The data are from a longitudinal clinical trial of contracepting women. In this trial women received an injection of either 100 mg or 150 mg of depot-medroxyprogesterone acetate (DMPA) on the day of randomization and three additional injections at 90-day intervals. There was a final follow-up visit 90 days after the fourth injection, i.e., one year after the first injection.

Throughout the study each woman completed a menstrual diary that recorded any vaginal bleeding pattern disturbances. The diary data were used to determine whether a women experienced amenorrhea, the absence of menstrual bleeding for a specified number of days.

A total of 1151 women completed the menstrual diaries and the diary data were used to generate a binary sequence for each woman according to whether or not she had experienced amenorrhea in the four successive three month intervals.

Reference: Machin D, Farley T, Busca B, Campbell M and d'Arcangues C. (1988). *Assessing changes in vaginal bleeding patterns in contracepting women*. **Contraception**, 38, 165-179.

**proc** **print** data = BIOS755.Amenorrhea (obs=**10**);

**run**;

|  |
| --- |
| The SAS System |

| **Obs** | **ID** | **TRT** | **TIME** | **Y** | **Ctime** | **prevy** |
| --- | --- | --- | --- | --- | --- | --- |
| **1** | 1 | 0 | 1 | 0 | 1 | . |
| **2** | 1 | 0 | 2 | . | 2 | 0 |
| **3** | 1 | 0 | 3 | . | 3 | . |
| **4** | 1 | 0 | 4 | . | 4 | . |
| **5** | 2 | 0 | 1 | 0 | 1 | . |
| **6** | 2 | 0 | 2 | . | 2 | 0 |
| **7** | 2 | 0 | 3 | . | 3 | . |
| **8** | 2 | 0 | 4 | . | 4 | . |
| **9** | 3 | 0 | 1 | 0 | 1 | . |
| **10** | 3 | 0 | 2 | . | 2 | 0 |

**Below, we’ll use a weighted GEE to analyze the data:**

**First we create a version of the data with the lagged outcome and a second time variable.**

**data** BIOS755.Amenorrhea;

set BIOS755.Amenorrhea;

Ctime = time;

prevy = lag(y);

**run**;

**Below the missmodel command is what estimates the weights.**

**For the weight model we are using categorical time (profile analysis), for the actual model we’re using continuous time. This is why we needed two time variables.**

ods graphics on;

**proc** **gee** data=BIOS755.Amenorrhea desc plots=histogram;

class ID Ctime;

missmodel Ctime Prevy trt trt\*Prevy / type=obslevel;

model Y = Time trt Time\*Time trt\*Time trt\*Time\*Time / dist=bin;

repeated subject=ID / within=Ctime corr=cs;

**run**;

This runs the following model:

which is used to estimate

| **Model Information** | | | |
| --- | --- | --- | --- |
| **Data Set** | BIOS755.AMENORRHEA |  | y |
| **Distribution** | Binomial |  |  |
| **Link Function** | Logit |  |  |
| **Dependent Variable** | Y |  |  |

|  |  |
| --- | --- |
| **Number of Observations Read** | 4604 |
| **Number of Observations Used** | 3616 |
| **Number of Events** | 1231 |
| **Number of Trials** | 3616 |
| **Number of Missing Values** | 988 |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 1151 | 1 2 3 4 5 6 7 8 9 10 …. 77 78 79 80 81 82 83 84 85 86 87 ... |
| **Ctime** | 4 | 1 2 3 4 |

| **Response Profile** | | |
| --- | --- | --- |
| **Ordered Value** | **Y** | **Total Frequency** |
| **1** | 1 | 1231 |
| **2** | 0 | 2385 |

|  |
| --- |
| ***PROC GEE is modeling the probability that Y='1'.*** |

| **GEE Model Information** | |
| --- | --- |
| **Correlation Structure** | Exchangeable |
| **Within-Subject Effect** | Ctime (4 levels) |
| **Subject Effect** | ID (1151 levels) |
| **Number of Clusters** | 1151 |
| **Clusters With Missing Values** | 437 |
| **Correlation Matrix Dimension** | 4 |
| **Maximum Cluster Size** | 4 |
| **Minimum Cluster Size** | 1 |

| **Missing Data Patterns** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Occasion** | | | | **Freq** | **Percent** |
| **1** | **2** | **3** | **4** |
| **1** | X | X | X | X | 714 | 62.03 |
| **2** | X | X | X | . | 84 | 7.30 |
| **3** | X | X | . | . | 155 | 13.47 |
| **4** | X | . | . | . | 198 | 17.20 |

| **Exchangeable Working Correlation** | |
| --- | --- |
| **Correlation** | 0.3949 |

