\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

\*\*\*\*\*\*\* Example Three (Unbalenced data) \*\*\*\*\*\*\*\*\*

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*;

\*The Six Cities Study of Air Pollution and Health was a

longitudinal study designed to characterize lung growth as

measured by changes in pulmonary function in children and

adolescents, and the factors that influence lung function growth.

A cohort of 13,379 children born on or after 1967 was enrolled

in six communities across the U.S.

.;

**data** air\_pol;

input ID Height Age INI\_Height INI\_Age Log\_FEV1;

datalines;

1 1.20 9.3415 1.20 9.3415 0.21511

1 1.28 10.3929 1.20 9.3415 0.37156

……………………..

300 1.62 17.0075 1.44 11.9617 1.12817

300 1.63 17.8645 1.44 11.9617 1.16938

;

**run**;

**Proc** **SGplot** data = air\_pol;

series x=Age y=Log\_FEV1 / group =ID LineAttrs= (pattern=**1** );

**run**;



**Proc** **SGplot** data = air\_pol;

series x=Height y=Log\_FEV1 / group =ID LineAttrs= (pattern=**1** );

**run**;



**data** air\_pol2;

set air\_pol;

lAge = log(Age);

Age\_fl = floor(Age);

**run**;

**proc** **print** data = air\_pol2 (obs=**10**);

**run**;

| **Obs** | **ID** | **Height** | **Age** | **INI\_Height** | **INI\_Age** | **Log\_FEV1** | **lAge** | **Age\_fl** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **1** | 1 | 1.20 | 9.3415 | 1.20 | 9.3415 | 0.21511 | 2.23447 | 9 |
| **2** | 1 | 1.28 | 10.3929 | 1.20 | 9.3415 | 0.37156 | 2.34112 | 10 |
| **3** | 1 | 1.33 | 11.4524 | 1.20 | 9.3415 | 0.48858 | 2.43820 | 11 |
| **4** | 1 | 1.42 | 12.4600 | 1.20 | 9.3415 | 0.75142 | 2.52252 | 12 |
| **5** | 1 | 1.48 | 13.4182 | 1.20 | 9.3415 | 0.83291 | 2.59661 | 13 |
| **6** | 1 | 1.50 | 15.4743 | 1.20 | 9.3415 | 0.89200 | 2.73918 | 15 |
| **7** | 1 | 1.52 | 16.3723 | 1.20 | 9.3415 | 0.87129 | 2.79559 | 16 |
| **8** | 2 | 1.13 | 6.5873 | 1.13 | 6.5873 | 0.30748 | 1.88514 | 6 |
| **9** | 2 | 1.19 | 7.6496 | 1.13 | 6.5873 | 0.35066 | 2.03465 | 7 |
| **10** | 2 | 1.49 | 12.7392 | 1.13 | 6.5873 | 0.75612 | 2.54468 | 12 |

Our options for covariance matrices for unbalanced data are limited. Here, we’ll make the data balanced by using age (floored), but we’ll also look at some covariance matrices that use the unbalanced data.

**proc** **mixed** data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height/solution;

random ID;

repeated Age\_fl/ subject=ID type=UN r rcorr;

**run**;

From log:

NOTE: An infinite likelihood is assumed in iteration 0 because of a nonpositive definite

estimated R matrix for ID 6.

NOTE: PROCEDURE MIXED used (Total process time):

real time 0.09 seconds

cpu time 0.06 seconds

**proc** **mixed** data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height/solution;

repeated Age\_fl / subject=ID type=CS rcorr;

**run**;

| **Dimensions** | |
| --- | --- |
| **Covariance Parameters** | 2 |
| **Columns in X** | 2 |
| **Columns in Z** | 0 |
| **Subjects** | 300 |
| **Max Obs per Subject** | 12 |

| **Number of Observations** | |
| --- | --- |
| **Number of Observations Read** | 1994 |
| **Number of Observations Used** | 1994 |
| **Number of Observations Not Used** | 0 |

| **Iteration History** | | | |
| --- | --- | --- | --- |
| **Iteration** | **Evaluations** | **-2 Res Log Like** | **Criterion** |
| **0** | 1 | -2760.23017893 |  |
| **1** | 2 | -4278.14652498 | 0.00030439 |
| **2** | 1 | -4279.47432273 | 0.00000866 |
| **3** | 1 | -4279.50940034 | 0.00000001 |

