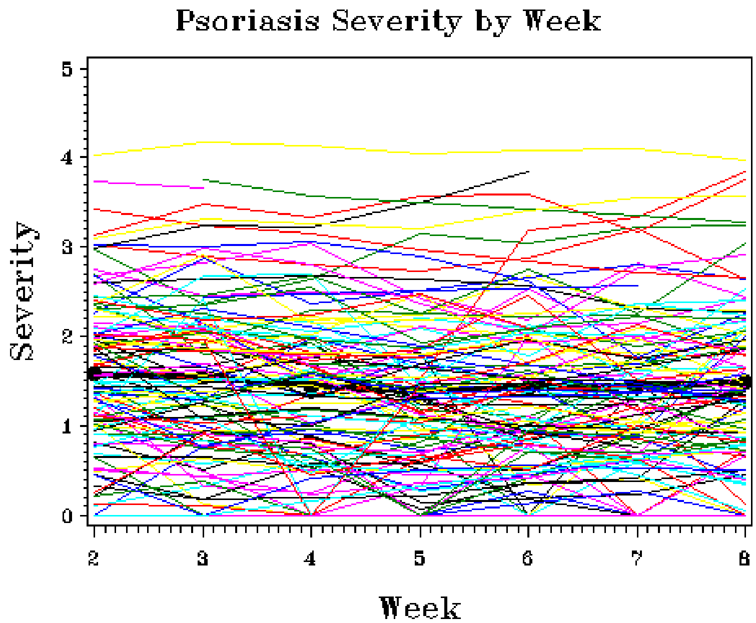
Example 4: Within-Person Fluctuation in Symptom Severity over Time
(complete syntax and output available for SAS, STATA, and R electronically)



These are real data from a study of weekly fluctuation in psoriasis severity. There was no intervention and no real reason to expect systematic growth (as shown by the mostly flat solid black line for the means).

But we still need ensure good fit for the model for the variance. The variances across occasions may need to differ, and the covariances across occasions may need to differ as well.

We will include just a fixed intercept in the model for the means and examine different ACS models for the variance, including R-only and G+R models for the variance.

To begin, let's see what the observed pattern of variances and covariances over time looks like by estimating an *n*-order unstructured (UN) **R** baseline model for the variance → each variance and covariance estimated is separately, with no constraints, so this is a description, not a predictive model. Btw, UN is equivalent to the "H1" model in SEM terminology with respect to the occasions' variances and covariances, but not with respect to the occasion means (we have only estimated one mean here instead of all possible means, as in the H1 model). *Note: you can only estimate an unstructured model if time is balanced across persons and you have more people than parameters estimated!*

This example uses the MIXED function in SAS and STATA, as well as three functions in R: `mmrm` (from the `mmrm` package) and `gls` and `lme` (from the `nlme` package). Each one has only some of the needed options ☹

***n*-order Unstructured (UN) R-only Model: the answer key of all possible variances and covariances estimated directly (rather than built from a pattern of fewer parameters)**

```
TITLE1 "SAS n-order Unstructured (UN) R-only Model";
* COVTEST adds SE for variances, IC=information criteria;
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
* CLASS needs categorical predictors and ID variables;
     CLASS subid week;
* MODEL y = x / print solution using Satterthwaite DDF;
     MODEL severity =  / SOLUTION DDFM=Satterthwaite;
* REPEATED timeIDvariable structures R matrix with TYPE;
     REPEATED week / TYPE=UN R RCORR SUBJECT=subid;
* ODS OUTPUT lists output tables to be saved as SAS datasets;
     ODS OUTPUT InfoCrit=FitUN; * Save for LRT;
RUN; TITLE1;

display "STATA n-order Unstructured R-only Model"
// subid: indicates nesting, noconstant removes random intercept
mixed severity , || subid: , noconstant reml nolog difficult  ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(unstructured,t(week))
display "-2LL = " e(ll)*-2      // Print -2LL for model
```

```
estat wcorrelation, covariance  // R matrix
estat wcorrelation              // RCORR matrix
estat ic                        // AIC and BIC
estimates store FitUN           // Save for LRT
# Convert my ID variables into factors as required by mmrm package
Example4$Fsubid=as.factor(Example4$subid)
Example4$Fweek=as.factor(Example4$week)

print("R mmrm Unstructured R-only Model")
UN = mmrm(data=Example4, formula=severity~1 + us(Fweek|Fsubid), reml=TRUE)
print("Show results adding -2LL and RCORR matrix")
deviance(UN); summary(UN); cov2cor(UN$cov)
```

R Output *(SAS and STATA output are very similar they but also have SEs for each R matrix term)*:

Note that given n=7, this model requires $n*(n+1) / 2 = 28$ covariance parameters!! You'd need at least 28 people to estimate it (and it may not be possible even then).

```
Formula:     severity ~ 1 + us(Fweek | Fsubid)
Data:        Example4 (used 770 observations from 124 subjects with maximum 7 timepoints)
Covariance:  unstructured (28 variance parameters)
Method:      Satterthwaite
Vcov Method: Asymptotic
Inference:   REML

Model selection criteria:
     AIC      BIC   logLik deviance → deviance = model -2LL
   949.1   1028.1   -446.6    893.1

Coefficients:
             Estimate Std. Error         df t value  Pr(>|t|)
(Intercept)  1.517786   0.074294 121.783000   20.43 < 2.2e-16

Covariance estimate: → This is the total (marginal) R variance-covariance matrix across
weeks 2-8
        2       3       4       5       6       7       8
2 0.74766 0.71901 0.68173 0.68075 0.61239 0.61821 0.63282
3 0.71901 0.82660 0.74284 0.74755 0.65714 0.66191 0.65410
4 0.68173 0.74284 0.83463 0.74985 0.65247 0.63899 0.61723
5 0.68075 0.74755 0.74985 0.83660 0.72929 0.72068 0.68058
6 0.61239 0.65714 0.65247 0.72929 0.82853 0.72810 0.73139
7 0.61821 0.66191 0.63899 0.72068 0.72810 0.79110 0.73527
8 0.63282 0.65410 0.61723 0.68058 0.73139 0.73527 0.84641

> cov2cor(UN$cov) → This is the RCORR matrix, the correlation version of the R matrix
        2       3       4       5       6       7       8
2 1.00000 0.91461 0.86300 0.86074 0.77807 0.80384 0.79550
3 0.91461 1.00000 0.89433 0.89895 0.79406 0.81853 0.78199
4 0.86300 0.89433 1.00000 0.89736 0.78462 0.78637 0.73435
5 0.86074 0.89895 0.89736 1.00000 0.87597 0.88586 0.80878
6 0.77807 0.79406 0.78462 0.87597 1.00000 0.89933 0.87339
7 0.80384 0.81853 0.78637 0.88586 0.89933 1.00000 0.89854
8 0.79550 0.78199 0.73435 0.80878 0.87339 0.89854 1.00000
```

The fit statistics for this n-order unstructured **R**-only model will serve as a baseline with which to compare more parsimonious models for the variance.

Ok, so this R matrix is what our models will be trying to reproduce… next we will try a few **R**-only models and see how they fit relative to this Unstructured answer key—can we use fewer parameters to capture these patterns and not decrease model fit?

Compound Symmetry (CS) R-only Model: equal total variances and covariances across weeks

```
TITLE1 "SAS Compound Symmetry (CS) R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     REPEATED week / TYPE=CS R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitCS; * Save for LRT;
RUN; TITLE1;
```

```
                  Covariance Parameter Estimates
                                          Standard         Z
Cov Parm      Subject      Estimate          Error     Value        Pr Z
CS            SUBID          0.6820        0.09019      7.56      <.0001 Var(U0)
Residual                     0.1306       0.007270     17.97      <.0001 Var(e)
```

SAS gives the parameters (= ingredients) that construct the R matrix:
CS = $\tau^2_{U_0}$ and Residual = σ^2_e

```
TITLE1 "Model comparison: CS not worse than UN?";
%FitTest(FitFewer=FitCS, FitMore=FitUN); TITLE1;
```

```
Likelihood Ratio Test for FitCS vs. FitUN
         Neg2Log
Name       Like      Parms     AIC      BIC    DevDiff    DFdiff    Pvalue
FitCS     1049.7        2   1053.7   1059.4       .          .         .
FitUN      893.1       28    949.1   1028.1    156.585      26         0
```

Is CS worse than UN? Yes!
$-2\Delta LL(26) = 156.6$, $p < 001$

```
display "STATA Compound Symmetry (CS) R-only Model"
mixed severity , || subid: , noconstant reml nolog  ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(exchangeable,t(week))
display "-2LL = " e(ll)*-2      // Print -2LL for model
estat wcorrelation, covariance  // R matrix
estat wcorrelation              // RCORR matrix
estat ic                        // AIC and BIC
estimates store FitCS           // Save for LRT
lrtest FitUN FitCS              // CS worse than UN?
```