| **Parameter Estimates for Response Model** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **with Empirical Standard Error Estimates** | | | | | | |
| **Parameter** | **Estimate** | **Standard Error** | **95% Confidence Limits** | | **Z** | **Pr > |Z|** |
| **Intercept** | -2.0381 | 0.2484 | -2.5251 | -1.5512 | -8.20 | <.0001 |
| **TIME** | 0.5453 | 0.2117 | 0.1303 | 0.9603 | 2.58 | 0.0100 |
| **TRT** | -0.4296 | 0.3540 | -1.1234 | 0.2643 | -1.21 | 0.2250 |
| **TIME\*TIME** | -0.0037 | 0.0405 | -0.0831 | 0.0757 | -0.09 | 0.9275 |
| **TRT\*TIME** | 0.6621 | 0.3021 | 0.0700 | 1.2542 | 2.19 | 0.0284 |
| **TRT\*TIME\*TIME** | -0.1264 | 0.0577 | -0.2395 | -0.0134 | -2.19 | 0.0284 |

| **Parameter Estimates for Missingness Model** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Parameter** |  | **Estimate** | **Standard Error** | **95% Confidence Limits** | | **Z** | **Pr > |Z|** |
| **Intercept** |  | 2.3967 | 0.1438 | 2.1149 | 2.6785 | 16.67 | <.0001 |
| **Ctime** | 1 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | . | . |
| **Ctime** | 2 | -0.7286 | 0.1439 | -1.0106 | -0.4466 | -5.06 | <.0001 |
| **Ctime** | 3 | -0.5919 | 0.1469 | -0.8798 | -0.3040 | -4.03 | <.0001 |
| **Ctime** | 4 | 0.0000 | 0.0000 | 0.0000 | 0.0000 | . | . |
| **prevy** |  | -0.4514 | 0.1619 | -0.7687 | -0.1341 | -2.79 | 0.0053 |
| **TRT** |  | 0.0680 | 0.1313 | -0.1893 | 0.3253 | 0.52 | 0.6046 |
| **prevy\*TRT** |  | -0.2381 | 0.2196 | -0.6685 | 0.1923 | -1.08 | 0.2782 |



**Comparing with the complete data analysis**

**proc** **gee** data=BIOS755.Amenorrhea desc plots=histogram;

class ID Ctime;

model Y = Time trt Time\*Time trt\*Time trt\*Time\*Time / dist=bin;

repeated subject=ID / within=Ctime corr=cs;

**run**;

| **Model Information** | | | |
| --- | --- | --- | --- |
| **Data Set** | BIOS755.AMENORRHEA |  | y |
| **Distribution** | Binomial |  |  |
| **Link Function** | Logit |  |  |
| **Dependent Variable** | Y |  |  |

|  |  |
| --- | --- |
| **Number of Observations Read** | 4604 |
| **Number of Observations Used** | 3616 |
| **Number of Events** | 1231 |
| **Number of Trials** | 3616 |
| **Number of Missing Values** | 988 |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 1151 | 1 2 3 4 ….. 75 76 77 78 79 80 81 82 83 84 85 86 87 ... |
| **Ctime** | 4 | 1 2 3 4 |

| **Response Profile** | | |
| --- | --- | --- |
| **Ordered Value** | **Y** | **Total Frequency** |
| **1** | 1 | 1231 |
| **2** | 0 | 2385 |

|  |
| --- |
| ***PROC GEE is modeling the probability that Y='1'.*** |

| **GEE Model Information** | |
| --- | --- |
| **Correlation Structure** | Exchangeable |
| **Within-Subject Effect** | Ctime (4 levels) |
| **Subject Effect** | ID (1151 levels) |
| **Number of Clusters** | 1151 |
| **Clusters With Missing Values** | 437 |
| **Correlation Matrix Dimension** | 4 |
| **Maximum Cluster Size** | 4 |
| **Minimum Cluster Size** | 1 |

| **Exchangeable Working Correlation** | |
| --- | --- |
| **Correlation** | 0.3626 |

| **GEE Fit Criteria** | |
| --- | --- |
| QIC | 4384.4585 |
| QICu | 4382.9860 |

| **Parameter Estimates for Response Model** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **with Empirical Standard Error Estimates** | | | | | | |
| **Parameter** | **Estimate** | **Standard Error** | **95% Confidence Limits** | | **Z** | **Pr > |Z|** |
| **Intercept** | -2.0022 | 0.2466 | -2.4856 | -1.5187 | -8.12 | <.0001 |
| **TIME** | 0.5097 | 0.2095 | 0.0990 | 0.9205 | 2.43 | 0.0150 |
| **TRT** | -0.4516 | 0.3514 | -1.1403 | 0.2371 | -1.29 | 0.1987 |
| **TIME\*TIME** | 0.0014 | 0.0401 | -0.0773 | 0.0801 | 0.03 | 0.9724 |
| **TIME\*TRT** | 0.6902 | 0.2988 | 0.1045 | 1.2760 | 2.31 | 0.0209 |
| **TIME\*TIME\*TRT** | -0.1299 | 0.0571 | -0.2419 | -0.0180 | -2.27 | 0.0229 |