| **Estimated R Correlation Matrix for ID 1** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** | **Col7** |
| **1** | 1.0000 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 |
| **2** | 0.7136 | 1.0000 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 |
| **3** | 0.7136 | 0.7136 | 1.0000 | 0.7136 | 0.7136 | 0.7136 | 0.7136 |
| **4** | 0.7136 | 0.7136 | 0.7136 | 1.0000 | 0.7136 | 0.7136 | 0.7136 |
| **5** | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 1.0000 | 0.7136 | 0.7136 |
| **6** | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 1.0000 | 0.7136 |
| **7** | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 0.7136 | 1.0000 |

| **Covariance Parameter Estimates** | | |
| --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** |
| **CS** | ID | 0.01140 |
| **Residual** |  | 0.004575 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4279.5 |
| **AIC (Smaller is Better)** | -4275.5 |
| **AICC (Smaller is Better)** | -4275.5 |
| **BIC (Smaller is Better)** | -4268.1 |

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height/solution;

repeated / subject=ID type=sp(exp)(Age) r rcorr;

run;

| **Dimensions** | |
| --- | --- |
| **Covariance Parameters** | 2 |
| **Columns in X** | 2 |
| **Columns in Z** | 0 |
| **Subjects** | 300 |
| **Max Obs per Subject** | 12 |

| **Number of Observations** | |
| --- | --- |
| **Number of Observations Read** | 1994 |
| **Number of Observations Used** | 1994 |
| **Number of Observations Not Used** | 0 |

|  |
| --- |
| Convergence criteria met. |

| **Estimated R Correlation Matrix for ID 1** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** | **Col7** |
| **1** | 1.0000 | 0.8058 | 0.6482 | 0.5271 | 0.4329 | 0.2838 | 0.2360 |
| **2** | 0.8058 | 1.0000 | 0.8045 | 0.6541 | 0.5372 | 0.3522 | 0.2929 |
| **3** | 0.6482 | 0.8045 | 1.0000 | 0.8131 | 0.6678 | 0.4378 | 0.3641 |
| **4** | 0.5271 | 0.6541 | 0.8131 | 1.0000 | 0.8214 | 0.5385 | 0.4478 |
| **5** | 0.4329 | 0.5372 | 0.6678 | 0.8214 | 1.0000 | 0.6556 | 0.5452 |
| **6** | 0.2838 | 0.3522 | 0.4378 | 0.5385 | 0.6556 | 1.0000 | 0.8316 |
| **7** | 0.2360 | 0.2929 | 0.3641 | 0.4478 | 0.5452 | 0.8316 | 1.0000 |

| **Covariance Parameter Estimates** | | |
| --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** |
| **SP(EXP)** | ID | 4.8692 |
| **Residual** |  | 0.01539 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4409.9 |
| **AIC (Smaller is Better)** | -4405.9 |
| **AICC (Smaller is Better)** | -4405.9 |
| **BIC (Smaller is Better)** | -4398.5 |

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height/solution;

repeated / subject=ID type=sp(exp)(**lAge**) r rcorr;

run;

| **Estimated R Correlation Matrix for ID 1** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** | **Col7** |
| **1** | 1.0000 | 0.7625 | 0.5958 | 0.4809 | 0.3983 | 0.2772 | 0.2402 |
| **2** | 0.7625 | 1.0000 | 0.7813 | 0.6306 | 0.5224 | 0.3636 | 0.3150 |
| **3** | 0.5958 | 0.7813 | 1.0000 | 0.8071 | 0.6685 | 0.4653 | 0.4032 |
| **4** | 0.4809 | 0.6306 | 0.8071 | 1.0000 | 0.8284 | 0.5765 | 0.4995 |
| **5** | 0.3983 | 0.5224 | 0.6685 | 0.8284 | 1.0000 | 0.6960 | 0.6030 |
| **6** | 0.2772 | 0.3636 | 0.4653 | 0.5765 | 0.6960 | 1.0000 | 0.8664 |
| **7** | 0.2402 | 0.3150 | 0.4032 | 0.4995 | 0.6030 | 0.8664 | 1.0000 |

| **Covariance Parameter Estimates** | | |
| --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** |
| **SP(EXP)** | ID | 0.3934 |
| **Residual** |  | 0.01516 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4449.3 |
| **AIC (Smaller is Better)** | -4445.3 |
| **AICC (Smaller is Better)** | -4445.3 |
| **BIC (Smaller is Better)** | -4437.9 |

