Bios 767 Homework 5

Problem 13.3.0

Table 1 presents simple descriptive statistics for the data being used. Based on this table, we see that more subjects reported a shorter time to fall asleep 2 weeks after follow-up than they did at baseline in both the placebo and hypnotic drug treatment groups.

Table 1: Reported time to fall asleep (in minutes) over the duration of the study for both treatment groups.

		Reported Time (in minutes)			
Treatment Group (N)	Time	< 20	20-30	30-60	> 60
Placebo (120)	Baseline	14	20	35	51
	2-week follow-up	31	29	35	25
Hypnotic Drug (119)	Baseline	12	20	40	47
	2-week follow-up	40	49	19	11

Problem 13.3.1

Using generalized estimating equations with a "working independence" assumption for the within-subject association, we fit a proportional odds model of the following form:

$$\log\left\{\frac{\Pr(Y_{ij} \leq k)}{\Pr(Y_{ij} > k)}\right\} = \alpha_k + \beta_1 Trt_i + \beta_2 Time_{ij} + \beta_3 Trt_i Time_{ij},$$

$$\text{where } Trt_i = \begin{cases} 1 & \text{if Hypnotic Drug} \\ 0 & \text{if Placebo} \end{cases}, \; Time_{ij} = \begin{cases} 1 & \text{if 2-week follow-up } (j = 1) \\ 0 & \text{if Baseline } (j = 0) \end{cases},$$

Y_{ij} is the i^{th} subject's reported time (in minutes) to fall asleep at occasion j,

$$k = \begin{cases} 1 & \text{if } < 20 \text{ minutes} \\ 2 & \text{if 20-30 minutes} \\ 3 & \text{if 30-60 minutes} \\ 4 & \text{if } > 60 \text{ minutes} \end{cases}, \text{ and } i = 1, ..., 239.$$

Parameter estimates are $\hat{\alpha}_1 = -2.267, \hat{\alpha}_2 = -0.9515, \hat{\alpha}_3 = 0.3517, \hat{\beta}_1 = 0.0336, \hat{\beta}_2 = 1.038, \text{and } \hat{\beta}_3 = 0.7078.$

Problem 13.3.2

$\beta_2 = \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i1} = 1)\} - \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i0} = 0)\} = (\alpha_k + \beta_2) - (\alpha_k)$
$\implies \hat{\beta}_2 = (\hat{\alpha}_k + \hat{\beta}_2) - \hat{\alpha}_k = 1.038.$

Relative to baseline, the log odds of a favorable response at 2 weeks has increased by $\hat{\beta}_2 = 1.038$ for the placebo group.

We can also interpret $\hat{\beta}_2$ as the log of the odds ratio of a more favorable response at week 2 relative to baseline for patients receiving placebo (calculation done in Problem 13.3.5).

Problem 13.3.3

$$
\begin{aligned}
\beta_3 &= \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 1, Time_{i1} = 1)\} - \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 1, Time_{i0} = 0)\} \\
&\qquad - \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i1} = 1)\} + \text{logit}\{\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i0} = 0)\} \\
&= \log\left\{\frac{odds(\Pr(Y_{ij} \le k \mid Trt_i = 1, Time_{i1} = 1))}{odds(\Pr(Y_{ij} \le k \mid Trt_i = 1, Time_{i0} = 0))}\right\} \\
&\qquad - \log\left\{\frac{odds(\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i1} = 1))}{odds(\Pr(Y_{ij} \le k \mid Trt_i = 0, Time_{i0} = 0))}\right\} \\
&= \log\left\{\frac{\exp(\alpha_k + \beta_1 + \beta_2 + \beta_3)}{\exp(\alpha_k + \beta_1)}\right\} - \log\left\{\frac{\exp(\alpha_k + \beta_2)}{\exp(\alpha_k)}\right\} \\
\implies \hat{\beta}_3 &= \log\left\{\frac{\exp(\hat{\alpha}_k + \hat{\beta}_1 + \hat{\beta}_2 + \hat{\beta}_3)}{\exp(\hat{\alpha}_k + \hat{\beta}_1)}\right\} - \log\left\{\frac{\exp(\hat{\alpha}_k + \hat{\beta}_2)}{\exp(\hat{\alpha}_k)}\right\} = 0.7078.
\end{aligned}
$$

We can interpret $\hat{\beta}_3 = 0.7078$ as the difference in the log odds ratio of a more favorable response at week 2 compared to baseline between patients receiving the hypnotic drug and patients receiving the placebo drug.

Problem 13.3.4

We will construct a test of the null hypothesis of no effect of treatment on changes in the cumulative log odds of response. We can rewrite our null hypothesis as $H_0 : \beta_1 = \beta_3 = 0$, or $H_0 : L\beta = 0$, where $L = \begin{bmatrix} 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$ and $\beta = [\alpha_1, \alpha_2, \alpha_3, \beta_1, \beta_2, \beta_3]^T$. Under H_0, a Wald test of this hypothesis yields a test statistic $X^2 = 12.47 \sim\ \chi^2_2$. At a 5% level of significance, we reject the null hypothesis ($p = 0.0020$) and conclude that treatment appears to have a significant effect on the cumulative log odds of favorable response.