**Creating monotone missing data in SAS data step**

First, read in the standard data file

**proc** **import** file= 'C:/Users/mclaina/OneDrive - University of South Carolina/Teaching/755\_Spring\_2022/Homework/ahead.csv' out=ahead dbms=csv replace;

getnames=Yes;

**run**;

Now, create lag variable to use in missingness model:

**data** ahead\_lag;

set ahead;

iadlany\_lag = lag(iadlany);

**run**;

**proc** **gee** data=ahead\_lag desc plots=histogram;

class id;

missmodel some missingness model / type=obslevel;

model iadlany = some model / dist=bin;

repeated subject=id / corr=cs;

**run**;

514

515 proc gee data=ahead\_lag desc plots=histogram;

516 class id;

517 missmodel some missingness model / type=obslevel;

518 model iadlany = some model / dist=bin;

519 repeated subject=id / corr=cs;

520 run;

**ERROR: Non-monotone missingness is not allowed.**

NOTE: The SAS System stopped processing this step because of errors.

NOTE: PROCEDURE GEE used (Total process time):

real time 0.21 seconds

cpu time 0.18 seconds

|  |
| --- |
| The SAS System |

The GEE Procedure

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.AHEAD\_LAG |
| **Distribution** | Binomial |
| **Link Function** | Logit |
| **Dependent Variable** | iadlany |

| **Missing Data Patterns** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Occasion** | | | | **Freq** | **Percent** |
| **1** | **2** | **3** | **4** |
| **1** | X | X | X | X | 3814 | 57.34 |
| **2** | X | X | X | . | 872 | 13.11 |
| **3** | X | X | . | X | 79 | 1.19 |
| **4** | X | X | . | . | 925 | 13.91 |
| **5** | X | . | X | X | 90 | 1.35 |
| **6** | X | . | X | . | 34 | 0.51 |
| **7** | X | . | . | X | 28 | 0.42 |
| **8** | X | . | . | . | 809 | 12.16 |

**data** ahead\_mono;

set ahead\_lag;

iadlany\_mono = **.**;

if iadlany\_lag ne **.** then iadlany\_mono=iadlany;

if year = **0** then iadlany\_mono=iadlany;

**run**;

**proc** **gee** data=ahead\_mono desc plots=histogram;

class id;

missmodel some missingness model / type=obslevel;

model iadlany\_mono = some model / dist=bin;

repeated subject=id / corr=cs;

**run**;

|  |
| --- |
| The SAS System |

The GEE Procedure

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.AHEAD\_MONO |
| **Distribution** | Binomial |
| **Link Function** | Logit |
| **Dependent Variable** | iadlany\_mono |

| **Missing Data Patterns** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Occasion** | | | | **Freq** | **Percent** |
| **1** | **2** | **3** | **4** |
| **1** | X | X | X | X | 3814 | 57.34 |
| **2** | X | X | X | . | 872 | 13.11 |
| **3** | X | X | . | . | 1004 | 15.10 |
| **4** | X | . | . | X | 90 | 1.35 |
| **5** | X | . | . | . | 871 | 13.10 |

**data** ahead\_mono2;

set ahead\_lag;

by id;

miss = **0**;

do i=**1** to **4**;

if first.id then miss = **0**;

if iadlany eq **.** then miss = **1**;

if lag(miss) eq **1** then miss = **1**;

iadlany\_mono = iadlany;

if miss = **1** then iadlany\_mono = **.**;

end;

output;

drop i miss;

**run**;

**proc** **gee** data=ahead\_mono2 desc plots=histogram;

class id;

missmodel some missingness model / type=obslevel;

model iadlany\_mono = some model / dist=bin;

repeated subject=id / corr=cs;