**Now that we’ve found a good covariance, we’ll move towards looked for the best way to represent the covariates height and age.**

proc mixed data=air\_pol2 method=ml;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height/solution;

repeated / subject=ID type=sp(exp)(lAge) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4463.4 |
| **AIC (Smaller is Better)** | -4455.4 |
| **AICC (Smaller is Better)** | -4455.4 |
| **BIC (Smaller is Better)** | -4440.6 |

proc mixed data=air\_pol2 method=ml;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height lAge/solution;

repeated / subject=ID type=sp(exp)(lAge) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4527.7 |
| **AIC (Smaller is Better)** | -4517.7 |
| **AICC (Smaller is Better)** | -4517.6 |
| **BIC (Smaller is Better)** | -4499.2 |

proc mixed data=air\_pol2 method=ml;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age/solution;

repeated / subject=ID type=sp(exp)(lAge) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4522.5 |
| **AIC (Smaller is Better)** | -4512.5 |
| **AICC (Smaller is Better)** | -4512.5 |
| **BIC (Smaller is Better)** | -4494.0 |

proc mixed data=air\_pol2 method=ml;  
class ID Age\_fl (ref='6');  
model Log\_FEV1 = Height Age Age\*Age/solution;  
repeated / subject=ID type=sp(exp)(lAge) rcorr;  
run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4533.2 |
| **AIC (Smaller is Better)** | -4521.2 |
| **AICC (Smaller is Better)** | -4521.2 |
| **BIC (Smaller is Better)** | -4499.0 |

proc mixed data=air\_pol2 method=ml;  
class ID Age\_fl (ref='6');  
model Log\_FEV1 = Height Age Height\*Height Age\*Age/solution;  
repeated / subject=ID type=sp(exp)(lAge) rcorr;  
run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4540.5 |
| **AIC (Smaller is Better)** | -4526.5 |
| **AICC (Smaller is Better)** | -4526.4 |
| **BIC (Smaller is Better)** | -4500.5 |

proc mixed data=air\_pol2 method=ml;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age\_fl/solution;

repeated / subject=ID type=sp(exp)(lAge) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | -4594.6 |
| **AIC (Smaller is Better)** | -4562.6 |
| **AICC (Smaller is Better)** | -4562.3 |
| **BIC (Smaller is Better)** | -4503.3 |

**Now we’ll go back to the covariance model fit:**

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age\_fl/solution;

repeated / subject=ID type=sp(exp)(lAge) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4482.4 |
| **AIC (Smaller is Better)** | -4478.4 |
| **AICC (Smaller is Better)** | -4478.4 |
| **BIC (Smaller is Better)** | -4471.0 |

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age\_fl/solution;

repeated / subject=ID type=sp(exp)(Age) rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4446.0 |
| **AIC (Smaller is Better)** | -4442.0 |
| **AICC (Smaller is Better)** | -4442.0 |
| **BIC (Smaller is Better)** | -4434.6 |

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age\_fl/solution;

repeated / subject=ID type=CS rcorr;

run;

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4486.4 |
| **AIC (Smaller is Better)** | -4482.4 |
| **AICC (Smaller is Better)** | -4482.4 |
| **BIC (Smaller is Better)** | -4475.0 |

Oh my!! Now we need to go back to the mean model fit and check those out again! I’ll save you the suspense, and tell you the same model was the best. Let’s take a look at the final results.

proc mixed data=air\_pol2;

class ID Age\_fl (ref='6');

model Log\_FEV1 = Height Age\_fl/solution;

repeated / subject=ID type=CS rcorr;

run;

