Consulting Report on The Effectiveness of Intervention on Mental Distress

Naitong Chen

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Abstract

In this report, change in mental distress over time is investigated in a group of participants that received mental health intervention and another control group that did not receive any treatment. The specific problems investigated are whether the participants' mental distresses decrease over time and whether the mental health intervention is effective in reducing the level of mental distress. Due to the longitudinal nature of the study, both the linear mixed effect models and the generalized estimating equation models are used to answer the two posed questions. It is found that while the participants' mental distresses in each of the two groups decrease significantly over time, mental health interventions do not seem to have a significant effect in reducing the level of mental distress.

1 Introduction

Nowadays, mental distress has become a common social issue and is affecting the quality of life of many people. According to the American Psychiatric Association, up to nineteen (19) percent of adults in the United States experience some degree of mental illness [**apastat**]. Particularly, amid the COVID-19 pandemic, the mental well-being of the general population has received an unprecedented amount of attention [**twenge2020mental**]. It is therefore important to study the effectiveness of mental health interventions on reducing the level of mental distress.

This study investigates changes in participants' mental distress over time in an intervention group and a control group. Specifically, we try to answer whether the participants' mental distresses decrease over time and whether the mental health intervention is effective in reducing the level of mental distress.

This report begins by introducing the data recorded for this study and drawing preliminary conclusions through some explorative data analysis. The reliability of these preliminary conclusions are then checked through some model-based statistical analysis. Finally, we provide a discussion on the implication of the findings in this study. The R code used for this report can be found at `https://github.com/NaitongChen/STAT550IndividualProject`.

2 Exploratory Data Analysis

We begin by giving an overview of the data recorded in the study. A description of each variable is shown in Table 1. Note that a higher GSI score indicates a higher level of mental distress. There are five recordings of the GSI score (response) for each participant, measured respectively at the beginning of the study (0), and three (3), six (6), eighteen (18), and sixty (60) months later, as indicated by the month variable. While none of the other variables change over time, the repeated GSI measurements make this study longitudinal.

Of all 271 participants in the study, 57.6% were randomly placed in the intervention group and the remaining 42.4% were in the control group. Excluding those whose gender are unknown, 34.1% of the participants are male and 65.9% are female (Table 12). While the split between the two treatment groups is roughly balanced, there may be a slight underrepresentation of male participants in the data. However, since there are as many as 271 participants in total, there are still many participants that are male. Therefore there should not be a major impact of the unbalanced gender proportions.

SN	subject number
treatment	treatment received by each subject (1 for intervention and 2 for control)
month	measurement time (in month)
gender	gender of each subject (1 for male and 2 for female)
education	education received by each subject (in years)
GSI	Global Severity Index: an index indicating level of mental distress

Table 1: Description of all variables recorded in the study

The means and standard deviations of all continuous variables are shown in Table 2. We see that the GSI scores decreases over time while the corresponding standard deviations roughly stay consistent. Another observation is that the GSI scores are much smaller in magnitude compared to the education and month variables. This difference in scale may make the estimated effects of these explanatory variables on GSI unusually small. To aviod getting results of low interpretability, the GSI scores are scaled by a factor of ten (10) for the remainder of this report.

A common issue in longitudinal studies is missing data. As expected, with the GSI scores recorded over the span of five years, some of the response values are missing. This is common as some of the participants may have dropped out of the study for various reasons. In addition, some participants' gender and amount of education received are also missing. The count of missing values and the corresponding proportion of missing values are shown in Table 3. It is clear that more participants dropped out of the study as time went on. With the missing rates as high as 38.7%, it is important that we address the sensitivity of our subsequent analysis to these missing data in Section 3.

	education	GSI (0)	GSI (3)	GSI (6)	GSI (18)	GSI (60)
mean	13.705	1.125	1.036	0.854	0.834	0.780
sd	2.360	0.722	0.702	0.638	0.559	0.625

Table 2: Summary statistics for continuous variables

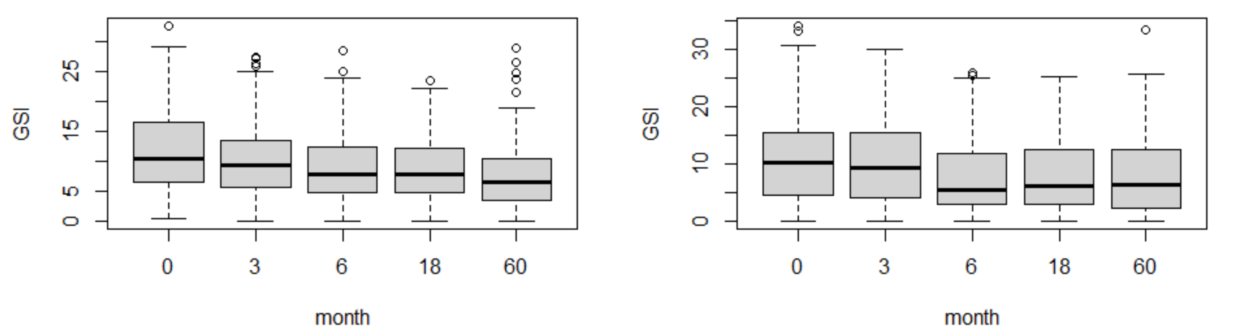
	gender	education	GSI (0)	GSI (3)	GSI (6)	GSI (18)	GSI (60)
count	4	7	10	38	52	105	98
proportion	0.015	0.026	0.037	0.140	0.192	0.387	0.362