**run**;

|  |
| --- |
| The SAS System |

The GEE Procedure

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.AHEAD\_MONO2 |
| **Distribution** | Binomial |
| **Link Function** | Logit |
| **Dependent Variable** | iadlany\_mono |

|  |  |
| --- | --- |
| **Number of Observations Read** | 26604 |
| **Number of Observations Used** | 20841 |
| **Number of Events** | 5555 |
| **Number of Trials** | 20841 |
| **Number of Missing Values** | 5763 |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **id** | 6651 | 1 10 100 1000 1001 1002 1003 1004 1005 1006 1007 1008 1009 101 1010 1011 1012 1013 1014 1015 1016 1017 1018 1019 102 1020 1021 1022 1023 1024 1025 1026 1027 1028 1029 103 1030 1031 1032 1033 1034 1035 1036 1037 1038 1039 104 1040 1041 1042 1043 1044 ... |

| **Response Profile** | | |
| --- | --- | --- |
| **Ordered Value** | **iadlany\_mono** | **Total Frequency** |
| **1** | 1 | 5555 |
| **2** | 0 | 15286 |

|  |
| --- |
| **PROC GEE is modeling the probability that iadlany\_mono='1'.** |

| **GEE Model Information** | |
| --- | --- |
| **Correlation Structure** | Exchangeable |
| **Subject Effect** | id (6651 levels) |
| **Number of Clusters** | 6651 |
| **Clusters With Missing Values** | 2837 |
| **Correlation Matrix Dimension** | 4 |
| **Maximum Cluster Size** | 4 |
| **Minimum Cluster Size** | 1 |

| **Missing Data Patterns** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **Occasion** | | | | **Freq** | **Percent** |
| **1** | **2** | **3** | **4** |
| **1** | X | X | X | X | 3814 | 57.34 |
| **2** | X | X | X | . | 872 | 13.11 |
| **3** | X | X | . | . | 1004 | 15.10 |
| **4** | X | . | . | . | 961 | 14.45 |

**Multiple Imputation in SAS**

**To impute longitudinal outcome data we use the monotone statement on the wide version of the dataset.**

**proc** **transpose** data=BIOS755.Amenorrhea out=Amenorrhea\_wide prefix=Y;

by id;

id time;

var y;

**run**;

**data** BIOS755.Amenorrhea\_wide;

merge BIOS755.Amenorrhea Amenorrhea\_wide;

by id;

if first.id;

drop y \_NAME\_ \_LABEL\_;

**run**;

**proc** **print** data = BIOS755.Amenorrhea\_wide (obs=**10**);

**run**;

| **Obs** | **ID** | **TRT** | **TIME** | **Y1** | **Y2** | **Y3** | **Y4** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **1** | 1 | 0 | 1 | 0 | . | . | . |
| **2** | 2 | 0 | 1 | 0 | . | . | . |
| **3** | 3 | 0 | 1 | 0 | . | . | . |

**proc** **sort** data = BIOS755.Amenorrhea\_wide;

by TRT;

**run**;

**With a MONOTONE statement, the variables with missing values are imputed sequentially in the order specified in the VAR statement.**

**proc** **mi** data=BIOS755.Amenorrhea\_wide NIMPUTE=**10** seed=**8675309** out=MI\_wide;

\* We could use the "by" statement to impute separately for each ID.

\* We don't want to do that here, but it's an option when there is lots of data per person/cluster;

\* by id;

class y1 - y4;

var trt y1 - y4;

monotone logistic (y2 = y1 trt);

monotone logistic (y3 = y2 y1 y1\*y2 trt);

monotone logistic (y4 = y3 y2 y1 y1\*y2 y3\*y2 trt);

\* We don’t specify link = logit, but that is what is used (by default).

With multinomial data,

* link = logit will use the cumulative logistic model for ordinal data,
* link = glogit for nominal data;

**run**;

| **Model Information** | |
| --- | --- |
| **Data Set** | BIOS755.AMENORRHEA\_WIDE |
| **Method** | Monotone |
| **Number of Imputations** | 10 |
| **Seed for random number generator** | 8675309 |

| **Monotone Model Specification** | |
| --- | --- |
| **Method** | **Imputed Variables** |
| Logistic Regression | Y2 Y3 Y4 |
| Discriminant Function | Y1 |

| **Missing Data Patterns** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Group** | **TRT** | **Y1** | **Y2** | **Y3** | **Y4** | **Freq** | **Percent** | **Group Means** |
| **TRT** |
| **1** | X | X | X | X | X | 714 | 62.03 | 0.494398 |
| **2** | X | X | X | X | . | 84 | 7.30 | 0.428571 |
| **3** | X | X | X | . | . | 155 | 13.47 | 0.561290 |
| **4** | X | X | . | . | . | 198 | 17.20 | 0.500000 |