**The Mixed Procedure**

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.AIR\_POL2 |
| **Dependent Variable** | Log\_FEV1 |
| **Covariance Structure** | Compound Symmetry |
| **Subject Effect** | ID |
| **Estimation Method** | REML |
| **Residual Variance Method** | Profile |
| **Fixed Effects SE Method** | Model-Based |
| **Degrees of Freedom Method** | Between-Within |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 300 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 |
| **Age\_fl** | 13 | 7 8 9 10 11 12 13 14 15 16 17 18 6 |

| **Dimensions** | |
| --- | --- |
| **Covariance Parameters** | 2 |
| **Columns in X** | 15 |
| **Columns in Z** | 0 |
| **Subjects** | 300 |
| **Max Obs per Subject** | 12 |

| **Number of Observations** | |
| --- | --- |
| **Number of Observations Read** | 1994 |
| **Number of Observations Used** | 1994 |
| **Number of Observations Not Used** | 0 |

| **Iteration History** | | | |
| --- | --- | --- | --- |
| **Iteration** | **Evaluations** | **-2 Res Log Like** | **Criterion** |
| **0** | 1 | -2851.77393747 |  |
| **1** | 2 | -4484.01011759 | 0.00050417 |
| **2** | 1 | -4486.30601741 | 0.00002294 |
| **3** | 1 | -4486.40220546 | 0.00000006 |
| **4** | 1 | -4486.40243953 | 0.00000000 |

|  |
| --- |
| Convergence criteria met. |

| **Estimated R Correlation Matrix for ID 1** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** | **Col7** |
| **1** | 1.0000 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 |
| **2** | 0.7449 | 1.0000 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 |
| **3** | 0.7449 | 0.7449 | 1.0000 | 0.7449 | 0.7449 | 0.7449 | 0.7449 |
| **4** | 0.7449 | 0.7449 | 0.7449 | 1.0000 | 0.7449 | 0.7449 | 0.7449 |
| **5** | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 1.0000 | 0.7449 | 0.7449 |
| **6** | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 1.0000 | 0.7449 |
| **7** | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 0.7449 | 1.0000 |

| **Covariance Parameter Estimates** | | |
| --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** |
| **CS** | ID | 0.01129 |
| **Residual** |  | 0.003866 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | -4486.4 |
| **AIC (Smaller is Better)** | -4482.4 |
| **AICC (Smaller is Better)** | -4482.4 |
| **BIC (Smaller is Better)** | -4475.0 |

| **Null Model Likelihood Ratio Test** | | |
| --- | --- | --- |
| **DF** | **Chi-Square** | **Pr > ChiSq** |
| 1 | 1634.63 | <.0001 |

| **Solution for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **Age\_fl** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | -1.6985 | 0.06282 | 299 | -27.04 | <.0001 |
| **Height** |  | 1.5699 | 0.05175 | 1681 | 30.34 | <.0001 |
| **Age\_fl** | 7 | 0.05777 | 0.01129 | 1643 | 5.12 | <.0001 |
| **Age\_fl** | 8 | 0.08168 | 0.01203 | 1643 | 6.79 | <.0001 |
| **Age\_fl** | 9 | 0.09790 | 0.01378 | 1643 | 7.10 | <.0001 |
| **Age\_fl** | 10 | 0.1119 | 0.01589 | 1643 | 7.04 | <.0001 |
| **Age\_fl** | 11 | 0.1203 | 0.01848 | 1643 | 6.51 | <.0001 |
| **Age\_fl** | 12 | 0.1490 | 0.02124 | 1643 | 7.01 | <.0001 |
| **Age\_fl** | 13 | 0.1791 | 0.02324 | 1643 | 7.70 | <.0001 |
| **Age\_fl** | 14 | 0.2205 | 0.02437 | 1643 | 9.05 | <.0001 |
| **Age\_fl** | 15 | 0.2463 | 0.02491 | 1643 | 9.88 | <.0001 |
| **Age\_fl** | 16 | 0.2535 | 0.02512 | 1643 | 10.09 | <.0001 |
| **Age\_fl** | 17 | 0.2581 | 0.02538 | 1643 | 10.17 | <.0001 |
| **Age\_fl** | 18 | 0.2527 | 0.02665 | 1643 | 9.48 | <.0001 |
| **Age\_fl** | 6 | 0 | . | . | . | . |

| **Type 3 Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **Height** | 1 | 1681 | 920.28 | <.0001 |
| **Age\_fl** | 12 | 1643 | 27.48 | <.0001 |

The datasets can be found at http://www.biostat.jhsph.edu/~fdominic/teaching/LDA/lda.html under "DATA SETS";

**data** hiv;

infile "C:\...\hivstudy.txt" dlm=tab;

input ID Month CD4 Group;