Table 3: Missing rates of all variables in the study

2.1 Visualization of GSI

We now use side-by-side boxplots to get a rough idea of how the two main questions laid out in Section 1 can be answered. We first visualize the changes in the GSI scores over time for both the intervention group and the control group. Note that the p-values of the ANOVA and Kruskal-Wallis tests are also included in the caption for each of the two groups. In this case, ANOVA, as a generalization of the commonly known t-test, tests whether the mean GSI scores are the same across each of the five time points. Since ANOVA assumes the data to be normally distributed, which may not hold, the Kruskal-Wallis test is also conducted as a non-parametric alternative. The Kruskal-Wallis test does not make the normality assumption and is relatively robust against outliers, which can be seen to be present in Figure 1. The Kruskal-Wallis test here serves as a reference to check the reliability of the results from the ANOVA tests.

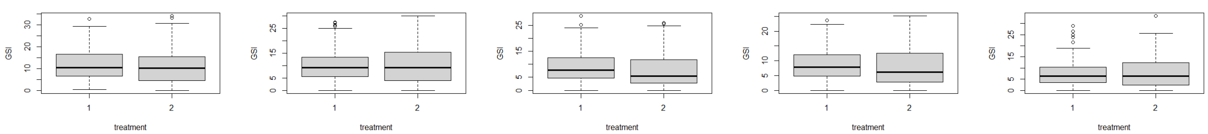
From Figure 1, we see that a downward trend of GSI over time is present in both groups. At the same time, the p-values from the ANOVA and Kruskal-Wallis tests (all < 0.021) indicate that there is moderate to strong evidence against that the mean GSI scores are the same across all five time points. It is then suggested that the participants' mental distresses in both groups decrease significantly over time.



(a) intervention group (ANOVA: 0, Kruskal-Wallis: 0) (b) control group (ANOVA: 0.021, Kruskal-Wallis: 0.006)

Figure 1: Side-by-side boxplots of the GSI scores across measurement times for each treatment group

To visualize whether the GSI scores are different between the intervention group and the control group at each of the five time points, we again use side-by-side boxplots. This is shown in Figure 2. Similarly, the p-values of two-sample t-tests and Wilcoxon tests are included in the caption to quantify the evidence we have against that the mean GSI scores are equal. Again, since the t-test assumes the data to be normally distributed and may be sensitive to outliers, the Wilcoxon test serves as a robust alternative. By the boxplots in Figure 2, the GSI scores of the two groups do not seem to differ much in any of the five times points. The p-values from the t-tests and Wilcoxon tests also indicate that, for the most part, there is no evidence against that the mean GSI scores between the two groups are the same.



(a) baseline (t-test: 0.457, Wilcoxon: 0.271) (b) 3 months (t-test: 0.995, Wilcoxon: 0.489) (c) 6 months (t-test: 0.332, Wilcoxon: 0.084) (d) 18 months (t-test: 0.405, Wilcoxon: 0.167) (e) 60 months (t-test: 0.826, Wilcoxon: 0.831)

Figure 2: Side-by-side boxplots of the GSI scores between two treatment groups across measurement times

2.2 Association between Explanatory Variables

Before summarizing our preliminary conclusions, it is worth inspecting the association between the two explanatory variables: gender and education. Since the gender variable is categorical, instead of computing the Pearson correlation coefficient, we use a side-by-side boxplot to study the association between the two variables Figure 3. Again, the p-values of t-test and Wilcoxon test are included in the caption. The plot suggests that the male participants as a group has received more education in terms of the number of years. The p-values (0.014 and 0.045) also indicates that there is moderate to strong evidence that the mean amount of education received in years among the male participants is different than that of the female participants. It is then possible that one of the two explanatory variables is enough to explain much of the variability present in the GSI scores of the corresponding participants. It is then worth inspecting whether including both of these explanatory variables leads to better fit models in Section 3.

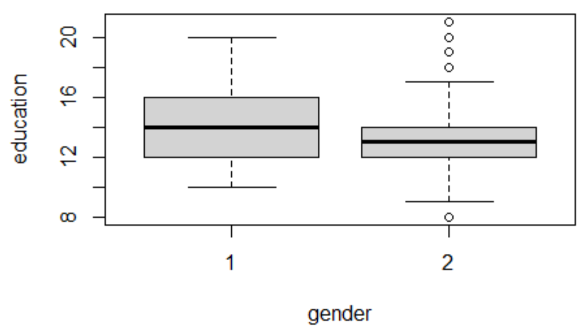


Figure 3: Side-by-side boxplot of education between the two genders (t-test: 0.014, Wilcoxon: 0.045)

2.3 Preliminary Conclusions

From the above graphical displays of the response variable, it is suggested that the participants' mental distresses in both the intervention group and the control group decrease over time. However, there does not seem to be a clear indication that the mental health intervention leads to a lower level of mental distress when compared to the control group. It is worth noting that the above preliminary conclusions are drawn without considering the gender and amount of education received of each participant. It is possible that these two explanatory variables exaggerate the effect of time or mask the effect of the mental health intervention on mental distress. Therefore, further analysis using various statistical models needs to be conducted to check the reliability of the conclusions drawn from the above exploratory data analysis.

