Effect of Three Treatments in Reduce Alcohol Usage

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Abstract

In this report, we use data getting from a randomized trial with 314 subjects known to suffer from alcohol dependence. Subjects were assigned to three different treatment and record follow-up information, total drinks numbers and relapse. By analyzing this data, I found that for the 30 days following randomization, the effect of Treatment 3 is the best. For the 30 days between the 30^{th} and 60^{th} day follow-up, the effect of Treatment 2 is the best. Changes patterns of total drinks number in Treatment 1 and Treatment 3 group is similar and both are different from Treatment 2 group. On baseline, female has less alcohol consumption and have better treatment effect for three types of intervention. Comparing to Treatment 2 and Treatment 1, Treatment 3 have more beneficial effect after treatments have stopped.

Introduction

Alcohol consumption has been identified as an important risk factor for illness, disability, and mortality. Almost all societies that consume alcohol show related health and social problems. In fact, in the last comparative risk assessment conducted by the World Health Organization (WHO), the detrimental impact of alcohol consumption on the global burden of disease and injury was surpassed only by unsafe sex and childhood underweight status but exceeded that of many classic risk factors, such as unsafe water and sanitation, hyper-tension, high cholesterol, or

tobacco use. The industrialization and production and globalization of marketing and promotion of alcohol have increased both the amount of worldwide consumption and the harms associated with it.

Considering the above facts, a group of researchers conducted a study to compare three types of interventions and to see if these interventions were helpful in reducing alcohol dependence.

By analyzing data getting from this study, I want to find out 1) treatment effects of three types of interventions in alcohol consumption; 2) the influence of gender in alcohol consumption and treatment effects; 3) effects of three types of interventions after treatments have stopped.

Methods

1. Study description

A randomized trial was conducted on 314 subjects known to suffer from alcohol dependence. The total number of drinks consumed in the 30 days immediately prior to randomization was recorded. After the assignment of treatment, the total number of drinks consumed in the past 30 days and between 30^{th} days and 60^{th} days since the beginning of treatment were recorded.

The subjects were randomly assigned into one of three treatment groups as follows:

I. Treatment 1: Subjects were given DVD, pamphlets and other instructional materials related alcohol dependency. The subjects kept track of their daily alcohol consumption and reported the total number of drinks consumed in the last 30 days on the 30^{th} and 60^{th} day.

II. Treatment 2: Subjects were given DVD, pamphlets and other instructional materials related alcohol dependency but were also required to report the number of drinks consumed at the end of every week.

III. Treatment 3: Subjects were given DVD, pamphlets and other instructional materials related alcohol dependency but were also required to report the number of drinks consumed daily using a toll-free phone number.

The subjects were also followed up 6 months after the end of treatment. Based on an a priori set criteria, the researchers classified the subjects as having relapsed into alcohol dependence or not.

2. Statistical Analysis

In order to find out treatment effects on alcohol consumptions, relapse and influence of gender, I used data to fit generalized linear models, generalized estimating equation models(GEE), and draw plots to get results.

Results

1. Data description

After study, we get data with 314 observations for 314 subjects and 7 variables, including sid(Subject ID), Treatment, Gender, ND0(Total Number of drinks consumed in the 30 days prior to randomization), ND30(Total Number of drinks consumed in the 30 days following randomization), ND60(Total Number of drinks consumed in the 30 days between the 30^{th} and 60^{th} day follow-up) and Relapse. **Table 1** shows summary of data.

2. Treatment effects on alcohol consumption

2.1 Treatment effects in a given 30-day period

First, I'm curious about treatment effects of three types of interventions in two given 30-day period. I fitted two generalized linear models for two given 30-day period.

For the first 30 days following randomization, we have dependent variable "ND30(Total Number of drinks consumed in the 30 days prior to randomization)" which follows poisson distribution and key predictor is "Treatment". We adjust for covariates "Gender" and "ND0(Total Number of drinks consumed in the 30 days prior to randomization)" and get following model.

$$\text{Model 1: } logE[ND30] = \beta_0 + \beta_1 Treatment + \beta_2 Gender + \beta_3 ND0$$

Table 2 shows results of Model 1. After taking exponential, we can find that the total number of drinks ratio between people who get Treatment 2 and people who get Treatment 1 is 0.984 on average and the total number of drinks ratio between people who get Treatment 3 and people who get Treatment 1 is 0.670 on average. This means for the 30 days following randomization, the effect of Treatment 3 is better than that of Treatment 2 and the effect of Treatment 2 is better than that of Treatment 1.

