

P8131 HW8

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The data (HEALTH.xlsx) are from a randomized, controlled trial among women of childbearing age to evaluate the effects of an educational intervention. One response variable of interest is the participants self-rating of health status as either good or poor. The researchers would like to assess the effect of the intervention on self-rated health across the follow-up period, as well as whether these effects are influenced by the mothers age. There are $n = 80$ women enrolled in this trial. These data were measured at 4 points in time: randomization, 3 months, 6 months, and 12 months post-randomization.

Problem a

Evaluate the bivariate, cross-sectional relationship between randomized group assignment and participants health self-rating at the time of randomization. Interpret and discuss these findings.

Answers

Table 1: Logistic Model Coefficients

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	-0.049	0.312	-0.156	0.876	-0.668	0.567
TRTIntervention	-0.314	0.451	-0.696	0.486	-1.208	0.568

The odds ratio of self-reporting “good” health for status intervention group vs. control group at randomization (baseline) is 0.73. However, the p value for the coefficient is $0.486 > 0.05$; therefore, we are 95% confident to conclude that there is not enough evidence to support association between treatment group assignment and health status at randomization.

Problem b

Perform a longitudinal data analysis across all study follow-up visits (but not at randomization) to describe the relationship of the participants self-ratings as a function of the effects of health self-rating at the baseline, treatment group, month post randomization, and age group as predictors. Fit a GEE with unstructured correlation structure. Interpret your results.

Answers

I transformed the TIME to its original scale, that is 0, 3, 6, 12.

The GEE model we are considering is

$$\log\left\{\frac{\Pr(Y_{ij} = 1|X_{ij})}{\Pr(Y_{ij} = 0|X_{ij})}\right\} = \log(\mu_{ij}) = \beta_0 + \beta_1 \times \text{BASELINEGood}_i + \beta_2 \times \text{Intervention}_i + \beta_3 \times \text{TIME}_i + \beta_4 \times \text{AGE:25-34}_i + \beta_5 \times \text{AGE:35+}_i$$

since the study design is unbalanced plus the response is binary

$$\text{Var}(Y_{ij}|X_{ij}) = \phi v(\mu_{ij}) = \mu_{ij}(1 - \mu_{ij})$$

finally, the within-subject association among the vector of repeated responses is assumed to have an unstructured pairwise log odds ratio pattern,

$$\log \text{OR}(Y_{ij}, Y_{ik}|X_{ij}, X_{ik}) = \alpha_{jk}$$

Table 2: Parameter estimates and standard errors from GEE model

	Estimate	Naive S.E.	Naive z	Robust S.E.	Robust z
(Intercept)	-1.690	0.500	-3.380	0.523	-3.230
BASELINE	1.814	0.490	3.706	0.510	3.560
TRTIntervention	2.102	0.488	4.310	0.538	3.909
TIME	0.032	0.037	0.885	0.048	0.682
AGEGROUP25-34	1.353	0.481	2.810	0.504	2.682
AGEGROUP35+	1.421	0.798	1.781	0.784	1.813

Table 3: Working correlation estimates from GEE model

obs	2	3	4
2	1.000	0.172	0.586
3	0.172	1.000	0.201
4	0.586	0.201	1.000

Interpretations:

- The odds ratio of participants self-rating “good” vs. “poor” is 6.136, between participants self-rating “good” or “poor” at baseline, if take average among all measurements and all subjects within the same subgroup.
- The odds ratio of participants self-rating “good” vs. “poor” is 8.185, between participants in “intervention” or “control” treatment group, if take average among all measurements and all subjects within the same subgroup.

- The odds ratio of participants self-rating “good” vs. “poor” is 1.033, for per month after randomization change, if take average among all measurements and all subjects within the same subgroup.
- The odds ratio of participants self-rating “good” vs. “poor” is 3.867, between 25-34 age group vs. 15-24 age group, if take average among all measurements and all subjects within the same subgroup.
- The odds ratio of participants self-rating “good” vs. “poor” is 4.139, between 35+ age group vs. 15-24 age group, if take average among all measurements and all subjects within the same subgroup.

Problem c

Fit a generalized linear mixed effects model with subject-specific random intercepts. Interpret your estimates. How are the interpretations different from the GEE model?