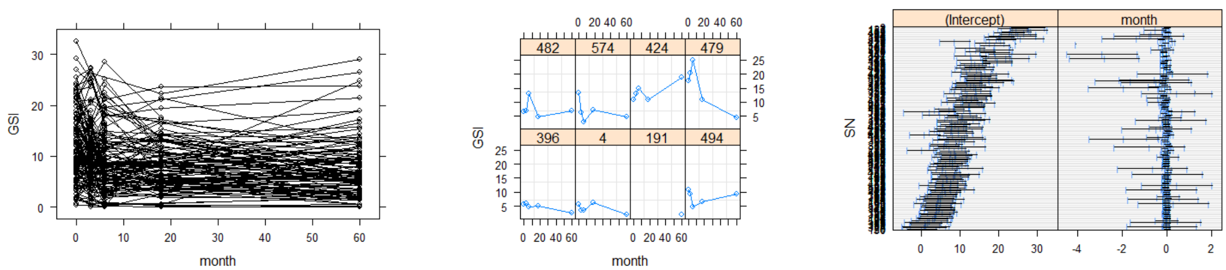
3 Model-Based Statistical Analysis

3.1 Model Selection

LRT [**wu2009mixed**]

	month	month + gender + education
month + gender	0	0.016
month + education	0.004	0

Table 4: P values of Likelihood Ratio tests between models with different covariates under the intervention group



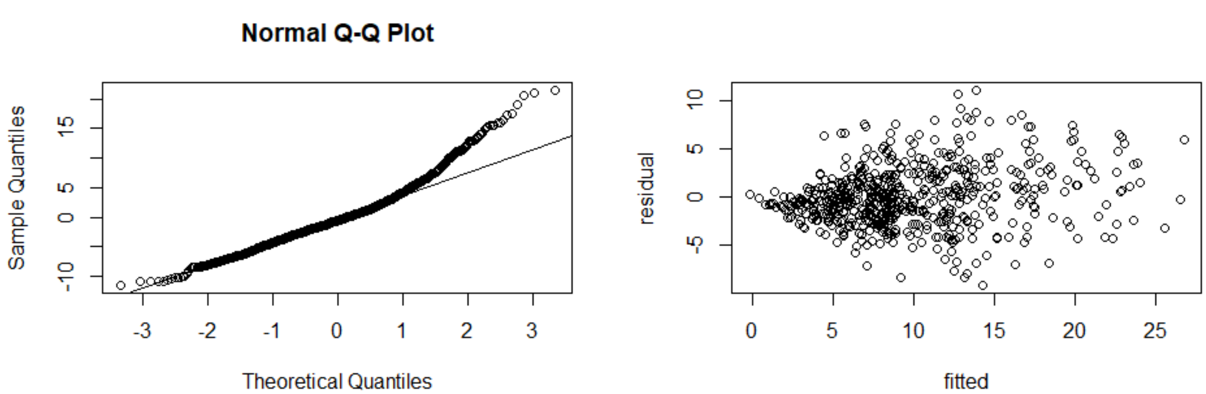
(a) trellis plot of all subjects in the intervention group (b) trellis plot of randomly selected subjects (c) confidence intervals of parameters from individual linear models

Figure 4: Diagnostic plots for selection of random effects for the intervention group

	no mixed effect	intercept	intercept + month
intercept	0	/	/
intercept + month	/	0.028	/
intercept + gender	/	0.784	/
intercept + education	/	0.998	/
intercept + month + gender	/	/	0.893
intercept + month + education	/	/	0.995

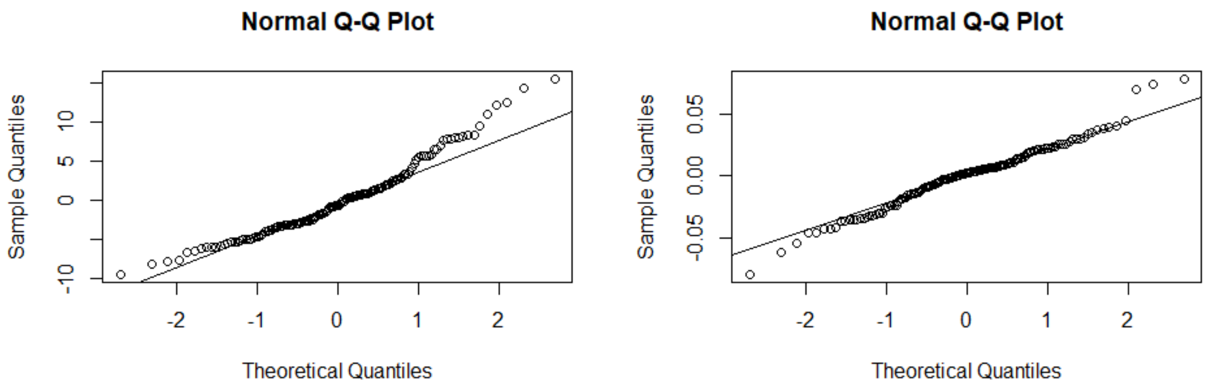
Table 5: P values of Likelihood Ratio tests between models with different mixed effects under the intervention group