For the 30 days between the 30th and 60th day follow-up, we have dependent variables "ND60(Total Number of drinks consumed in the 30 days between the 30th and 60th day follow-up)" which follows poisson distribution, key predictor "Treatment" and covariates "Gender", "ND0" and "ND30".

$$\text{Model 2: } logE[ND60] = \beta_0 + \beta_1 Treatment + \beta_2 Gender + \beta_3 ND0 + \beta_4 ND30$$

Table 3 shows results of Model 2. According to results above, we can find that the total number of drinks ratio between people who get Treatment 2 and people who get Treatment 1 is 0.6771 on average and the total number of drinks ratio between people who get Treatment 3 and people who get Treatment 1 is 0.7024 on average. This means for the 30 days between the 30th and 60th day follow-up, the effect of Treatment 2 is slightly better than that of Treatment 3 and the effect of Treatment 3 is better than that of Treatment 1.

2.2 Change patterns of three treatment groups

We also curious about whether the change patterns in three treatment groups are different. **Figure 1** shows how total numbers of drinks change from 30-day period prior to randomization to 30-day period between the 30th and 60th day follow-up. We can find that all treatments have significant effect on decreasing total numbers of drinks in the 30 days following randomization. But in the 30 days between the 30th and 60th day follow-up, treatment effects of Treatment 1 and Treatment 3 decrease, but Treatment 2 still shows significant treatment effect on decreasing total alcohol consumption.

I also fitted a generalized estimating equation model(GEE). Let y_{ij} be the numbers of drinks consumed in the 30 days for subject $i = 1,2,\ldots,314$ at visit $j = 0,1,2$. Assume y_{ij} follows poisson distribution.

Model 3 : $log(E[y_{ij}]) = \beta_0 + \beta_1 time_{ij} + \beta_2 treatment_{ij} + \beta_3 treatment_{ij} * time_{ij} + \beta_4 ND0.$

Table 4 shows results of Model 3. According to model results, we can find that the ratio of drinks consumed changes between ND30 and ND60 for group in Treatment 2 versus Treatment 1 is significant with value equals to 0.6884 and the ratio of drinks consumed changes between ND30

and ND60 for group in Treatment 3 versus Treatment 1 is not significant with value equals to 1.0048. So the pattern of change in the number of drinks consumed between the Treatment 1 group and Treatment 2 group is difference and the same between the Treatment 1 group and Treatment 3 group.

3. Influence of gender on alcohol consumption and treatment effects

Alcohol-use disorders are among the most disabling disease categories for the global burden of disease especially for men, so we want to know influence of gender on alcohol consumption and treatment effects.

3.1 Influence of gender on baseline alcohol consumption

First, we need to find out whether different gender have different influence on baseline alcohol consumption. I fitted a generalized linear model with dependent variable "ND0" and predictor "Gender".

$$\text{Model4: } logE[ND0] = \beta_0 + \beta_1 Gender$$

Table 5 shows results of Model 4. According to above results, we can find that confidence interval of Gender across 0, which means coefficient of Gender is significant with value equals to 0.9975. This means on average, total number drinks male consumed in baseline 30-day period is 2.712 times compared to that of female on average.

3.2 Influence of gender on treatment effects

We are also curious about whether gender influence treatment effects of three interventions, thus I fitted a generalized estimating equation model(GEE) with interaction between treatment

and gender. Let y_{ij} be the numbers of drinks consumed in the 30 days for subject $i = 1,2,\ldots,314$ at visit $j = 0,1,2$. Assume y_{ij} follows poisson distribution.

Model 5 : $log(y_{ij}) = \beta_0 + \beta_1 * time_{ij} + \beta_2 treatment_{ij} + \beta_3 treatment_{ij} * time_{ij} + \beta_4 * ND0 + \beta_5 * Gender$.