**run**;

ods rtf file="C:\...\Examples\09 - Profile and Parametric examples2.rtf";

**proc** **print** data = hiv (obs=**10**);

**run**;

| **Obs** | **ID** | **Month** | **CD4** | **Group** |
| --- | --- | --- | --- | --- |
| **1** | 1 | 0 | 658 | 1 |
| **2** | 1 | 2 | 543 | 1 |
| **3** | 1 | 4 | 520 | 1 |
| **4** | 1 | 6 | 563 | 1 |
| **5** | 1 | 8 | 389 | 1 |
| **6** | 1 | 10 | 371 | 1 |
| **7** | 2 | 0 | 500 | 1 |
| **8** | 2 | 2 | 419 | 1 |
| **9** | 2 | 4 | 431 | 1 |
| **10** | 2 | 6 | 285 | 1 |

\*Now we will include the mean line on the graph by TRT;

**proc** **sort** data=hiv;

by Group Month;

\*Calculate the mean by week;

**proc** **means** mean data=hiv noprint;

by Group Month;

var CD4;

output out = MN\_GRP\_dat mean = mn\_GRP\_CD4;

**run**;

\*First, let's look at the mean by TRT group;

**Proc** **SGplot** data = MN\_GRP\_dat;

series x=Month y=mn\_GRP\_CD4 / group =Group LineAttrs= (pattern=**1** thickness=**3**);

**run**;



**data** hiv\_spline;

set hiv;

sp\_mn1 = min(month,**4**);

sp\_mn2 = max(**0**,month-**4**);

**run**;

**proc** **mixed** data=hiv\_spline;

class ID month group(ref='1');

model CD4 = group sp\_mn1 sp\_mn2 group\*sp\_mn1 group\*sp\_mn2/solution;

repeated month/ subject=ID type=UN r rcorr;

**run**;

| **Estimated R Matrix for ID 1** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **1** | 7117.69 | 3537.34 | 3177.50 | 4137.80 | 4777.74 | 3782.56 |
| **2** | 3537.34 | 6983.79 | 3060.69 | 5319.00 | 4664.03 | 3768.19 |
| **3** | 3177.50 | 3060.69 | 6584.21 | 3731.95 | 4082.94 | 3125.07 |
| **4** | 4137.80 | 5319.00 | 3731.95 | 9845.98 | 5991.41 | 5417.86 |
| **5** | 4777.74 | 4664.03 | 4082.94 | 5991.41 | 9356.51 | 5239.18 |
| **6** | 3782.56 | 3768.19 | 3125.07 | 5417.86 | 5239.18 | 7730.21 |

| **Estimated R Correlation Matrix for ID 1** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **1** | 1.0000 | 0.5017 | 0.4642 | 0.4943 | 0.5855 | 0.5099 |
| **2** | 0.5017 | 1.0000 | 0.4514 | 0.6414 | 0.5770 | 0.5129 |
| **3** | 0.4642 | 0.4514 | 1.0000 | 0.4635 | 0.5202 | 0.4380 |
| **4** | 0.4943 | 0.6414 | 0.4635 | 1.0000 | 0.6242 | 0.6210 |
| **5** | 0.5855 | 0.5770 | 0.5202 | 0.6242 | 1.0000 | 0.6160 |
| **6** | 0.5099 | 0.5129 | 0.4380 | 0.6210 | 0.6160 | 1.0000 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | 8126.7 |
| **AIC (Smaller is Better)** | 8168.7 |
| **AICC (Smaller is Better)** | 8170.1 |
| **BIC (Smaller is Better)** | 8227.3 |

**proc** **mixed** data=hiv\_spline;

class ID month group(ref='1');

model CD4 = group sp\_mn1 sp\_mn2 group\*sp\_mn1 group\*sp\_mn2/solution;

repeated month/ subject=ID type=CSH r rcorr;

**run**;

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | 8146.2 |
| **AIC (Smaller is Better)** | 8160.2 |
| **AICC (Smaller is Better)** | 8160.4 |
| **BIC (Smaller is Better)** | 8179.7 |

**proc** **mixed** data=hiv\_spline; \*This is the final model;

class ID month group(ref='1');

model CD4 = group sp\_mn1 sp\_mn2 group\*sp\_mn1 group\*sp\_mn2/solution outpm=pred;

repeated month/ subject=ID type=CS r rcorr;

