

A pharmaceutical company examined effects of three drugs on respiratory ability of asthma patients. The drugs were randomly assigned to 24 patients each. The assigned drug as administered to each patient. Then a standard measure of respiratory called FEV1 was measured hourly for eight hours following treatment. FEV1 was also measured immediately prior to administration of the drugs.

```
title1 " ";
options nodate nonumber ls=80 nocenter;
data fev1mult;
input PATIENT BASEFEV1 FEV11H FEV12H FEV13H FEV14H FEV15H FEV16H FEV17H FEV18H DRUG $;
cards;
201 2.46 2.68 2.76 2.50 2.30 2.14 2.40 2.33 2.20 a
202 3.50 3.95 3.65 2.93 2.53 3.04 3.37 3.14 2.62 a
...
232 2.88 3.04 3.00 3.24 3.37 2.69 2.89 2.89 2.76 p
;
```

```
data fev1uni; set fev1mult;
drop fev11h fev12h fev13h fev14h fev15h fev16h fev17h fev18h;
hour=1; fev1=fev11h; output;
hour=2; fev1=fev12h; output;
hour=3; fev1=fev13h; output;
hour=4; fev1=fev14h; output;
hour=5; fev1=fev15h; output;
hour=6; fev1=fev16h; output;
hour=7; fev1=fev17h; output;
hour=8; fev1=fev18h; output;
run;
```

```
symbol1 i=j line=1 v=plus c=black;
symbol2 i=j line=5 v=square c=black;
symbol3 i=j line=10 v=triangle c=black;
```

