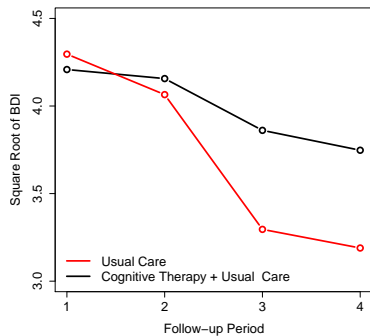


Figure: Mean of \sqrt{BDI} for the study sample.

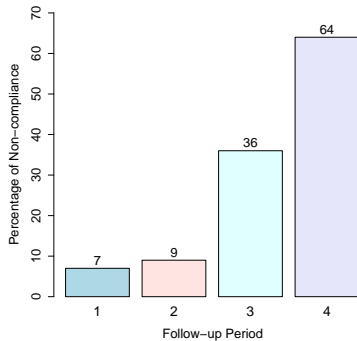


Figure: Rate of non-compliance for patients randomized to the cognitive therapy group.

Outline

- 1 Motivating Study
- 2 Markov Compliance Behaviors and Outcomes Model
- 3 Main Results
- 4 Conclusions

Research Background

- Compliance classes in the two-arm treatment trial consist of
 - **Compliers**: Subjects who take treatment if and only if assigned to it
 - **Never-takers**: Subjects who do not take treatment regardless of assignment
 - **Always-takers**: Subjects who take treatment regardless of assignment
 - **Defiers**: Subjects who take treatment if and only if assigned to control
- Compliance class, which is a pre-treatment covariate, was generalized to principal stratification.

Research Background

- Previous research focused on estimating causal effect of treatment within each compliance class
- We use the longitudinal nature of the study to estimate
 1. How treatment assignment changes the expected outcome among compliers (causal effect of treatment)
 2. How the current causal effect of treatment impacts future compliance behavior

Notation

- For subject i at follow-up time t ,
 - Z_i — Randomization assignment. $Z_i = 1$ for cognitive therapy and $Z_i = 0$ for usual care.
 - X_i — Baseline covariates.
 - $Y_{i,t}(Z_i = 1), Y_{i,t}(Z_i = 0)$ — Potential outcomes under cognitive therapy or usual care.
 - $D_{i,t}(Z_i = 1), D_{i,t}(Z_i = 0)$ — Treatment taken under assignment to cognitive therapy or usual care.
 - $C_{i,t}$ — Compliance class at time t .
Patients randomized in the usual care group cannot access cognitive therapy, therefore there are only compliers and never-takers.

$$C_{i,t} = \begin{cases} c & (\text{compliers, } D_{i,t}(Z_i = z)) \\ n & (\text{never-takers, } D_{i,t}(Z_i = 0)) \end{cases}$$

Two Key Assumptions

1. Randomization Assumption

$$Z_i \perp Y_{i,t}(1), Y_{i,t}(0), C_{i,t}, \text{ for all } i, t$$

2. Stable Unit Treatment Value Assumption

- $C_{i,t} \perp Z_j$, for $i \neq j$.
- $Y_{i,t}(1), Y_{i,t}(0) \perp Z_j, C_{j,t}$, for $i \neq j$.

Complete Data Likelihood

For subject i , the joint distribution of potential outcomes and compliance classes is

$$L(Y_{i,1}(1), Y_{i,1}(0), \dots, Y_{i,4}(1), Y_{i,4}(0), C_{i,1}, \dots, C_{i,4} | \vec{X}_i, \vec{\alpha}, \vec{\beta}, \vec{\theta}, \vec{\gamma}) \\ = f_1(C_{i,1} | X_i, \vec{\alpha}) \tag{1}$$

$$\times f_2(Y_{i,1}(1), Y_{i,1}(0) | C_{i,1}, \vec{\beta}) \tag{2}$$

$$\times \prod_{t=2}^4 f_3(C_{i,t} | C_{i,t-1}, Y_{i,t-1}(1), Y_{i,t-1}(0), \vec{\theta}) \tag{3}$$

$$\times \prod_{t=2}^4 f_4(Y_{i,t}(1), Y_{i,t}(0) | C_{i,t}, Y_{i,t-1}(1), Y_{i,t-1}(0), \vec{\gamma}) \tag{4}$$

Parametric Models for (1) and (2)

1. Compliance classes during the 1st follow up period

$$P(C_{i,1} = c | X_i, \vec{\alpha}) = \Phi(\alpha_0 + \vec{\alpha}_1^T X_i)$$

2. Potential outcomes at the end of 1st follow up period

$(Y_{i,1}(1), Y_{i,1}(0) | C_{i,1}, \vec{\beta}) \sim MVN(\mu_{i,1}, \Sigma)$, where
 $\mu_{i,1} = (\beta_1 + \beta_{c1}I(C_{i,1} = c), \beta_0 + \beta_{c0}I(C_{i,1} = c))$

$$\Sigma = \begin{pmatrix} \sigma^2 & \rho\sigma^2 \\ \rho\sigma^2 & \sigma^2 \end{pmatrix}$$