Table 6 shows results of Model 5. According to results, we can find that for Treatment 1, counts ratio of total drinks number for male versus female is 1.7132 on average, which indicates Treatment 1 has better treatment effect on female versus male. For Treatment 2, counts ratio of total drinks number for male versus female is 1.8273(1.7132*1.0666) on average, which indicates Treatment 2 has better treatment effect on female versus male. For Treatment 3, counts ratio of total drinks number for male versus female is 1.7708 on average, which indicates Treatment 2 has better treatment effect on female versus male.

Overall, treatment effects of three interventions have better effect on female versus male and the treatment effect difference of Treatment 2 between female and male is the highest.

4. Effects of three types of interventions after treatments have stopped

4.1 Treatment effects on relapse

I fitted a generalized linear model to find out the influence of three types of interventions on relapsing into alcohol dependence adjusted for “Gender” and “ND0”. Assume “Relapse” follows binomial distribution.

$$\text{Model 6 : } log\frac{P(Relapse=1)}{P(Relapse=0)} = \beta_0 + \beta_1 Treatment + \beta_2 Gender + \beta_3 ND0$$

Table 7 shows results of Model 6. As 95% confidence interval of coefficients for treatment 2 and treatment 3 do not across 0, we can conclude that treatment effects difference between treatment 2, treatment 3 versus treatment 1 are significant. The odd ratio of relapse between people in treatment 2 versus people in treatment 1 is 0.1826 and the odd ratio of relapse between people in treatment 2 versus people in treatment 1 is 0.0345. In general, treatment 3 have best treatment effect on preventing relapse and treatment effect of treatment 2 is better than treatment 1.

4.2 Beneficial effects after treatment stopped

According to **Figure 1**, we can find that for people in Treatment group 1 and 3, the treatment effects decrease in the 30 days between the 30^{th} and 60^{th} day follow-up. Total numbers of drinks consumed in the 30 days following randomization are similar to total numbers of drinks consumed in the 30 days between the 30^{th} and 60^{th} day follow-up. While total numbers of drinks consumed in 30 days keep decrease for people in Treatment group2. According to these trends, treatment 2 might be beneficial once the treatment has stopped.

As “Relapse” were recorded 6 months after the end of treatment. The probability of relapsing also indicates whether three interventions have beneficial effect after treatments have stopped.

Figure 2 shows three boxplots for probabilities of relapse in different treatment groups. According to this plot, we can find that probabilities of relapse in Treatment 1 are higher than Treatment 2 and higher than Treatment 1. Most subjects in Treatment 2 and Treatment 3 groups have relapse probabilities less than 0.5. This means Treatment 2 and Treatment 3 have beneficial effect after treatments have stopped.

Discussion

According to analysis above, we can find that for the 30 days following randomization, the effect of Treatment 3 is better than that of Treatment 2 and the effect of Treatment 2 is better than that of Treatment 1. For the 30 days between the 30^{th} and 60^{th} day follow-up, the effect of Treatment 2 is slightly better than that of Treatment 3 and the effect of Treatment 3 is better than that of Treatment 1. Changes patterns of total drinks number in Treatment 1 and Treatment 3 group is similar and both are different from Treatment 2 group. On baseline, female has less alcohol consumption and have better treatment effect for three types of intervention. Comparing to Treatment 2 and Treatment 1, Treatment 3 have more beneficial effect after treatments have stopped.

However, there are some limitations in this study. First, as there are only two follow-up 30-day period, we can only know the roughly trend of effects for three interventions. Even though Treatment 2 doesn't perform well at first, it shows a continuous effect on decreasing total drinks number and might be the best treatment in long term. Due to limited data, we cannot verify it.

For further study, we can collect more follow-up data to find out effects of different treatments. We can also collect more covariates information to have a more accurate association relationship of treatment and alcohol consumptions. Based on current data, data from other sources can also be included to do further analysis.

Reference

[1]Rehm J. The risks associated with alcohol use and alcoholism. Alcohol Res Health. 2011;34(2):135–143.