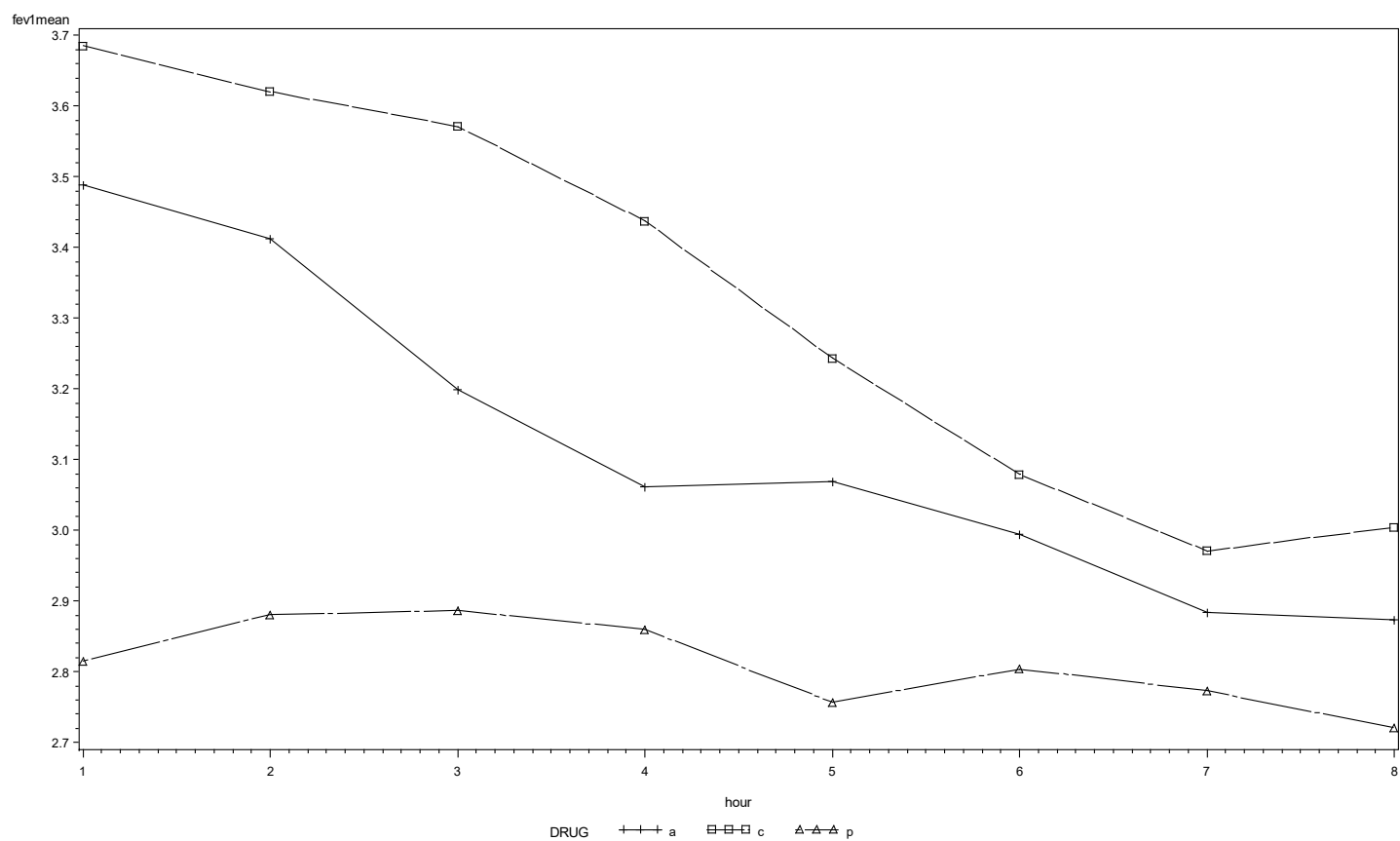
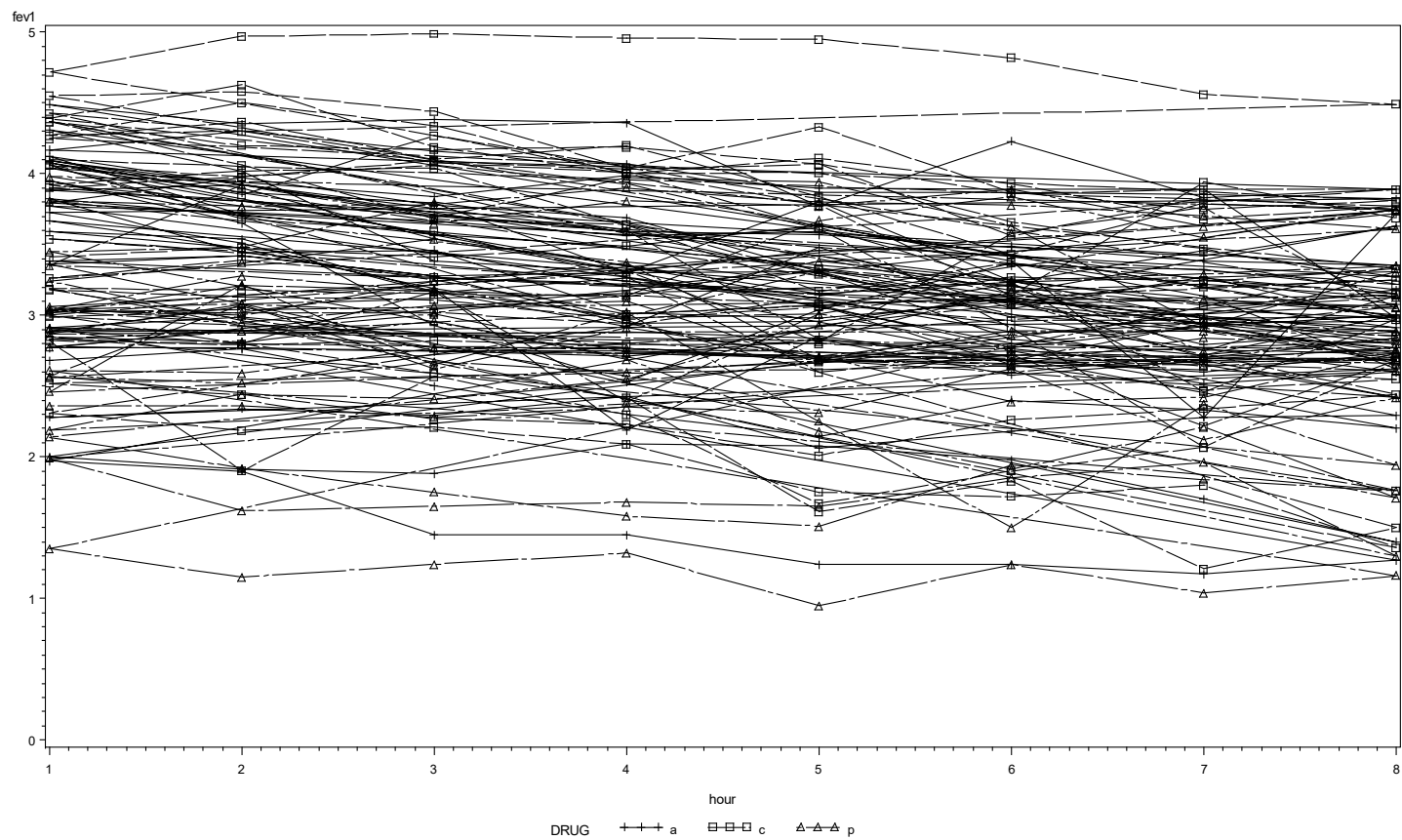
```
proc gplot data=fev1uni;
plot fev1*hour =drug;
run;
```

```
proc sort data=fev1uni;
by drug hour;
run;
```

```
proc means data=fev1uni;
var fev1;
by drug hour;
output out=fev1mean mean=fev1mean;
run;
```

```
proc print;
run;
```

```
proc gplot data=fev1mean;
plot fev1mean*hour = drug;
run;
```



```

proc glm data=fev1uni;
class drug patient hour;
model fev1=drug patient(drug) hour drug*hour / ss3;
random patient(drug)/test;
lsmeans drug / pdiff cl adj=tukey e=patient(drug);
contrast "a-c overall" drug 1 -1 0 / e=patient(drug);
contrast "a-c at hour1" drug 1 -1 0 drug*hour 1 0 0 0 0 0 0 -1 0 0 0 0 0 0;
run;