**run**;

| **Estimated R Matrix for ID 1** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **1** | 7932.96 | 4252.14 | 4252.14 | 4252.14 | 4252.14 | 4252.14 |
| **2** | 4252.14 | 7932.96 | 4252.14 | 4252.14 | 4252.14 | 4252.14 |
| **3** | 4252.14 | 4252.14 | 7932.96 | 4252.14 | 4252.14 | 4252.14 |
| **4** | 4252.14 | 4252.14 | 4252.14 | 7932.96 | 4252.14 | 4252.14 |
| **5** | 4252.14 | 4252.14 | 4252.14 | 4252.14 | 7932.96 | 4252.14 |
| **6** | 4252.14 | 4252.14 | 4252.14 | 4252.14 | 4252.14 | 7932.96 |

| **Estimated R Correlation Matrix for ID 1** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Row** | **Col1** | **Col2** | **Col3** | **Col4** | **Col5** | **Col6** |
| **1** | 1.0000 | 0.5360 | 0.5360 | 0.5360 | 0.5360 | 0.5360 |
| **2** | 0.5360 | 1.0000 | 0.5360 | 0.5360 | 0.5360 | 0.5360 |
| **3** | 0.5360 | 0.5360 | 1.0000 | 0.5360 | 0.5360 | 0.5360 |
| **4** | 0.5360 | 0.5360 | 0.5360 | 1.0000 | 0.5360 | 0.5360 |
| **5** | 0.5360 | 0.5360 | 0.5360 | 0.5360 | 1.0000 | 0.5360 |
| **6** | 0.5360 | 0.5360 | 0.5360 | 0.5360 | 0.5360 | 1.0000 |

| **Covariance Parameter Estimates** | | |
| --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** |
| **CS** | ID | 4252.14 |
| **Residual** |  | 3680.82 |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Likelihood** | 8153.7 |
| **AIC (Smaller is Better)** | 8157.7 |
| **AICC (Smaller is Better)** | 8157.7 |
| **BIC (Smaller is Better)** | 8163.3 |

| **Null Model Likelihood Ratio Test** | | |
| --- | --- | --- |
| **DF** | **Chi-Square** | **Pr > ChiSq** |
| 1 | 298.84 | <.0001 |

| **Solution for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **Group** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | 512.86 | 13.4974 | 117 | 38.00 | <.0001 |
| **Group** | 2 | 8.2469 | 19.0882 | 117 | 0.43 | 0.6665 |
| **Group** | 3 | 2.1689 | 19.0882 | 117 | 0.11 | 0.9097 |
| **Group** | 1 | 0 | . | . | . | . |
| **sp\_mn1** |  | -21.5651 | 3.1123 | 594 | -6.93 | <.0001 |
| **sp\_mn2** |  | -20.4803 | 2.0586 | 594 | -9.95 | <.0001 |
| **sp\_mn1\*Group** | 2 | -2.6579 | 4.4014 | 594 | -0.60 | 0.5462 |
| **sp\_mn1\*Group** | 3 | -0.9908 | 4.4014 | 594 | -0.23 | 0.8220 |
| **sp\_mn1\*Group** | 1 | 0 | . | . | . | . |
| **sp\_mn2\*Group** | 2 | 19.4280 | 2.9113 | 594 | 6.67 | <.0001 |
| **sp\_mn2\*Group** | 3 | 31.7622 | 2.9113 | 594 | 10.91 | <.0001 |
| **sp\_mn2\*Group** | 1 | 0 | . | . | . | . |

| **Type 3 Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **Group** | 2 | 117 | 0.10 | 0.9046 |
| **sp\_mn1** | 1 | 594 | 160.74 | <.0001 |
| **sp\_mn2** | 1 | 594 | 8.27 | 0.0042 |
| **sp\_mn1\*Group** | 2 | 594 | 0.19 | 0.8301 |
| **sp\_mn2\*Group** | 2 | 594 | 60.50 | <.0001 |

**proc** **mixed** data=hiv\_spline method=ml;

class ID month group(ref='1');

model CD4 = group month group\*month/solution;

repeated month/ subject=ID type=CS r rcorr;