**Then, I’ll do the same things I did before. Comparing the means of the imputed variables we the means of the observed variables.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Obs** | **TRT** | **NImpute** | **Parm** | **Estimate** | **StdErr** | **LCLMean** | **UCLMean** | **DF** | **Min** | **Max** | **Theta0** | **tValue** | **Probt** |
| **1** | 0 | 10 | mn\_Y1 | 0.18576 | 0.01622 | . | . | . | 0.18576 | 0.18576 | 0 | . | . |
| **2** | 0 | 10 | mn\_Y2 | 0.26892 | 0.01986 | 0.2299 | 0.30795 | 505.4 | 0.26042 | 0.27951 | 0 | 13.54 | <.0001 |
| **3** | 0 | 10 | mn\_Y3 | 0.39983 | 0.02587 | 0.34815 | 0.45151 | 63.42 | 0.37326 | 0.42361 | 0 | 15.46 | <.0001 |
| **4** | 0 | 10 | mn\_Y4 | 0.51962 | 0.02529 | 0.46936 | 0.56988 | 87.05 | 0.49653 | 0.54167 | 0 | 20.55 | <.0001 |
| **5** | 1 | 10 | mn\_Y1 | 0.20522 | 0.01686 | . | . | . | 0.20522 | 0.20522 | 0 | . | . |
| **6** | 1 | 10 | mn\_Y2 | 0.34661 | 0.02164 | 0.30405 | 0.38917 | 360.9 | 0.33391 | 0.35652 | 0 | 16.01 | <.0001 |
| **7** | 1 | 10 | mn\_Y3 | 0.51478 | 0.02513 | 0.46488 | 0.56469 | 92.81 | 0.49044 | 0.5287 | 0 | 20.48 | <.0001 |
| **8** | 1 | 10 | mn\_Y4 | 0.5673 | 0.02477 | 0.51815 | 0.61646 | 97.76 | 0.54087 | 0.58435 | 0 | 22.9 | <.0001 |

The MEANS Procedure

trt=0

| **Variable** | **Mean** | **Std Dev** | **Lower 95% CL for Mean** | **Upper 95% CL for Mean** |
| --- | --- | --- | --- | --- |
| |  | | --- | | **Y1** | | **Y2** | | **Y3** | | **Y4** | | |  | | --- | | 0.1857639 | | 0.2620545 | | 0.3887531 | | 0.5013850 | | |  | | --- | | 0.3892541 | | 0.4402138 | | 0.4880641 | | 0.5006920 | | |  | | --- | | 0.1539083 | | 0.2224488 | | 0.3413121 | | 0.4495614 | | |  | | --- | | 0.2176194 | | 0.3016603 | | 0.4361940 | | 0.5532087 | |

trt=1

| **Variable** | **Mean** | **Std Dev** | **Lower 95% CL for Mean** | **Upper 95% CL for Mean** |
| --- | --- | --- | --- | --- |
| |  | | --- | | **Y1** | | **Y2** | | **Y3** | | **Y4** | | |  | | --- | | 0.2052174 | | 0.3361345 | | 0.4935733 | | 0.5354108 | | |  | | --- | | 0.4042120 | | 0.4728825 | | 0.5006026 | | 0.4994524 | | |  | | --- | | 0.1721088 | | 0.2935446 | | 0.4436707 | | 0.4831289 | | |  | | --- | | 0.2383259 | | 0.3787243 | | 0.5434759 | | 0.5876926 | |

**Go from wide to long:**

**data** MI\_wide\_long;

set MI\_wide;

time=**1**;

Y=Y1;

output;

time=**2**;

Y=Y2;

output;

time=**3**;

Y=Y3;

output;

time=**4**;

Y=Y4;

output;

drop Y1-Y4;

**run**;

**run**;

**Now, we’ll analyze the data using proc glimmix by \_Imputation\_:**

**proc** **glimmix** data=MI\_wide\_long method=QUAD(qpoints=**50**);

by \_Imputation\_;

class ID;

model Y = Time trt Time\*Time trt\*Time trt\*Time\*Time / dist=bin solution covb;

random intercept / subject=id;

ods output ParameterEstimates=mixparms CovB=mixcovb;

run;

**The output from the first 2 imputations:**

|  |
| --- |
| The SAS System |

The GLIMMIX Procedure

Imputation Number=1

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.MI\_WIDE\_LONG |
| **Response Variable** | Y |
| **Response Distribution** | Binomial |
| **Link Function** | Logit |
| **Variance Function** | Default |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Maximum Likelihood |
| **Likelihood Approximation** | Gauss-Hermite Quadrature |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 1151 | 1 2 3 4 5 6 7 8 9 ……. 1151 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 4604 |
| **Number of Observations Used** | 4604 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 1 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 1 |
| **Subjects (Blocks in V)** | 1151 |
| **Max Obs per Subject** | 4 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 7 |
| **Lower Boundaries** | 1 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Not Profiled |
| **Starting From** | GLM estimates |
| **Quadrature Points** | 50 |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Evaluations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | 4 | 5076.0941281 | . | 1097.241 |
| **1** | **0** | 4 | 5067.7387036 | 8.35542455 | 201.1249 |
| **2** | **0** | 2 | 5049.0448135 | 18.69389005 | 726.9587 |
| **3** | **0** | 3 | 5029.056989 | 19.98782452 | 192.037 |
| **14** | **0** | 3 | 4963.0965641 | 0.00157926 | 0.169368 |
| **15** | **0** | 3 | 4963.096537 | 0.00002709 | 0.015629 |