3.2 Assumption Check



(a) residual QQ plot (b) fitted value vs. residual (t-test: 1, Wilcoxon: 0.204)

Figure 5: Visualizing the residuals of the LME model under the intervention group



(a) QQ plot for the random effects on the intercept (t-test: 1, Wilcoxon: 0.335)

(b) QQ plot for the random effects on the slope (t-test: 1, Wilcoxon: 0.781)

Figure 6: Visualizing the random effects under the intervention group

3.3 Analysis results

3.3.1 Changes in Mental Distress over Time

	Value	Std.Error	DF	t-value	p-value
(Intercept)	11.933	2.758	465	4.326	0.000
month	-0.047	0.008	465	-5.671	0.000
gender2	2.764	0.925	141	2.990	0.003
education	-0.249	0.190	141	-1.314	0.191

Table 6: Output of Linear Mixed Model under the intervention group

	Estimate	Naive S.E.	Naive z	Robust S.E.	Robust z
(Intercept)	11.162	2.484	4.494	2.538	4.397
month	-0.047	0.010	-4.477	0.008	-5.852
gender2	2.827	0.834	3.391	0.869	3.253
education	-0.194	0.170	-1.146	0.173	-1.125

Table 7: Output of GEE model under the intervention group

	Value	Std.Error	DF	t-value	p-value
(Intercept)	19.235	4.151	308	4.634	0.000
month	-0.020	0.008	308	-2.394	0.017
gender2	2.606	1.383	95	1.884	0.063
education	-0.822	0.273	95	-3.015	0.003

Table 8: Output of Linear Mixed Model under the control group

	Estimate	Naive S.E.	Naive z	Robust S.E.	Robust z
(Intercept)	19.267	3.433	5.613	3.229	5.967
month	-0.027	0.013	-2.019	0.010	-2.606
gender2	2.220	1.148	1.935	1.216	1.825
education	-0.809	0.225	-3.596	0.203	-3.994

Table 9: Output of GEE model under the control group

3.3.2 Effectiveness of Mental Health Intervention

	Value	Std.Error	DF	t-value	p-value
(Intercept)	15.418	2.341	774	6.586	0.000
treatment2	-0.193	0.731	238	-0.264	0.792
month	-0.037	0.006	774	-5.893	0.000
gender2	2.737	0.776	238	3.527	0.001
education	-0.516	0.157	238	-3.295	0.001

Table 10: Output of Linear Mixed Model

	Estimate	Naive S.E.	Naive z	Robust S.E.	Robust z
(Intercept)	14.685	2.046	7.176	2.053	7.154
treatment2	-0.430	0.641	-0.671	0.735	-0.586
month	-0.039	0.008	-4.666	0.006	-6.040
gender2	2.693	0.680	3.961	0.716	3.763
education	-0.455	0.136	-3.337	0.139	-3.278

Table 11: Output of GEE model

3.4 Handling Missing Data

[**little2019statistical**]

4 Conclusions and Discussion

A Summary statistics for categorical variables

	treatment		gender
intervention	0.576	male	0.341
control	0.424	female	0.659

Table 12: Summary statistics (proportion) for categorical variables

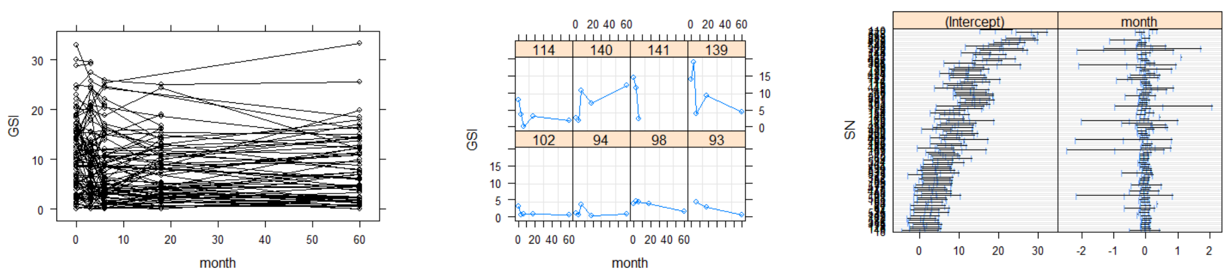
B Additional Model Selection Tables and Plots

B.1 Covariate Selection for The Control Group

	month	month + gender + education
month + gender	0	0
month + education	0	0

Table 13: P values of Likelihood Ratio tests between models with different covariates under the control group