Tables and plots

Table 1 Summary of variables stratified by treatments

	Stratified by Treatment		
	Treatment1	Treatment2	Treatment3
n	106	107	101
Gender = Male (%)	52 (49.1)	62 (57.9)	57 (56.4)
ND0 (mean (SD))	125.71 (62.70)	134.08 (59.11)	131.02 (59.62)
ND30 (mean (SD))	84.78 (42.16)	89.27 (41.83)	59.69 (27.63)
ND60 (mean (SD))	83.13 (42.26)	60.26 (28.39)	58.81 (28.46)
Relapse = 1 (%)	87 (82.1)	49 (45.8)	14 (13.9)

Table 2 Results of Model 1

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	3.5442	34.6123	0.0267	3.4919	3.5964
Treatment2	-0.0156	0.9845	0.0148	-0.0446	0.0133
Treatment3	-0.4000	0.6703	0.0167	-0.4328	-0.3672
GenderMale	0.5593	1.7494	0.0395	0.4818	0.6367
ND0	0.0039	1.0039	0.0003	0.0033	0.0045

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

Table 3 Results of Model 2

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	3.4741	32.2692	0.0304	3.4144	3.5337
Treatment2	-0.3899	0.6771	0.0165	-0.4222	-0.3577
Treatment3	-0.3531	0.7025	0.0251	-0.4024	-0.3039
GenderMale	0.5568	1.7450	0.0439	0.4708	0.6427
ND0	0.0034	1.0034	0.0004	0.0026	0.0042

ND30	0.0012	1.0012	0.0005	0.0002	0.0023

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

Table 4 Results of Model 3

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	3.3012	27.1448	0.0227	3.2567	3.3456
Treatment2	0.0049	1.0049	0.0228	-0.0398	0.0497
Treatment3	-0.3769	0.6860	0.0250	-0.4259	-0.3279
time60	-0.0197	0.9805	0.0234	-0.0655	0.0261
ND0	0.0081	1.0081	0.0001	0.0078	0.0083
Treatment2:time60	-0.3733	0.6884	0.0320	-0.4360	-0.3106
Treatment3:time60	0.0048	1.0048	0.0341	-0.0620	0.0716

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

Table 5 Results of Model 4

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	4.2110	67.427	0.0102	4.1910	4.231
GenderMale	0.9975	2.712	0.0116	0.9747	1.020

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

Table 6 Results of Model 5

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	3.5519	34.8811	0.0246	3.5036	3.6003
Treatment2	-0.0656	0.9365	0.0264	-0.1174	-0.0139
Treatment3	-0.4247	0.6539	0.0287	-0.4811	-0.3684
time60	-0.0197	0.9805	0.0178	-0.0545	0.0151
ND0	0.0040	1.0040	0.0002	0.0035	0.0044
GenderMale	0.5383	1.7132	0.0346	0.4706	0.6061
Treatment2:time60	-0.3733	0.6884	0.0246	-0.4216	-0.3250
Treatment3:time60	0.0048	1.0048	0.0263	-0.0467	0.0563
Treatment2:GenderMale	0.0644	1.0666	0.0274	0.0108	0.1181
Treatment3:GenderMale	0.0330	1.0336	0.0300	-0.0257	0.0918

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

Table 7 Results of Model 6

	Estimate	Exp.Est	Std.Error	CIL	CIU
(Intercept)	1.8188	6.1646	0.5980	0.6656	3.0171
Treatment2	-1.7006	0.1826	0.3208	-2.3492	-1.0873

Treatment3	-3.3667	0.0345	0.3862	-4.1601	-2.6406
GenderMale	0.4970	1.6438	0.9073	-1.2896	2.2790
ND0	-0.0043	0.9957	0.0075	-0.0190	0.0105

CIL indicates lower bound of 95% confidence interval and CIU indicates upper bound of 95% confidence interval