|  |
| --- |
| Convergence criterion (GCONV=1E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 4963.10 |
| **AIC (smaller is better)** | 4977.10 |
| **AICC (smaller is better)** | 4977.12 |
| **BIC (smaller is better)** | 5012.44 |
| **CAIC (smaller is better)** | 5019.44 |
| **HQIC (smaller is better)** | 4990.44 |

| **Fit Statistics for Conditional Distribution** | |
| --- | --- |
| **-2 log L(Y | r. effects)** | 2950.53 |
| **Pearson Chi-Square** | 2486.32 |
| **Pearson Chi-Square / DF** | 0.54 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **Intercept** | **ID** | 4.8233 | 0.4605 |

| **Solutions for Fixed Effects** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Effect** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** | -3.5029 | 0.3822 | 1149 | -9.16 | <.0001 |
| **TIME** | 0.9244 | 0.3135 | 3449 | 2.95 | 0.0032 |
| **TRT** | -0.6139 | 0.5237 | 3449 | -1.17 | 0.2412 |
| **TIME\*TIME** | -0.00429 | 0.06015 | 3449 | -0.07 | 0.9432 |
| **TIME\*TRT** | 1.0102 | 0.4383 | 3449 | 2.30 | 0.0213 |
| **TIME\*TIME\*TRT** | -0.1831 | 0.08420 | 3449 | -2.17 | 0.0298 |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **TIME** | 1 | 3449 | 8.70 | 0.0032 |
| **TRT** | 1 | 3449 | 1.37 | 0.2412 |
| **TIME\*TIME** | 1 | 3449 | 0.01 | 0.9432 |
| **TIME\*TRT** | 1 | 3449 | 5.31 | 0.0213 |
| **TIME\*TIME\*TRT** | 1 | 3449 | 4.73 | 0.0298 |

| **Covariance Matrix for Fixed Effects** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **Intercept** | **1** | 0.1461 | -0.1090 | -0.1392 | 0.01924 | 0.1060 | -0.01897 |
| **TIME** | **2** | -0.1090 | 0.09826 | 0.1075 | -0.01850 | -0.09762 | 0.01844 |
| **TRT** | **3** | -0.1392 | 0.1075 | 0.2743 | -0.01929 | -0.2112 | 0.03785 |
| **TIME\*TIME** | **4** | 0.01924 | -0.01850 | -0.01929 | 0.003618 | 0.01852 | -0.00362 |
| **TIME\*TRT** | **5** | 0.1060 | -0.09762 | -0.2112 | 0.01852 | 0.1921 | -0.03627 |
| **TIME\*TIME\*TRT** | **6** | -0.01897 | 0.01844 | 0.03785 | -0.00362 | -0.03627 | 0.007090 |

|  |
| --- |
| The SAS System |

The GLIMMIX Procedure

Imputation Number=2

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.MI\_WIDE\_LONG |
| **Response Variable** | Y |
| **Response Distribution** | Binomial |
| **Link Function** | Logit |
| **Variance Function** | Default |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Maximum Likelihood |
| **Likelihood Approximation** | Gauss-Hermite Quadrature |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 1151 | 1 2 3 4 5 6…. 1151 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 4604 |
| **Number of Observations Used** | 4604 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 1 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 1 |
| **Subjects (Blocks in V)** | 1151 |
| **Max Obs per Subject** | 4 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 7 |
| **Lower Boundaries** | 1 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Not Profiled |
| **Starting From** | GLM estimates |
| **Quadrature Points** | 50 |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Evaluations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | 4 | 5002.670221 | . | 989.6732 |
| **1** | **0** | 4 | 4995.2095204 | 7.46070063 | 208.1282 |
| **10** | **0** | 3 | 4873.2681437 | 0.00026587 | 0.172507 |
| **11** | **0** | 4 | 4873.2677845 | 0.00035921 | 2.552924 |

|  |
| --- |
| Convergence criterion (GCONV=1E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 4873.27 |
| **AIC (smaller is better)** | 4887.27 |
| **AICC (smaller is better)** | 4887.29 |
| **BIC (smaller is better)** | 4922.61 |
| **CAIC (smaller is better)** | 4929.61 |
| **HQIC (smaller is better)** | 4900.61 |

| **Fit Statistics for Conditional Distribution** | |
| --- | --- |
| **-2 log L(Y | r. effects)** | 2815.05 |
| **Pearson Chi-Square** | 2376.58 |
| **Pearson Chi-Square / DF** | 0.52 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **Intercept** | **ID** | 5.4393 | 0.5186 |