**run**;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 8189.6 |
| **AIC (Smaller is Better)** | 8229.6 |
| **AICC (Smaller is Better)** | 8230.8 |
| **BIC (Smaller is Better)** | 8285.4 |

| **Null Model Likelihood Ratio Test** | | |
| --- | --- | --- |
| **DF** | **Chi-Square** | **Pr > ChiSq** |
| 1 | 302.11 | <.0001 |

| **Solution for Fixed Effects** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **Month** | **Group** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  |  | 305.10 | 13.9247 | 117 | 21.91 | <.0001 |
| **Group** |  | 2 | 108.90 | 19.6926 | 117 | 5.53 | <.0001 |
| **Group** |  | 3 | 192.40 | 19.6926 | 117 | 9.77 | <.0001 |
| **Group** |  | 1 | 0 | . | . | . | . |
| **Month** | 0 |  | 208.68 | 13.4431 | 585 | 15.52 | <.0001 |
| **Month** | 2 |  | 162.80 | 13.4431 | 585 | 12.11 | <.0001 |
| **Month** | 4 |  | 122.58 | 13.4431 | 585 | 9.12 | <.0001 |
| **Month** | 6 |  | 81.6000 | 13.4431 | 585 | 6.07 | <.0001 |
| **Month** | 8 |  | 36.9750 | 13.4431 | 585 | 2.75 | 0.0061 |
| **Month** | 10 |  | 0 | . | . | . | . |
| **Month\*Group** | 0 | 2 | -101.33 | 19.0115 | 585 | -5.33 | <.0001 |
| **Month\*Group** | 0 | 3 | -193.00 | 19.0115 | 585 | -10.15 | <.0001 |
| **Month\*Group** | 0 | 1 | 0 | . | . | . | . |
| **Month\*Group** | 2 | 2 | -104.63 | 19.0115 | 585 | -5.50 | <.0001 |
| **Month\*Group** | 2 | 3 | -186.68 | 19.0115 | 585 | -9.82 | <.0001 |
| **Month\*Group** | 2 | 1 | 0 | . | . | . | . |
| **Month\*Group** | 4 | 2 | -116.88 | 19.0115 | 585 | -6.15 | <.0001 |
| **Month\*Group** | 4 | 3 | -186.88 | 19.0115 | 585 | -9.83 | <.0001 |
| **Month\*Group** | 4 | 1 | 0 | . | . | . | . |
| **Month\*Group** | 6 | 2 | -67.8750 | 19.0115 | 585 | -3.57 | 0.0004 |
| **Month\*Group** | 6 | 3 | -147.23 | 19.0115 | 585 | -7.74 | <.0001 |
| **Month\*Group** | 6 | 1 | 0 | . | . | . | . |
| **Month\*Group** | 8 | 2 | -27.9250 | 19.0115 | 585 | -1.47 | 0.1424 |
| **Month\*Group** | 8 | 3 | -64.3000 | 19.0115 | 585 | -3.38 | 0.0008 |
| **Month\*Group** | 8 | 1 | 0 | . | . | . | . |
| **Month\*Group** | 10 | 2 | 0 | . | . | . | . |
| **Month\*Group** | 10 | 3 | 0 | . | . | . | . |
| **Month\*Group** | 10 | 1 | 0 | . | . | . | . |

| **Type 3 Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **Group** | 2 | 117 | 8.46 | 0.0004 |
| **Month** | 5 | 585 | 63.21 | <.0001 |
| **Month\*Group** | 10 | 585 | 18.11 | <.0001 |

**proc** **mixed** data=hiv\_spline method=ml;

class ID month group(ref='1');

model CD4 = group sp\_mn1 sp\_mn2 group\*sp\_mn1 group\*sp\_mn2/solution outpm=pred;

repeated month/ subject=ID type=CS r rcorr;

**run**;

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 8199.6 |
| **AIC (Smaller is Better)** | 8233.3 |
| **AICC (Smaller is Better)** | 8233.8 |
| **BIC (Smaller is Better)** | 8285.4 |

**Let’s compare these two models graphically:**

**proc** **mixed** data=hiv\_spline;

class ID month group(ref='1');

model CD4 = group month group\*month/solution outpm=pred2;

repeated month/ subject=ID type=CS r rcorr;

**run**;

**proc** **sgplot** data=pred;

series y=pred x=month / group=group;

**run**;

**proc** **sgplot** data=pred2;

series y=pred x=month / group=group;

**run**;