Problem 13.3.5

The odds ratio of a more favorable response at week 2 relative to baseline for patients receiving placebo is given by

$$\frac{\exp(\text{logit}\{\Pr(Y_{ij} \leq k \mid Trt_i = 0, Time_{i1} = 1)\})}{\exp(\text{logit}\{\Pr(Y_{ij} \leq k \mid Trt_i = 0, Time_{i0} = 0)\})} = \frac{\exp(\alpha_k + \beta_2)}{\exp(\alpha_k)} = \exp(\beta_2).$$

An estimate of this odds ratio is therefore $\exp(\hat{\beta}_2) = \exp(1.038) = 2.824$.

Problem 13.3.6

The odds ratio of a more favorable response at week 2 relative to baseline for patients receiving the hypnotic drug is given by

$$\frac{\exp(\text{logit}\{\Pr(Y_{ij} \leq k \mid Trt_i = 1, Time_{i1} = 1)\})}{\exp(\text{logit}\{\Pr(Y_{ij} \leq k \mid Trt_i = 1, Time_{i0} = 0)\})} = \frac{\exp(\alpha_k + \beta_2 + \beta_3)}{\exp(\alpha_k)} = \exp(\beta_2 + \beta_3).$$

An estimate of this odds ratio is therefore $\exp(\hat{\beta}_2 + \hat{\beta}_3) = \exp(1.038 + 0.7078) = 5.731$.

Problem 13.3.7

We want to find $F_{i1} \equiv \Pr(Y_{ij} \leq 1 \mid Trt_i = 1, Time_{i1} = 1)\}) = \Pr(Y_{ij} = 1 \mid Trt_i = 1, Time_{i1} = 1)\})$. Define $\eta_{i1} \equiv \alpha_1 + \beta_1 + \beta_2 + \beta_3$.

$$\text{logit}\{F_{i1}\} = \log\left\{\frac{F_{i1}}{1-F_{i1}}\right\} = \eta_{i1} \implies \frac{F_{i1}}{1-F_{i1}} = \exp(\eta_{i1}) \implies F_{i1} = \exp(\eta_{i1})[1-F_{i1}]$$

$$\implies F_{i1} = \exp(\eta_{i1}) - F_{i1}\exp(\eta_{i1}) \implies F_{i1} + F_{i1}\exp(\eta_{i1}) = \exp(\eta_{i1}) \implies F_{i1} = \frac{\exp(\eta_{i1})}{1+\exp(\eta_{i1})}$$

Therefore, the estimated probability that a patient receiving the hypnotic drug reports falling asleep in less than 20 minutes (i.e. the estimated probability of response level 1) at week 2 is $\hat{F}_{i1} = \frac{\exp(\hat{\eta}_{ij})}{1+\exp(\hat{\eta}_{ij})} = \frac{\exp(\hat{\alpha}_1+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)}{1+\exp(\hat{\alpha}_1+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)} = \frac{\exp(-2.267+0.0336+1.038+0.7078)}{1+\exp(-2.267+0.0336+1.038+0.7078)} = 0.3805$.

Problem 13.3.8

We will first find $F_{i3} \equiv \Pr(Y_{ij} \leq 3 \mid Trt_i = 1, Time_{i1} = 1)\})$ and $F_{i2} \equiv \Pr(Y_{ij} \leq 2 \mid Trt_i = 1, Time_{i1} = 1)\})$ Define $\eta_{i3} \equiv \alpha_3 + \beta_1 + \beta_2 + \beta_3$ and $\eta_{i2} \equiv \alpha_2 + \beta_1 + \beta_2 + \beta_3$.

Using the same calculations as done in Problem 13.3.7, we can obtain $F_{i3} = \frac{\exp(\eta_{i3})}{1+\exp(\eta_{i3})}$ and $F_{i2} = \frac{\exp(\eta_{i2})}{1+\exp(\eta_{i2})}$.

Then $\Pr(Y_{ij} = 3 \mid Trt_i = 1, Time_{i1} = 1)\}) = F_{i3} - F_{i2} = \frac{\exp(\eta_{i3})}{1+\exp(\eta_{i3})} - \frac{\exp(\eta_{i2})}{1+\exp(\eta_{i2})}$.

The estimated probability that patients receiving the hypnotic drug report falling asleep in 30-60 minutes (i.e. the estimated probability of response level 3) is $\hat{F}_{i3} - \hat{F}_{i2} = \frac{\exp(\hat{\eta}_{i3})}{1+\exp(\hat{\eta}_{i3})} - \frac{\exp(\hat{\eta}_{i2})}{1+\exp(\hat{\eta}_{i2})} = \frac{\exp(\hat{\alpha}_3+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)}{1+\exp(\hat{\alpha}_3+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)} - \frac{\exp(\hat{\alpha}_2+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)}{1+\exp(\hat{\alpha}_2+\hat{\beta}_1+\hat{\beta}_2+\hat{\beta}_3)} = \frac{\exp(0.3517+0.0336+1.038+0.7078)}{1+\exp(0.3517+0.0336+1.038+0.7078)} - \frac{\exp(-0.9515+0.0336+1.038+0.7078)}{1+\exp(-0.9515+0.0336+1.038+0.7078)} = 0.8939 - 0.6959 = 0.1980$.