B.2 Random Effect Selection for The Control Group



(a) trellis plot of all subjects in the control group

(b) trellis plot of randomly selected subjects

(c) confidence intervals of parameters from individual linear models

Figure 7: Diagnostic plots for selection of random effects for the control group

	no mixed effect	intercept
intercept	0	/
intercept + month	/	0.166
intercept + gender	/	0.638
intercept + education	/	0.981

Table 14: P values of Likelihood Ratio tests between models with different mixed effects under the control group

B.3 Covariate Selection for Both Groups Combined

	treatment + month	treatment + month + gender + education
treatment + month + gender	0	0
treatment + month + education	0	0

Table 15: P values of Likelihood Ratio tests between models with different covariates

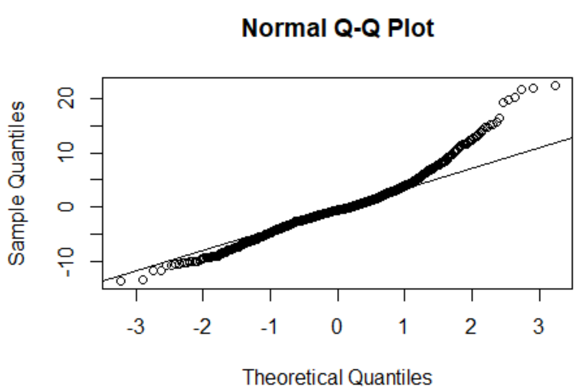
B.4 Random Effect Selection for Both Groups Combined

	no mixed effect	intercept	intercept + month
intercept	0	/	/
intercept + month	/	0.005	/
intercept + treatment	/	0.208	/
intercept + gender	/	0.487	/
intercept + education	/	0.999	/
intercept + month + treatment	/	/	0.343
intercept + month + gender	/	/	0.690
intercept + month + education	/	/	0.997

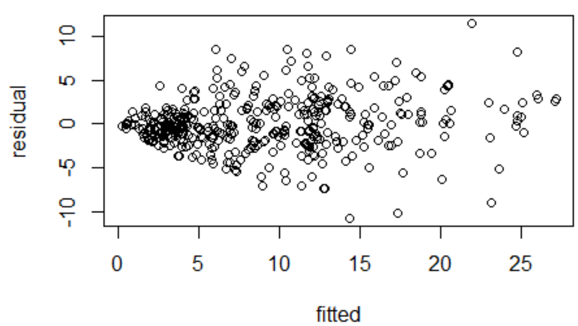
Table 16: P values of Likelihood Ratio tests between models with different mixed effects

C Additional Assumption Check Plots

C.1 Control Group



(a) residual QQ plot



(b) fitted value vs. residual (t-test: 1, Wilcoxon: 0.501)

Figure 8: Visualizing the residuals of the LME model under the control group

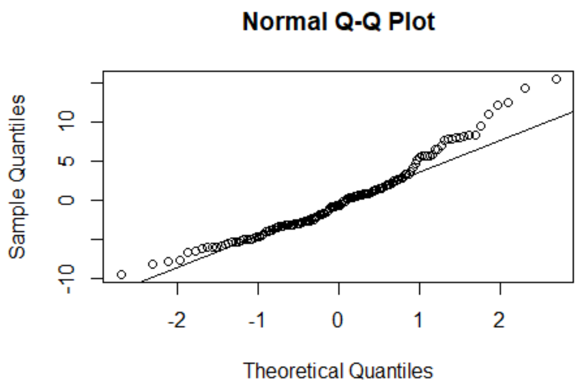
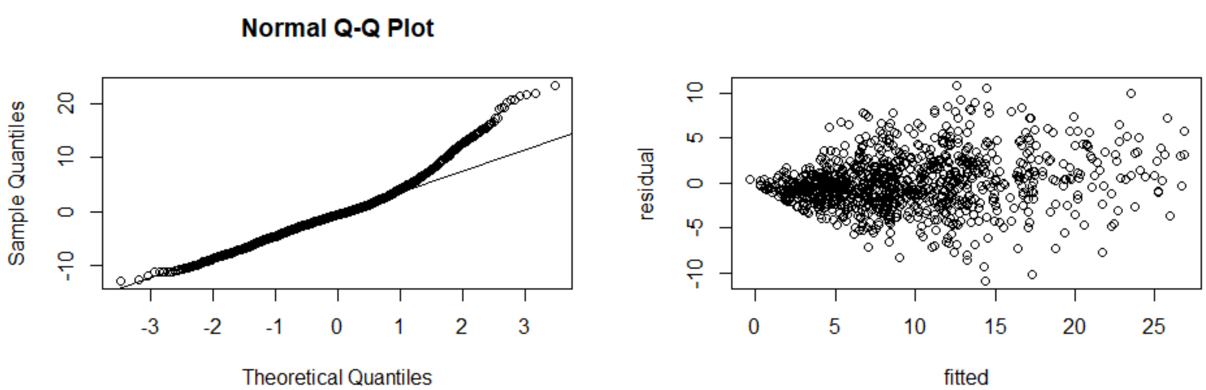


Figure 9: QQ plot for the random effects on the intercept (t-test: 1, Wilcoxon: 0.405)