```

Source	Type III Expected Mean Square
DRUG	Var(Error) + 8 Var(PATIENT(DRUG)) + Q(DRUG, DRUG*hour)
PATIENT(DRUG)	Var(Error) + 8 Var(PATIENT(DRUG))
hour	Var(Error) + Q(hour, DRUG*hour)
DRUG*hour	Var(Error) + Q(DRUG*hour)

The GLM Procedure
Tests of Hypotheses for Mixed Model Analysis of Variance

Dependent Variable: fev1

Source	DF	Type III SS	Mean Square	F Value	Pr > F
DRUG	2	25.782567	12.891284	3.60	0.0327
Error	69	247.412491	3.585688		
Error: MS (PATIENT (DRUG))					

Source	DF	Type III SS	Mean Square	F Value	Pr > F
PATIENT(DRUG)	69	247.412491	3.585688	56.80	<.0001
hour	7	17.170399	2.452914	38.86	<.0001
DRUG*hour	14	6.280066	0.448576	7.11	<.0001
Error: MS (Error)	483	30.490259	0.063127		

Least Squares Means

Adjustment for Multiple Comparisons: Tukey

Standard Errors and Probabilities Calculated Using the Type III MS for
PATIENT(DRUG) as an Error Term

DRUG	fev1 LSMEAN	LSMEAN Number
a	3.12276042	1
c	3.32645833	2
p	2.81192708	3

Least Squares Means for effect DRUG

Pr > |t| for H0: LSMean(i)=LSMean(j)

Dependent Variable: fev1

i/j	1	2	3
1		0.5457	0.2490
2	0.5457		0.0258
3	0.2490	0.0258	

DRUG	fev1 LSMEAN	95% Confidence Limits	
a	3.122760	2.850135	3.395386
c	3.326458	3.053833	3.599084
p	2.811927	2.539301	3.084553

Least Squares Means for Effect DRUG

i	j	Difference Between Means	Simultaneous 95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	-0.203698	-0.666627	0.259231
1	3	0.310833	-0.152096	0.773762
2	3	0.514531	0.051602	0.977460

Dependent Variable: fev1

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c at hour1	1	0.46216875	0.46216875	7.32	0.0071

Tests of Hypotheses Using the Type III MS for PATIENT(DRUG) as an Error Term

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c overall	1	3.98331276	3.98331276	1.11	0.2956

```
proc glm data=fev1mult;
class drug;
model fev11h fev12h fev13h fev14h fev15h fev16h fev17h fev18h=drug / nouni;
repeated hour/printe;
run;
```

Sphericity Tests

Variables	DF	Mauchly's Criterion	Chi-Square	Pr > ChiSq
Transformed Variates	27	0.0033417	378.86425	<.0001
Orthogonal Components	27	0.0654899	181.13982	<.0001 ←