Answers

The GLMM model we are considering is

$$\log\left\{\frac{\Pr(Y_{ij} = 1|b_i)}{\Pr(Y_{ij} = 0|b_i)}\right\} = \beta_0 + \beta_1 \times \text{BASELINEGood}_{ij} + \beta_2 \times \text{Intervention}_{ij} + \beta_3 \times \text{TIME}_{ij} + \beta_4 \times \text{AGE:25-34}_{ij} + \beta_5 \times \text{AGE:35+}_{ij} + b_i$$

Table 4: Estimated fixed effect for random intercept model

	Estimate	Std. Error	z value	Pr(> z)
(Intercept)	-2.581	1.042	-2.477	0.013
BASELINE	2.776	0.984	2.822	0.005
TRTIntervention	3.413	1.073	3.182	0.001
TIME	0.037	0.069	0.536	0.592
AGEGROUP25-34	2.257	1.009	2.237	0.025
AGEGROUP35+	1.982	1.381	1.435	0.151

Table 5: Covariance matrix for the estimates of fixed effects

	(Intercept)	BASELINE	TRTIntervention	TIME	AGEGROUP25-34	AGEGROUP35+
(Intercept)	1.085	-0.648	-0.712	-0.030	-0.656	-0.608
BASELINE	-0.648	0.968	0.473	0.001	0.376	0.373
TRTIntervention	-0.712	0.473	1.151	0.004	0.427	0.305
TIME	-0.030	0.001	0.004	0.005	0.001	-0.001
AGEGROUP25-34	-0.656	0.376	0.427	0.001	1.018	0.543
AGEGROUP35+	-0.608	0.373	0.305	-0.001	0.543	1.908

Table 6: Estimated random intercept

Group	Variable	vcov	sd
ID	(Intercept)	5.721	2.392

Interpretation:

- For the same subject, the odds ratio of participants self-rating “good” vs. “poor” is 1.038, for per month after randomization change, while holding other covariates fixed.
- For the same subject, The odds ratio of participants self-rating “good” vs. “poor” is 16.056, for participants self-rating “good” vs. “poor” at baseline, while holding other covariates fixed.
- For the same subject, The odds ratio of participants self-rating “good” vs. “poor” is 30.363, for participants in “intervention” vs. “control” treatment group, while holding other covariates fixed.

- For the same subject, The odds ratio of participants self-rating “good” vs. “poor” is 9.55, for participants in 25-34 age group vs. 15-24 age group, while holding other covariates fixed.
- For the same subject, The odds ratio of participants self-rating “good” vs. “poor” is 7.259, for participants in 35+ age group vs. 15-24 age group, while holding other covariates fixed.

Difference between the GEE and GLMM parameter interpretations:

- GEE is a marginal model focus on inferences about the study population.
- GLMM focus on inference about individuals.
- The parameters in GLMM measure the change in expected value of response while holding other covariates and *random effect* constant. On the contrary, the parameters in GEE measures the change in expected value of response, for *sub-populations* defined by fixed and known covariate values.

Appendix

```
knitr::opts_chunk$set(echo = F,
                      message = F,
                      warning = F,
                      comment = "")

library(tidyverse)
library(readxl)
library(gee)
library(lme4)
library(nlme)
health.df = read_excel("./HW8-HEALTH.xlsx") %>%
  rename(TRT = TXT) %>%
  mutate(TRT = as.factor(TRT),
         HEALTH = as.numeric(HEALTH == "Good"),
         TIME = as.integer(TIME))
randomized.df = health.df %>% filter(TIME == 1)
randomized.fit = glm(HEALTH ~ TRT,
                    data = randomized.df,
                    family = binomial(link = "logit"))
randomized.fit %>% broom::tidy(conf.int = T) %>% knitr::kable(digits = 3, caption = "Logistic Model Coe-
#randomized.fit %>% broom::glance() %>% knitr::kable(caption = "Logistic Model Goodness-of-Fit statisti
# remove the participants with randomization only, which is 108 and 115
health.lda = health.df %>%
  filter(!ID %in% names(which(table(health.df$ID) == 1)))
health.baseline = subset(health.lda, TIME == "1")
health.lda$BASELINE = rep(health.baseline$HEALTH, as.numeric(table(health.lda$ID)))
health.lda$TIME = health.lda$TIME - 1
health.lda = subset(health.lda, TIME > 0)
health.lda$TIME = case_when(health.lda$TIME == 1 ~ 3,
                           health.lda$TIME == 2 ~ 6,
                           health.lda$TIME == 3 ~ 12)

gee.fit = gee(HEALTH ~ BASELINE + TRT + TIME + AGEGROUP,
             data = health.lda,
             id = ID,
             family = "binomial",
```

```

      corstr = "unstructured",
      scale.fix = TRUE,
      scale.value = 1,

    )

gee.sum = summary(gee.fit)
gee.sum$coefficients %>% knitr::kable(digits = 3, caption = "Parameter estimates and standard errors fr
data.frame(gee.sum$working.correlation) %>% mutate(obs = c("2", "3","4")) %>% select(obs,everything()) %
glmm.fit = glmer(HEALTH ~ BASELINE + TRT + TIME + AGEGROUP + (1 | ID),
  data = health.lda,
  family = binomial)
glmm.sum = summary(glmm.fit)
glmm.sum$coefficients %>% knitr::kable(digits = 3, caption = "Estimated fixed effect for random intercep
as.data.frame(as.matrix(glmm.sum$vcov)) %>% knitr::kable(digits = 3, caption = "Covariance matrix for t
as.data.frame(glmm.sum$varcor) %>% select(-var2) %>% knitr::kable(digits = 3, caption = "Estimated rand

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