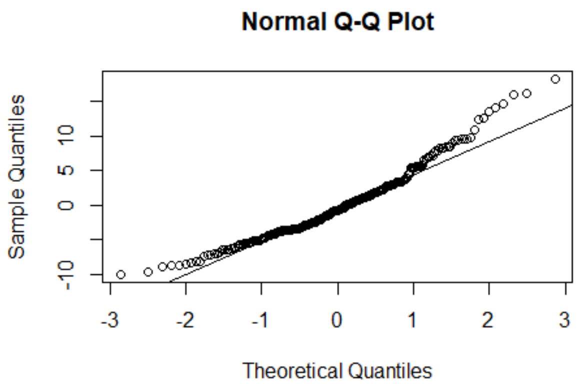
C.2 Both Groups Combined



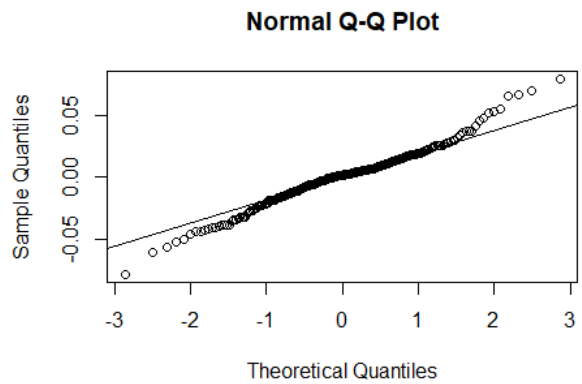
(a) residual QQ plot

(b) fitted value vs. residual (t-test: 1, Wilcoxon: 0.143)

Figure 10: Visualizing the residuals of the LME model



(a) QQ plot for the random effects on the intercept (t-test: 1, Wilcoxon: 0.207)



(b) QQ plot for the random effects on the slope (t-test: 1, Wilcoxon: 0.786)

Figure 11: Visualizing the random effects

D Pooled Analysis Results from Multiple Imputation

D.1 Intervention Group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	11.526	2.809	4.104	231.840	0.000
month	-0.045	0.011	-3.999	23.557	0.001
gender2	2.734	0.968	2.824	239.207	0.005
education	-0.222	0.199	-1.115	107.937	0.268

Table 17: Output of pooled Linear Mixed Model under the intervention group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	11.102	2.789	3.981	158.677	0.000
month	-0.048	0.012	-4.090	12.698	0.001
gender2	2.733	0.942	2.902	355.509	0.004
education	-0.188	0.198	-0.947	78.666	0.347

Table 18: Output of pooled GEE model (naive) under the intervention group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	11.102	2.692	4.124	137.732	0.000
month	-0.048	0.012	-3.939	14.758	0.001
gender2	2.733	0.908	3.009	307.277	0.003
education	-0.188	0.191	-0.985	67.256	0.328

Table 19: Output of pooled GEE model (robust) under the intervention group

D.2 Control Group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	19.695	4.011	4.910	1786.900	0.000
month	-0.032	0.012	-2.571	10.407	0.027
gender2	2.277	1.315	1.732	5112.727	0.083
education	-0.828	0.268	-3.096	802.808	0.002

Table 20: Output of pooled Linear Mixed Model under the control group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	20.598	4.119	5.000	208.709	0.000
month	-0.027	0.014	-1.999	14.750	0.064
gender2	1.821	1.328	1.371	440.506	0.171
education	-0.870	0.280	-3.103	105.337	0.002

Table 21: Output of pooled GEE model (naive) under the control group

	Estimate	Std.Error	t.value	df	P value
(Intercept)	20.598	3.695	5.575	135.062	0.000
month	-0.027	0.014	-1.949	16.329	0.069
gender2	1.821	1.302	1.399	406.382	0.163
education	-0.870	0.242	-3.590	58.813	0.001

Table 22: Output of pooled GEE model (robust) under the control group

D.3 Both Groups Combined

	Estimate	Std.Error	t.value	df	P value
(Intercept)	14.858	2.439	6.091	135.244	0.000
treatment2	-0.171	0.733	-0.234	802.931	0.815
month	-0.039	0.009	-4.167	15.060	0.001
gender2	2.604	0.829	3.139	108.962	0.002
education	-0.467	0.172	-2.715	58.348	0.009

Table 23: Output of pooled Linear Mixed Model

	Estimate	Std.Error	t.value	df	P value
(Intercept)	14.644	2.449	5.980	98.809	0.000
treatment2	-0.223	0.724	-0.307	832.892	0.759
month	-0.039	0.011	-3.678	8.707	0.005
gender2	2.591	0.810	3.197	140.824	0.002
education	-0.446	0.173	-2.582	48.524	0.013

Table 24: Output of pooled GEE model (naive)

	Estimate	Std.Error	t.value	df	P value
(Intercept)	14.644	2.356	6.215	84.692	0.000
treatment2	-0.223	0.742	-0.300	917.614	0.764
month	-0.039	0.011	-3.594	9.554	0.005
gender2	2.591	0.786	3.298	124.401	0.001
education	-0.446	0.168	-2.655	43.400	0.011

Table 25: Output of pooled GEE model (robust)