| **Solutions for Fixed Effects** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Effect** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** | -3.3388 | 0.3893 | 1149 | -8.58 | <.0001 |
| **TIME** | 0.6620 | 0.3198 | 3449 | 2.07 | 0.0385 |
| **TRT** | -1.0295 | 0.5360 | 3449 | -1.92 | 0.0549 |
| **TIME\*TIME** | 0.04142 | 0.06155 | 3449 | 0.67 | 0.5010 |
| **TIME\*TRT** | 1.4343 | 0.4483 | 3449 | 3.20 | 0.0014 |
| **TIME\*TIME\*TRT** | -0.2567 | 0.08612 | 3449 | -2.98 | 0.0029 |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **TIME** | 1 | 3449 | 4.28 | 0.0385 |
| **TRT** | 1 | 3449 | 3.69 | 0.0549 |
| **TIME\*TIME** | 1 | 3449 | 0.45 | 0.5010 |
| **TIME\*TRT** | 1 | 3449 | 10.24 | 0.0014 |
| **TIME\*TIME\*TRT** | 1 | 3449 | 8.88 | 0.0029 |

| **Covariance Matrix for Fixed Effects** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **Intercept** | **1** | 0.1515 | -0.1124 | -0.1441 | 0.01989 | 0.1091 | -0.01957 |
| **TIME** | **2** | -0.1124 | 0.1023 | 0.1113 | -0.01931 | -0.1018 | 0.01926 |
| **TRT** | **3** | -0.1441 | 0.1113 | 0.2873 | -0.02004 | -0.2203 | 0.03947 |
| **TIME\*TIME** | **4** | 0.01989 | -0.01931 | -0.02004 | 0.003788 | 0.01938 | -0.00379 |
| **TIME\*TRT** | **5** | 0.1091 | -0.1018 | -0.2203 | 0.01938 | 0.2010 | -0.03795 |
| **TIME\*TIME\*TRT** | **6** | -0.01957 | 0.01926 | 0.03947 | -0.00379 | -0.03795 | 0.007417 |

**Now, we’ll pool the imputed analyses into one set of parameter estimates with proc mialalyze:**

**proc** **mianalyze** parms=mixparms covb(effectvar=rowcol)=mixcovb ;

\*The covb is only needed for multi-variate results (i.e., type III tests or contrast statements);

modeleffects Intercept Time trt Time\*Time trt\*Time trt\*Time\*Time;

title 'MIANALYZE Results';

**run**;

|  |
| --- |
| MIANALYZE Results |

The MIANALYZE Procedure

| **Model Information** | |
| --- | --- |
| **PARMS Data Set** | WORK.MIXPARMS |
| **COVB Data Set** | WORK.MIXCOVB |
| **Number of Imputations** | 10 |

| **Variance Information (10 Imputations)** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Variance** | | | **DF** | **Relative Increase in Variance** | **Fraction Missing Information** | **Relative Efficiency** |
| **Between** | **Within** | **Total** |
| **Intercept** | 0.023032 | 0.143971 | 0.169306 | 401.93 | 0.175972 | 0.153840 | 0.984849 |
| **Time** | 0.025113 | 0.097413 | 0.125037 | 184.4 | 0.283573 | 0.229240 | 0.977590 |
| **trt** | 0.042740 | 0.272122 | 0.319136 | 414.7 | 0.172769 | 0.151400 | 0.985086 |
| **Time\*Time** | 0.000937 | 0.003597 | 0.004628 | 181.35 | 0.286626 | 0.231205 | 0.977402 |
| **Time\*trt** | 0.058482 | 0.191145 | 0.255475 | 141.94 | 0.336551 | 0.262130 | 0.974457 |
| **Time\*Time\*trt** | 0.002635 | 0.007060 | 0.009959 | 106.25 | 0.410524 | 0.304022 | 0.970495 |

| **Parameter Estimates (10 Imputations)** | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Parameter** | **Estimate** | **Std Error** | **95% Confidence Limits** | | **DF** | **Minimum** | **Maximum** | **Theta0** | **t for H0: Parameter=Theta0** | **Pr > |t|** |
| **Intercept** | -3.374046 | 0.411468 | -4.18294 | -2.56515 | 401.93 | -3.680824 | -3.104243 | 0 | -8.20 | <.0001 |
| **Time** | 0.821449 | 0.353606 | 0.12382 | 1.51908 | 184.4 | 0.627280 | 1.182889 | 0 | 2.32 | 0.0213 |
| **trt** | -0.769218 | 0.564921 | -1.87968 | 0.34125 | 414.7 | -1.029541 | -0.426314 | 0 | -1.36 | 0.1741 |
| **Time\*Time** | 0.014475 | 0.068028 | -0.11975 | 0.14870 | 181.35 | -0.058471 | 0.043144 | 0 | 0.21 | 0.8317 |
| **Time\*trt** | 1.170986 | 0.505445 | 0.17181 | 2.17016 | 141.94 | 0.757193 | 1.460007 | 0 | 2.32 | 0.0219 |
| **Time\*Time\*trt** | -0.222907 | 0.099794 | -0.42075 | -0.02506 | 106.25 | -0.301403 | -0.134900 | 0 | -2.23 | 0.0276 |