STATA gives a different version of the parameters that construct the R matrix:
var(e) = total variance and cov(e) = $\tau^2_{U_0}$

```
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
subid:                (empty) |
-----------------------------+------------------------------------------------
Residual: Exchangeable       |
                      var(e) |   .8126927   .0903725      .6535391    1.010604  Total var
                      cov(e) |   .6820625   .0901958      .5052819     .858843  Var(U0)
------------------------------------------------------------------------------
```

```
print("R mmrm Compound Symmetry R-only Model")
CS = mmrm(data=Example4, formula=severity~1 + cs(Fweek|Fsubid), reml=TRUE)
print("Show results adding -2LL and RCORR matrix")
deviance(CS); summary(CS); cov2cor(CS$cov)
```

```
Covariance:  compound symmetry (2 variance parameters)

Model selection criteria:
     AIC      BIC   logLik deviance
  1053.7   1059.4   -524.9   1049.7

Coefficients:
            Estimate Std. Error       df t value Pr(>|t|)
(Intercept)   1.4767     0.0755 122.6000    19.6   <2e-16
```

```
Covariance estimate: → R matrix
      2     3     4     5     6     7     8
2 0.813 0.682 0.682 0.682 0.682 0.682 0.682
3 0.682 0.813 0.682 0.682 0.682 0.682 0.682
4 0.682 0.682 0.813 0.682 0.682 0.682 0.682
5 0.682 0.682 0.682 0.813 0.682 0.682 0.682
6 0.682 0.682 0.682 0.682 0.813 0.682 0.682
7 0.682 0.682 0.682 0.682 0.682 0.813 0.682
8 0.682 0.682 0.682 0.682 0.682 0.682 0.813
```

The intraclass correlation in RCORR can be computed as: $\text{ICC} = \dfrac{0.682}{0.813} = .839$

```
> cov2cor(CS$cov) → RCORR matrix
        2       3       4       5       6       7       8
2 1.00000 0.83926 0.83926 0.83926 0.83926 0.83926 0.83926
3 0.83926 1.00000 0.83926 0.83926 0.83926 0.83926 0.83926
4 0.83926 0.83926 1.00000 0.83926 0.83926 0.83926 0.83926
5 0.83926 0.83926 0.83926 1.00000 0.83926 0.83926 0.83926
6 0.83926 0.83926 0.83926 0.83926 1.00000 0.83926 0.83926
7 0.83926 0.83926 0.83926 0.83926 0.83926 1.00000 0.83926
8 0.83926 0.83926 0.83926 0.83926 0.83926 0.83926 1.00000
```

```
# mmrm does not appear to have any built-in LRTs (or use with anova), so I made it myself
print("LRT: Is CS worse than UN?")
devUNCS = deviance(CS)-deviance(UN); devUNCS              # difference in -2LL
dfUNCS = length(UN$jac_list)-length(CS$jac_list); dfUNCS  # difference in # parms
pchisq(devUNCS, dfUNCS, lower.tail=FALSE)                 # p-value for LRT
```

Auto-Regressive (AR) R-only Model: equal total variances and an AR1 total correlation

```
TITLE1 "SAS Auto-Regressive (AR1) R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     REPEATED week / TYPE=AR(1) R RCORR SUBJECT=subid;
* Use this version for unbalanced time;
     *REPEATED week / TYPE=SP(POW)(week) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitAR1; * Save for LRT;
RUN; TITLE1;
```

SAS gives the parameters that construct the R matrix: **AR1 corr** and Residual = total var

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr Z	
AR(1)	SUBID	0.8955	0.01148	78.01	<.0001	**Total AR1 correlation**
Residual		0.7999	0.08044	9.94	<.0001	**Total variance (equal across weeks)**

```
TITLE1 "Model comparison: AR1 not worse than UN?";
%FitTest(FitFewer=FitAR1, FitMore=FitUN); TITLE1;
```

Likelihood Ratio Test for FitAR1 vs. FitUN

Name	Neg2Log Like	Parms	AIC	BIC	DevDiff	DFdiff	Pvalue
FitAR1	990.9	2	994.9	1000.5	.	.	.
FitUN	893.1	28	949.1	1028.1	**97.7472**	**26**	**3.0326E-10**

Is AR1 worse than UN? Yes! $-2\Delta LL(26) = 97.7$, $p < 001$

```
display "STATA Auto-Regressive (AR1) R-only Model"
mixed severity , || subid: , noconstant reml nolog  ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(ar1,t(week))
display "-2LL = " e(ll)*-2       // Print -2LL for model
estat wcorrelation, covariance   // R matrix
estat wcorrelation               // RCORR matrix
estat ic                         // AIC and BIC
estimates store FitAR1           // Save for LRT
lrtest FitUN FitAR1              // AR worse than UN?
```