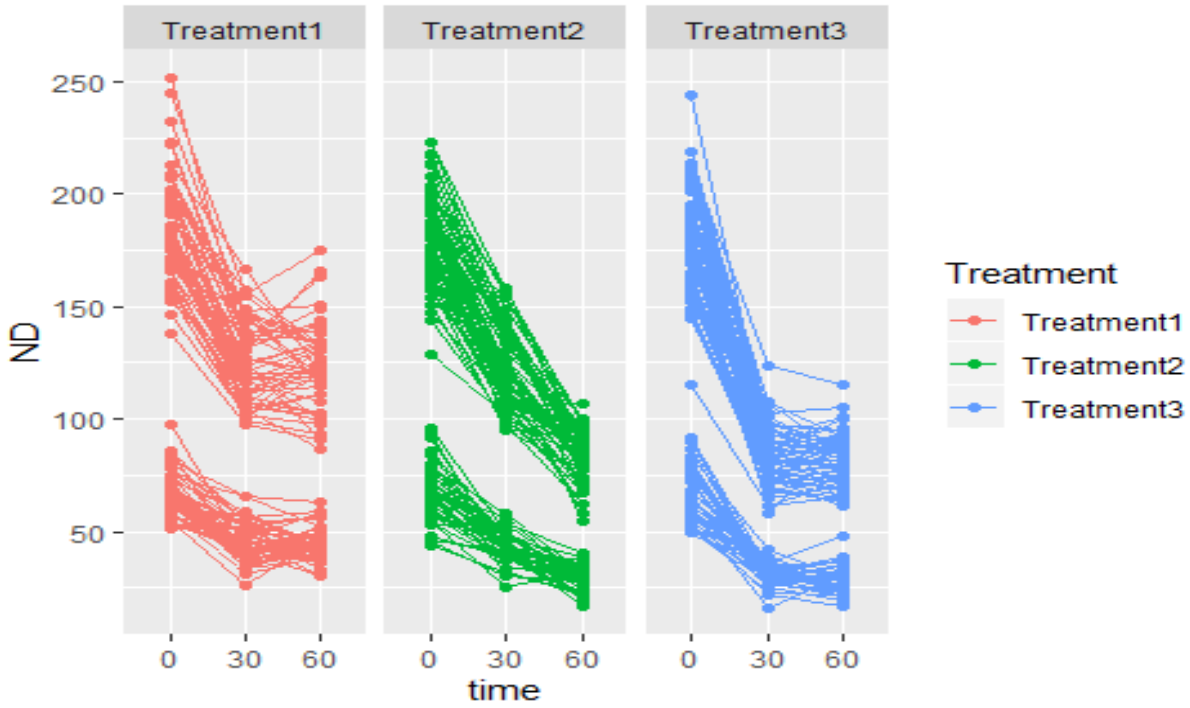

Figure 1 Changes of total numbers of drinks in 30-day periods

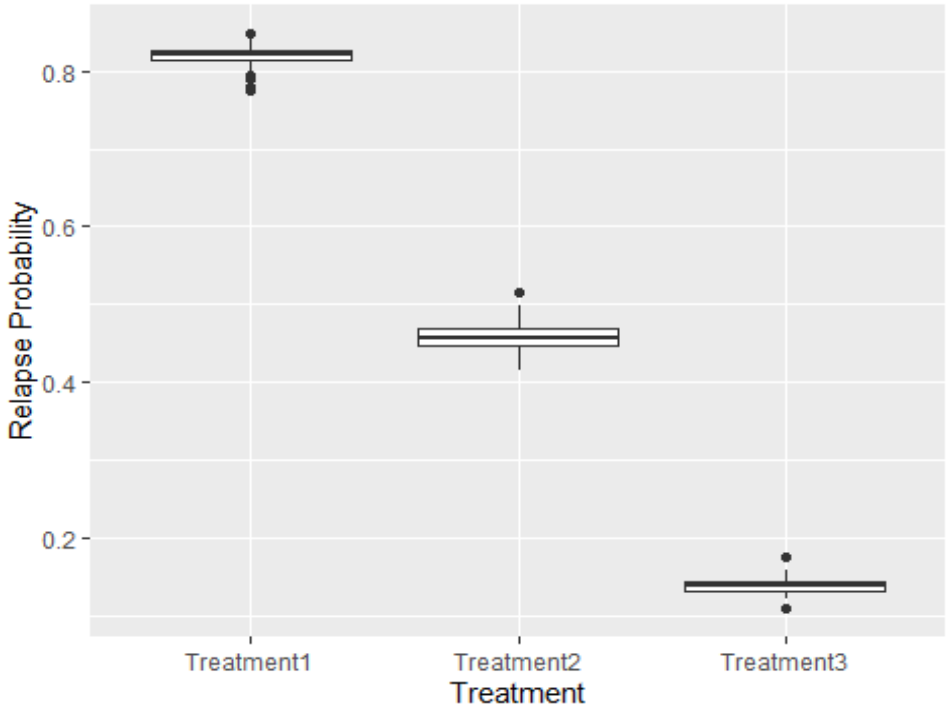

Figure 2 Probabilities of relapse in different treatment groups

Appendix

```
library(gee)
library(tidyverse)
library(geepack)
library(nlme)
library(tableone)
data = read.csv("./ALCDEP.txt", sep = "\t") %>%
  mutate(Gender = ifelse(Gender==0, "Male", "Female"),
         Gender = as.factor(Gender),
         Treatment = as.factor(Treatment),
         Relapse = as.factor(Relapse))
summary(data)
# Table1
factorVars <- c("Treatment","Gender","Relapse")
vars <- c("Gender","ND0", "ND30", "ND60", "Relapse")
tableOne <- CreateTableOne(vars = vars, strata = "Treatment", data = data,
factorVars = factorVars)
tableOne %>% kableone()
# Table2
glm.model1 = glm(ND30~Treatment+Gender+ND0, family = poisson(), data = data)
```

```r
summary(glm.model1)
confint_glm <- function(object, parm, level = 0.95, ...) {
  coef = coef(summary(object)) %>% as.data.frame()
  coef_CI = object %>% confint() %>% as.data.frame()
  table = cbind(coef, coef_CI) %>%
    mutate(Exp.Est = round(exp(Estimate),4),
           CIL = round(`2.5 %`,4),
           CIU = round(`97.5 %`,4),
           Std.Error = round(`Std. Error`,4),
           Estimate = round(Estimate,4)) %>%
    select(Estimate, Exp.Est, Std.Error, CIL, CIU)
  rownames(table) <- rownames(coef)
  return(table)
}
confint_glm(glm.model1) %>% knitr::kable()
# Table 3
glm.model2 = glm(ND60~Treatment+Gender+ND0 + ND30, family = poisson(), data =
data)
summary(glm.model2)
confint_glm(glm.model2) %>% knitr::kable()
# Figure1
seq_data = data %>%
  gather(key = "time", value = "ND", ND0:ND60) %>%
  mutate(time = str_replace(time, "ND", "")) %>%
  mutate(Gender = as.factor(Gender),
         Treatment = str_c("Treatment",Treatment))