E R Code Excerpt (Intervention Group)

```r
# load packages
library(nlme)
library(gee)
library(corrplot)
library(lattice)
library(lmtest)
library(mitml)

# load data
dat = read.csv("data_dep.txt", TRUE, " ")

# removing variables not in the description
# the remaining variables are:
# subject #, treatment, gender, education, month, GSI
dat = dat[,c(1,2,3,5,10,20)]

# make SN, treatment and gender factors
dat[,2] = as.factor(dat[,2])
dat[,3] = as.factor(dat[,3])

# scale GSI by 10
dat[,6] = 10 * dat[,6]

dat = as.data.frame(dat)
colnames(dat)[2] = "treatment"
colnames(dat)[3] = "gender"
colnames(dat)[4] = "education"

# EDA

# summary statistics
# treatment
print(length(which(dat$treatment == 1)) / length(dat$SN))
print(length(which(dat$treatment == 2)) / length(dat$SN))
# gender (ignore missing)
print(length(which(dat$gender == 1)) / (length(which(dat$gender == 1)) +
                                        length(which(dat$gender == 2))))
print(length(which(dat$gender == 2)) / (length(which(dat$gender == 1)) +
                                        length(which(dat$gender == 2))))
# education
print(mean(dat$education, na.rm = T))
print(sd(dat$education, na.rm = T))
# GSI
# month = 0
print(mean(dat$GSI[which(dat$month == 0)], na.rm = T))
print(sd(dat$GSI[which(dat$month == 0)], na.rm = T))
# month = 3
print(mean(dat$GSI[which(dat$month == 3)], na.rm = T))
print(sd(dat$GSI[which(dat$month == 3)], na.rm = T))
# month = 6
print(mean(dat$GSI[which(dat$month == 6)], na.rm = T))
print(sd(dat$GSI[which(dat$month == 6)], na.rm = T))
# month = 18
```

```r
print(mean(dat$GSI[which(dat$month == 18)], na.rm = T))
print(sd(dat$GSI[which(dat$month == 18)], na.rm = T))
# month = 60
print(mean(dat$GSI[which(dat$month == 60)], na.rm = T))
print(sd(dat$GSI[which(dat$month == 60)], na.rm = T))

# missing rates
# gender
print(sum(is.na(dat[,3]))/5)
print((sum(is.na(dat[,3]))/5)/(length(dat[,1])/5))
# education
print(sum(is.na(dat[,4]))/5)
print((sum(is.na(dat[,4]))/5)/(length(dat[,1])/5))
# GSI
# month = 0
print(sum(is.na(dat$GSI[which(dat$month == 0)])))
print(sum(is.na(dat$GSI[which(dat$month == 0)]))/(length(dat[,1])/5))
# month = 3
print(sum(is.na(dat$GSI[which(dat$month == 3)])))
print(sum(is.na(dat$GSI[which(dat$month == 3)]))/(length(dat[,1])/5))
# month = 6
print(sum(is.na(dat$GSI[which(dat$month == 6)])))
print(sum(is.na(dat$GSI[which(dat$month == 6)]))/(length(dat[,1])/5))
# month = 18
print(sum(is.na(dat$GSI[which(dat$month == 18)])))
print(sum(is.na(dat$GSI[which(dat$month == 18)]))/(length(dat[,1])/5))
# month = 60
print(sum(is.na(dat$GSI[which(dat$month == 60)])))
print(sum(is.na(dat$GSI[which(dat$month == 60)]))/(length(dat[,1])/5))

# boxplots over time
dat_control = dat[which(dat$treatment == 2),]
boxplot(GSI ~ month, dat_control)
summary(aov(GSI ~ month, dat_control))
kruskal.test(GSI ~ month, dat_control)$p.value

dat_trt = dat[which(dat$treatment == 1),]
boxplot(GSI ~ month, dat_trt)
summary(aov(GSI ~ month, dat_trt))
kruskal.test(GSI ~ month, dat_trt)$p.value

# boxplots between groups
dat_t1 = dat[which(dat$month == 0),]
boxplot(GSI ~ treatment, dat_t1)
t.test(GSI ~ treatment, dat_t1)
wilcox.test(GSI ~ treatment, dat_t1)

dat_t2 = dat[which(dat$month == 3),]
boxplot(GSI ~ treatment, dat_t2)
t.test(GSI ~ treatment, dat_t2)
wilcox.test(GSI ~ treatment, dat_t2)

dat_t3 = dat[which(dat$month == 6),]
boxplot(GSI ~ treatment, dat_t3)
t.test(GSI ~ treatment, dat_t3)
wilcox.test(GSI ~ treatment, dat_t3)

dat_t4 = dat[which(dat$month == 18),]
boxplot(GSI ~ treatment, dat_t4)
t.test(GSI ~ treatment, dat_t4)
wilcox.test(GSI ~ treatment, dat_t4)

dat_t5 = dat[which(dat$month == 60),]
boxplot(GSI ~ treatment, dat_t5)
t.test(GSI ~ treatment, dat_t5)
wilcox.test(GSI ~ treatment, dat_t5)
```

```r
# association between covariates
# keep one row from each SN
inds = seq(1, length(dat[,1]), 5)
dat_single = dat[inds,]

boxplot(education ~ gender, dat_single)
t.test(education ~ gender, dat_single)
wilcox.test(education ~ gender, dat_single)

# confirmatory data analysis
# group data
dat_cc = na.omit(dat)
dat_cc = dat_cc[-c(1:21),]
dat_cc_g = groupedData(GSI ~ month | SN, data = dat_cc)
dat_cc_trt = dat_cc[which(dat_cc$treatment == 1),]
dat_cc_trt_g = groupedData(GSI ~ month | SN, data = dat_cc_trt)

# covariate selection
model_base = lm(GSI ~ month, data = dat_cc_trt)
model_d1 = lm(GSI ~ month + gender, data = dat_cc_trt)
model_d4 = lm(GSI ~ month + education, data = dat_cc_trt)
model_both = lm(GSI ~ month + gender + education, data = dat_cc_trt)

lrtest(model_base, model_d1)
lrtest(model_base, model_d4)

lrtest(model_d1, model_both)
lrtest(model_d4, model_both)

# diagnostic plots
xyplot(GSI ~ month, group = SN, data = dat_cc_trt, col="black", type="b")
plot(dat_cc_trt_g[335:370,])

fit_lm = lmList(GSI ~ month | SN, dat_cc_trt_g)
plot(intervals(fit_lm))

# selecting random effects
model_base = lm(GSI ~ month + gender + education, data = dat_cc_trt)
model_intercept = lme(GSI ~ month + gender + education,
                      random= ~ 1 | SN, data = dat_cc_trt_g,
                      control = lmeControl(opt='optim'))
model_month = lme(GSI ~ month + gender + education,
                  random= ~ month | SN, data = dat_cc_trt_g,
                  control = lmeControl(opt='optim'))

model_d1 = lme(GSI ~ month + gender + education,
               random= ~ gender | SN, data = dat_cc_trt_g,
               control = lmeControl(opt='optim'))

model_d4 = lme(GSI ~ month + gender + education,
               random= ~ education | SN, data = dat_cc_trt_g,
               control = lmeControl(opt='optim'))

model_d1d4 = lme(GSI ~ month + gender + education,
                 random= ~ gender + education | SN, data = dat_cc_trt_g,
                 control = lmeControl(opt='optim'))

model_monthd1 = lme(GSI ~ month + gender + education,
                    random= ~ month + gender | SN, data = dat_cc_trt_g,
                    control = lmeControl(opt='optim'))

model_monthd4 = lme(GSI ~ month + gender + education,
                    random= ~ month + education | SN, data = dat_cc_trt_g,
                    control = lmeControl(opt='optim'))

anova(model_intercept, model_base)

