Fitting a mixed model with unstructured covariance, and unstructured time trend for a controlled trial

- 1. Select from menu bar: Analyze>Mixed Model>linear
 - Put the patient ID in the subjects box
 - Put visit # in the Repeated box
 - Select "Unstructured: Correlation Metric" from the "Repeated" drop down menu (note: is you want a different structure, just select it instead)



- 2. Define your variables of interest
 - Put your outcome variable in the "Dependent Variable" box
 - Put Treatment group, and visit # in the "Factor" box

Linear Mixed Models			$\overline{\mathbf{X}}$
 Patients Unique ID [subnun site week HAM total 1-17 [hamtot17] visit=1 visit=6 visit=8 (FIL) 	•	Dependent Variable: CDRS Total Score [cdrstot] Factor(s): Comparison Factor(s): Factor(s): Factor(s): Comparison Factor(s): Comparison Compa	OK Paste Reset Cancel Help
	•	Covariate(s):	
Fixed Random	Estimatio	Don) Statistics EM Means	Save

- 3. Click on fixed effects
 - Put treatment group, visit # and their interaction into the model
 - Click continue

Linear Mixed Models: Fixed	d Effects		
Fixed Effects			
 Build terms 	O Build nested te	rms	
Factors and Covariates:		Model:	
druggroup(F) visit(F)	Factorial 💌	druggroup visit druggroup*visit	
By* (Within) Build Term:	Clear Term	Add Remove	
✓ Include Intercept Su	um of squares:	ype III 💌 Continue Cancel Help]

- 4. Click on "Statistics"
 - Check the Parameter estimates box
 - Click "Continue" and the "OK"

🗖 Linear Mixed Models			
			drugaron
Patients Unique ID (subnur	Dependent Variable:	ΠΚ	Linear Mixed Models: Statistics
Site	CDRS Total Score [cdrstot]	Paste	Summary Statistics
HAM total 1-17 [hamtot17]	Exchar(a):	Beset	Descriptive statistics
🔗 visit=1 visit=6 visit=8 (FIL)	druggroup	Cancel	1. Case Processing Summary
	🕨 🛷 visit	Help	Model Statistics Help
			Parameter estimates
	Covariate(s):		Tests for covariance parameters
			Correlations of parameter estimates
	•		Covariances of parameter estimates
			Covariances of random effects
	Residual Weight:		Covariances of residuals
			Contrast coefficient matrix
Fixed Random	Estimation Statistics EM Means	Save	Confidence interval: 95 %
	N 5.00000 1		
→	XO		

Linear Mixed Models				
Patients Unique ID [subnun Site Week AM total 1-17 [hamtot17] Visit=1 visit=6 visit=8 (FIL)	Dependent Variable: CDRS Total Score [cdrstot] Paste Factor(s): Reset druggroup visit Help	, , , , ,	Linear Mixed Models: Statistics	Continue Cancel Help
•	Covariate(s):		Tests for covariance parameters Correlations of parameter estimates Covariances of parameter estimates Covariances of random effects Covariances of residuals Contrast coefficient matrix	
Fixed Random Estimat	on Statistics EM Means Save	_	Confidence interval: 95 %	

The Output

1. F-tests of fixed effects

Type III Tests of Fixed Effects(a)

Source	Numerator df	Denominator df	F	Sig.
Intercept	1	91.487	246.581	.000
druggroup	1	91.487	14.096	.000
visit	2	79.042	23.274	.000
druggroup * visit	2	79.042	1.876	.160

a Dependent Variable: CDRS Total Score.

- Drug group is significant (<0.001): thus there is an overall difference between the groups
- Visit is significant (<0.001): Subjects change over time.
- The interaction of drug group and time is not significant (0.160): There is not enough evidence to conclude that the treatment groups progress differently over time. (Note: the interaction is the most important test when considering a treatment effect because the placebo and treatments should progress differently. The treatment should improve relative to the placebo)
- 2. Parameter estimates

Parameter	Estimate	Std. Error	df	t	Sig.	95% Confidence Interval	
Intercept	2.787863	.546934	78.889	5.097	.000	1.699195	3.876531
[druggroup=1.00000]	3.032488	.800008	78.132	3.791	.000	1.439837	4.625139
[druggroup=2.00000]	0(a)	0					
[visit=1.00000]	2.966854	.576155	86.204	5.149	.000	1.821534	4.112174
[visit=6.00000]	147509	.455714	70.537	324	.747	-1.056281	.761262
[visit=8.00000]	0(a)	0					
[visit=1.00000] * [druggroup=1.00000]	-1.603531	.841622	85.810	-1.905	.060	-3.276674	.069612
[visit=6.00000] * [druggroup=1.00000]	466091	.669651	70.355	696	.489	-1.801549	.869366
[visit=8.00000] * [druggroup=1.00000]	0(a)	0					
[visit=1.00000] * [druggroup=2.00000]	0(a)	0					
[visit=6.00000] * [druggroup=2.00000]	0(a)	0					
[visit=8.00000] * [druggroup=2.00000]	0(a)	0					

Estimates of Fixed Effects(b)

a This parameter is set to zero because it is redundant.

b Dependent Variable: CDRS Total Score.

- All tests of parameters are relative to the reference categories (i.e. the redundant parameters)
- Druggroup=1 (placebo) is significant, and it is relative to Druggroup=2, and visit=8, so, the groups are significantly different at the endpoint (visit 8)