**Comparing with the complete data analysis**

**proc** **glimmix** data=BIOS755.Amenorrhea method=QUAD(qpoints=**50**);

class ID;

model Y = Time trt Time\*Time trt\*Time trt\*Time\*Time / dist=bin solution;

random intercept / subject=id;

run;

| **Model Information** | |
| --- | --- |
| **Data Set** | BIOS755.AMENORRHEA |
| **Response Variable** | Y |
| **Response Distribution** | Binomial |
| **Link Function** | Logit |
| **Variance Function** | Default |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Maximum Likelihood |
| **Likelihood Approximation** | Gauss-Hermite Quadrature |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 1151 | 1 …. 1150 1151 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 4604 |
| **Number of Observations Used** | 3616 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 1 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 1 |
| **Subjects (Blocks in V)** | 1151 |
| **Max Obs per Subject** | 4 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 7 |
| **Lower Boundaries** | 1 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Not Profiled |
| **Starting From** | GLM estimates |
| **Quadrature Points** | 50 |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Evaluations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | 4 | 3961.1107127 | . | 754.8834 |
| **1** | **0** | 4 | 3954.5188083 | 6.59190441 | 170.3103 |
| **2** | **0** | 2 | 3935.2222761 | 19.29653216 | 501.6977 |
| **3** | **0** | 3 | 3916.3366324 | 18.88564370 | 125.6327 |
| **4** | **0** | 2 | 3895.3759089 | 20.96072351 | 37.89303 |
| **5** | **0** | 4 | 3875.3319661 | 20.04394273 | 102.5231 |
| **6** | **0** | 3 | 3867.4836672 | 7.84829892 | 86.57043 |
| **7** | **0** | 3 | 3867.1121884 | 0.37147880 | 3.268637 |
| **8** | **0** | 3 | 3866.9314898 | 0.18069861 | 35.01058 |
| **9** | **0** | 3 | 3866.8928583 | 0.03863151 | 3.791026 |
| **10** | **0** | 3 | 3866.8913504 | 0.00150794 | 0.307824 |
| **11** | **0** | 2 | 3866.8899544 | 0.00139600 | 1.891312 |
| **12** | **0** | 2 | 3866.8877416 | 0.00221279 | 0.181709 |
| **13** | **0** | 3 | 3866.8874462 | 0.00029532 | 0.43449 |
| **14** | **0** | 3 | 3866.8874348 | 0.00001144 | 0.012497 |

|  |
| --- |
| Convergence criterion (GCONV=1E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 3866.89 |
| **AIC (smaller is better)** | 3880.89 |
| **AICC (smaller is better)** | 3880.92 |
| **BIC (smaller is better)** | 3916.23 |
| **CAIC (smaller is better)** | 3923.23 |
| **HQIC (smaller is better)** | 3894.23 |

| **Fit Statistics for Conditional Distribution** | |
| --- | --- |
| **-2 log L(Y | r. effects)** | 2169.87 |
| **Pearson Chi-Square** | 1741.85 |
| **Pearson Chi-Square / DF** | 0.48 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **Intercept** | ID | 5.0798 | 0.5855 |

| **Solutions for Fixed Effects** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Effect** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** | -3.3943 | 0.4146 | 1149 | -8.19 | <.0001 |
| **TIME** | 0.7978 | 0.3551 | 2461 | 2.25 | 0.0248 |
| **TRT** | -0.8049 | 0.5636 | 2461 | -1.43 | 0.1534 |
| **TIME\*TIME** | 0.01966 | 0.06968 | 2461 | 0.28 | 0.7779 |
| **TIME\*TRT** | 1.2194 | 0.4978 | 2461 | 2.45 | 0.0144 |
| **TIME\*TIME\*TRT** | -0.2296 | 0.09770 | 2461 | -2.35 | 0.0188 |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **TIME** | 1 | 2461 | 5.05 | 0.0248 |
| **TRT** | 1 | 2461 | 2.04 | 0.1534 |
| **TIME\*TIME** | 1 | 2461 | 0.08 | 0.7779 |
| **TIME\*TRT** | 1 | 2461 | 6.00 | 0.0144 |
| **TIME\*TIME\*TRT** | 1 | 2461 | 5.52 | 0.0188 |