```

```r
anova(model_month, model_intercept) # winner
anova(model_d1, model_intercept)
anova(model_d4, model_intercept)

anova(model_monthd1, model_month)
anova(model_monthd4, model_month)

# fit lme
model_month = lme(GSI ~ month + gender + education,
                  random= ~ month | SN, data = dat_cc_trt_g,
                  control = lmeControl(opt='optim'))
summary(model_month)$tTable

# lme assumption check
qqnorm(model_month$residuals)
qqline(model_month$residuals)
fitted = fitted(model_month)
residual = resid(model_month)
plot(fitted, residual)
t.test(resid(model_month))
wilcox.test(resid(model_month))

qqnorm(ranef(model_month)[,1])
qqline(ranef(model_month)[,1])
t.test(ranef(model_month)[,1])
wilcox.test(ranef(model_month)[,1])

qqnorm(ranef(model_month)[,2])
qqline(ranef(model_month)[,2])
t.test(ranef(model_month)[,2])
wilcox.test(ranef(model_month)[,2])

# fit gee
gee_trt <- gee(GSI ~ month + gender + education, SN, corstr = "unstructured",
               data = dat_cc_trt)
summary(gee_trt)$coef

# multiple imputation
dat_to_impute = dat[-c(1:130),]
type_vec = c(-2, 2, 1, 1, 3, 1)
imp = jomoImpute(dat_to_impute, type = type_vec, seed = 1, m = 5)
implist <- mitmlComplete(imp)

implist_trt = implist
for (i in 1:5) {
  implist_trt[[i]] = implist[[i]][which(implist[[i]]$treatment == 1),]
}

# pool lme
lme.p1.control <- with(implist_con,
                       lme(GSI ~ month + gender + education,
                           random= ~ 1 | SN,
                           control = lmeControl(opt='optim')))
testEstimates(lme.p1.control)

# pool gee
gee.p1.treatment <- with(implist_trt,
                         gee(GSI ~ month + gender + education, SN,
                             corstr = "unstructured"))
qhat <- sapply(gee.p1.treatment, coef)

# robust
uhat <- qhat
for (i in 1:5) {
  uhat[,i] = diag(gee.p1.treatment[[i]]$robust.variance)
}

```

```
testEstimates(qhat = qhat, uhat = uhat)

# naive
uhat <- qhat
for (i in 1:5) {
  uhat[,i] = diag(gee.p1.treatment[[i]]$naive.variance)
}

testEstimates(qhat = qhat, uhat = uhat)
```