seq_data %>%
  ggplot(aes(x = time, y = ND, group = sid, color = Treatment)) +
  geom_point()+
  geom_line()+
  facet_grid(. ~ Treatment)
# Table4
spr_data = data %>%
  gather(key = "time", value = "ND", ND30:ND60) %>%
  mutate(time = str_replace(time, "ND", "")) %>%
  mutate(Gender = as.factor(Gender),
         Treatment = as.factor(Treatment))
gee.model = geeglm(ND ~ Treatment + time + Treatment*time + ND0, id = sid,
data = spr_data, family = poisson(), corstr="ar1")
summary(gee.model)
confint_geeglm <- function(object, parm, level = 0.95, ...) {
    cc <- coef(summary(object))
    mult <- qnorm((1+level)/2)
    citab <- with(as.data.frame(cc),
                  cbind(Estimate = round(Estimate,4),
                        Exp.Est = round(exp(Estimate),4),
                        Std.Error = round(Std.err,4),
                        CIL=round(Estimate-mult*Std.err,4),
                        CIU=round(Estimate+mult*Std.err,4)))
    rownames(citab) <- rownames(cc)
```

```
    citab[parm,]
}

confint_geeglm(gee.model) %>% knitr::kable()
# Table5
glm.model3 = glm(ND0 ~ Gender, data = data, family = poisson())
summary(glm.model3)
confint_glm(glm.model3) %>% knitr::kable()
# Table6
gee.model2 = geeglm(ND ~ Treatment + time + Treatment*time + ND0 +
Gender*Treatment, id = sid, data = spr_data, family = poisson(),
corstr="ar1")
summary(gee.model2)
confint_geeglm(gee.model2)%>% knitr::kable()
# Table7
glm.model3 = glm(Relapse ~ Treatment + Gender + ND0, data = data, family =
binomial(link = "logit"))
summary(glm.model3)
confint_glm(glm.model3) %>% knitr::kable()
# Figure2
data %>%
  mutate(Response_p = predict(glm.model3,type="response"),
         Treatment = str_c("Treatment", Treatment)) %>%
  ggplot(aes(y = Response_p, x = Treatment)) +
  geom_boxplot() +
  scale_y_continuous(name="Relapse Probability")
```