The GLM Procedure
Repeated Measures Analysis of Variance
Tests of Hypotheses for Between Subjects Effects

Source	DF	Type III SS	Mean Square	F Value	Pr > F
DRUG	2	25.7825670	12.8912835	3.60	0.0327
Error	69	247.4124906	3.5856883		

The GLM Procedure
Repeated Measures Analysis of Variance
Univariate Tests of Hypotheses for Within Subject Effects

Source	DF	Type III SS	Mean Square	F Value	Pr > F
hour	7	17.17039931	2.45291419	38.86	<.0001
hour*DRUG	14	6.28006632	0.44857617	7.11	<.0001
Error (hour)	483	30.49025937	0.06312683		

Source	Adj G - G	Pr > F H - F
hour	<.0001	<.0001
hour*DRUG	<.0001	<.0001
Error (hour)		

Greenhouse-Geisser Epsilon 0.4971
Huynh-Feldt Epsilon 0.5419

The summary option in the repeated statement provides univariate anova results of contrast variables ... the contrasts are differences between each hour and hour 8. For example hour.1 is the difference between hour 1 and hour 8. For each contrast variable there are tests labeled mean, drug, and a-c. These results are what you would obtain if you created the differences in a SAS data set and ran univariate analyses on the contrasts. Since they are univariate analyses, their validity does not depend on the covariance structure.

Some care is required to correctly interpret the tests ... consider the variable hour.1. The F-text for drug is highly significant ... this is evidence that the means of the variable hour.1 for the three drugs are different ... but since the variable hour.1 is the difference between hours 1 and 8, the test for drug is really a test of whether the change from hour 1 to hour 8 differs between the drugs. Thus the test for drug is really a test for the interaction between drugs and the contrast hour 1 minus hour 8.

Likewise,

test a-c : test for the interaction b/w drug contrast a-c and the hour contrast 1-8.

The test for mean

... is a test for whether the average value of hour.1 over the drugs differ from zero.

```

proc glm data=fevlmult;
class drug;
model fev11h fev12h fev13h fev14h fev15h fev16h fev17h fev18h=drug / nouni;
contrast 'a-c' drug 1 -1 0;
repeated hour/printe summary;
run;

```

The GLM Procedure
 Repeated Measures Analysis of Variance
 Analysis of Variance of Contrast Variables

hour_N represents the contrast between the nth level of hour and the last

Contrast Variable: hour_1

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	15.47533889	15.47533889	81.76	<.0001
DRUG	2	4.95388611	2.47694306	13.09	<.0001
Error	69	13.05957500	0.18926920		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.05135208	0.05135208	0.27	0.6041

Contrast Variable: hour_2

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	13.84256806	13.84256806	82.37	<.0001
DRUG	2	2.85541111	1.42770556	8.50	0.0005
Error	69	11.59632083	0.16806262		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.07207500	0.07207500	0.43	0.5147

Contrast Variable: hour_3

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	8.96761250	8.96761250	62.21	<.0001
DRUG	2	1.95842500	0.97921250	6.79	0.0020
Error	69	9.94626250	0.14414873		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.69841875	0.69841875	4.85	0.0311

Contrast Variable: hour_4

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	4.63093889	4.63093889	31.57	<.0001
DRUG	2	1.19181111	0.59590556	4.06	0.0215
Error	69	10.12265000	0.14670507		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.72030000	0.72030000	4.91	0.0300

Contrast Variable: hour_5

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	1.77347222	1.77347222	19.50	<.0001
DRUG	2	0.54738611	0.27369306	3.01	0.0559
Error	69	6.27594167	0.09095568		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.02296875	0.02296875	0.25	0.6169

Contrast Variable: hour_6

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	0.62533472	0.62533472	9.28	0.0033
DRUG	2	0.02916944	0.01458472	0.22	0.8058
Error	69	4.64719583	0.06735066		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.02566875	0.02566875	0.38	0.5390

Contrast Variable: hour_7

Source	DF	Type III SS	Mean Square	F Value	Pr > F
Mean	1	0.00700139	0.00700139	0.07	0.7953
DRUG	2	0.08841944	0.04420972	0.43	0.6535
Error	69	7.12547917	0.10326781		

Contrast	DF	Contrast SS	Mean Square	F Value	Pr > F
a-c	1	0.02296875	0.02296875	0.22	0.6387