Parametric Models for (3)

3. Compliance class during each of the follow up periods 2 to 4 depends on previous compliance status, previous treatment effect, and their interaction.

$$\begin{aligned}
 & P(C_{i,t} = c | Y_{i,t-1}(1), Y_{i,t-1}(0), C_{i,t-1}, \vec{\theta}) \\
 = & \Phi(\theta_{0t} + \theta_{y0} Y_{i,t-1}(1) + \theta_y (Y_{i,t-1}(0) - Y_{i,t-1}(1)) + \\
 & \theta_c I(C_{i,t-1} = c) + \theta_{yc} I(C_{i,t-1} = c)(Y_{i,t-1}(0) - Y_{i,t-1}(1)))
 \end{aligned}$$

Parametric Models for (4)

4. Potential outcomes at the end of the follow up periods 2 to 4 follows a multivariate model as well.

$$(Y_{i,t}(1), Y_{i,t}(0) | Y_{i,t-1}(1), Y_{i,t-1}(0), C_{i,t}, \vec{\gamma}) \sim MVN(\mu_{i,t}, \Sigma)$$

$$\mu_{i,t}^T =$$

$$\begin{pmatrix} \gamma_{1t} + \gamma_{y0} Y_{i,t-1}(1) + \gamma_{y1} (Y_{i,t-1}(0) - Y_{i,t-1}(1)) + \gamma_{c1t} I(C_{i,t} = c) \\ \gamma_{0t} + \gamma_{y0} Y_{i,t-1}(1) + \gamma_{y1} (Y_{i,t-1}(0) - Y_{i,t-1}(1)) + \gamma_{c0t} I(C_{i,t} = c) \end{pmatrix}$$

$$\Sigma = \begin{pmatrix} \sigma^2 & \rho\sigma^2 \\ \rho\sigma^2 & \sigma^2 \end{pmatrix}$$

Unobservable Variables

1. Potential outcomes for the randomized arm other than the one assigned
2. Compliance classes of the subjects randomized to the usual care group

⇒ Bayesian paradigm with Markov Chain Monte Carlo becomes the natural approach.

Outline

- 1 Motivating Study
- 2 Markov Compliance Behaviors and Outcomes Model
- 3 Main Results**
- 4 Conclusions

Main Results

- Causal effect of cognitive therapy at the end of follow up period t

For compliers: $E(Y_{i,t}(1) - Y_{i,t}(0) | C_{i,t} = c)$

For never takers: $E(Y_{i,t}(1) - Y_{i,t}(0) | C_{i,t} = n)$

- Posterior means and 95% credible intervals of the causal effect of cognitive therapy on the \sqrt{BDI}

Follow up Period	Compliers	Never-takers
1	-0.6 (-1.2, -0.1)	1.5 (-0.1, 2.8)
2	-0.8 (-1.4, -0.1)	1.6 (-0.2, 3.0)
3	-1.2 (-1.9, -0.5)	0.1 (-0.9, 0.9)
4	-2.2 (-3.4, -1.1)	-0.2 (-1.0, 0.7)

Main Results

Posterior means and 95% credible intervals

- $\theta_y = 1.6$ (-0.2, 3.8)
 - Effect of a unit change in \sqrt{BDI} for **never takers** at time $t - 1$ on the compliance behavior at time t
- $\theta_y + \theta_{yc} = 2.4$ (0.1, 5.1)
 - Effect of a unit change in \sqrt{BDI} for **compliers** at time $t - 1$ on the compliance behavior at time t

Conclusions:

- The greater the causal treatment effect is at time $t - 1$, the more likely the patient will be complies to the randomization assignment during the next follow up period.
- The association is stronger for compliers at time $t - 1$.

Main Results

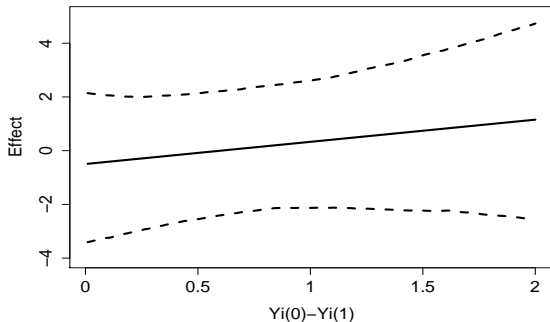


Figure: Effect of compliance in the follow up period $t - 1$ on compliance in the follow up period t

Outline

- 1 Motivating Study
- 2 Markov Compliance Behaviors and Outcomes Model
- 3 Main Results
- 4 Conclusions**

Conclusions

- The causal effect of cognitive therapy increases as time increases for compliers. At the end of the 4th follow up period, the cognitive therapy is expected to decrease the \sqrt{BDI} by 2.2.
- The more effective the cognitive therapy is at the end of the follow up period $t - 1$, the more likely the patient complies to the randomization assignment during the follow up period t .

Thank You.