Option for AR1 using unbalanced time are not available in STATA MIXED as far as I know

```
----------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+----------------------------------------------
subid:                (empty) |
-----------------------------+----------------------------------------------
Residual: AR(1)               |
                          rho |   .8955408   .0114794      .8706121    .9158826  Total AR1 corr
                       var(e) |    .799881   .0804445      .6567794     .974162  Total variance
----------------------------------------------------------------------------
```

```
print("R mmrm Auto-Regressive R-only Model")
AR1 = mmrm(data=Example4, formula=severity~1 + ar1(Fweek|Fsubid), reml=TRUE)
print("Show results adding -2LL and RCORR matrix")
deviance(AR1); summary(AR1); cov2cor(AR1$cov)
```

```
Covariance:  auto-regressive order one (2 variance parameters)

Model selection criteria:
     AIC       BIC    logLik deviance
   994.9    1000.5    -495.4    990.9

Coefficients:
            Estimate Std. Error        df t value Pr(>|t|)
(Intercept)   1.5148     0.0703 128.7000    21.5   <2e-16

Covariance estimate: → R matrix
      2     3     4     5     6     7     8
2 0.800 0.716 0.641 0.574 0.514 0.461 0.413
3 0.716 0.800 0.716 0.641 0.574 0.514 0.461
4 0.641 0.716 0.800 0.716 0.641 0.574 0.514
5 0.574 0.641 0.716 0.800 0.716 0.641 0.574
6 0.514 0.574 0.641 0.716 0.800 0.716 0.641
7 0.461 0.514 0.574 0.641 0.716 0.800 0.716
8 0.413 0.461 0.514 0.574 0.641 0.716 0.800
```

For unbalanced time, you can use **corCAR1** in **gls** instead

```
> cov2cor(AR1$cov) → RCORR matrix
        2       3       4       5       6       7       8
2 1.00000 0.89554 0.80199 0.71822 0.64319 0.57601 0.51584
3 0.89554 1.00000 0.89554 0.80199 0.71822 0.64319 0.57601
4 0.80199 0.89554 1.00000 0.89554 0.80199 0.71822 0.64319
5 0.71822 0.80199 0.89554 1.00000 0.89554 0.80199 0.71822
6 0.64319 0.71822 0.80199 0.89554 1.00000 0.89554 0.80199
7 0.57601 0.64319 0.71822 0.80199 0.89554 1.00000 0.89554
8 0.51584 0.57601 0.64319 0.71822 0.80199 0.89554 1.00000
```

AR1 also forces all variances equal, but with correlations declining sharply with time (r, r^2, r^3... = .8955, .8020, .7182…). Relative to the UN model, the BIC (but not the AIC) is happier.

```
print("LRT: Is AR1 worse than UN?")
devUNAR1 = deviance(AR1)-deviance(UN); devUNAR1                # difference in -2LL
dfUNAR1 = length(UN$jac_list)-length(AR1$jac_list); dfUNAR1   # difference in # parms
pchisq(devUNAR1, dfUNAR1, lower.tail=FALSE)                   # p-value for LRT
```

Toeplitz(*n*) R-only Model: equal total variances and 6 lagged total covariances across weeks

```
TITLE1 "SAS Toeplitz (n=7 total bands, lag-6) R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     REPEATED week / TYPE=TOEP(7) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitTP7; * Save for LRT;
RUN; TITLE1;
```

For Toeplitz in SAS, (*n*) indicates the total number of bands including the total variance on the diagonal + 6 total covariances for the 7 occasions.

```
                  Covariance Parameter Estimates
                                           Standard         Z
Cov Parm      Subject       Estimate        Error       Value        Pr Z
TOEP(2)       SUBID           0.7257      0.09004        8.06      <.0001   Total covariance for t-1 (lag 1)
TOEP(3)       SUBID           0.6974      0.08997        7.75      <.0001   Total covariance for t-2 (lag 2)
TOEP(4)       SUBID           0.6576      0.09003        7.30      <.0001   Total covariance for t-3 (lag 3)
TOEP(5)       SUBID           0.6394      0.09019        7.09      <.0001   Total covariance for t-4 (lag 4)
TOEP(6)       SUBID           0.6368      0.09066        7.02      <.0001   Total covariance for t-5 (lag 5)
TOEP(7)       SUBID           0.6541      0.09179        7.13      <.0001   Total covariance for t-6 (lag 6)
Residual                      0.8103      0.09014        8.99      <.0001   Total variance (equal across weeks)
```

```
TITLE1 "Model comparison: TP7 not worse than UN?";
%FitTest(FitFewer=FitTP7, FitMore=FitUN); TITLE1;
```

```
Likelihood Ratio Test for FitToep7 vs. FitUN
            Neg2Log
Name          Like    Parms     AIC      BIC     DevDiff     DFdiff      Pvalue
FitToep7      926.0      7     940.0    959.7       .           .           .
FitUN         893.1     28     949.1   1028.1    32.8656        21      0.047729
```

The TOEP(*n*) model fits almost not worse than the *n*-order UN model, $-2\Delta LL(21) = 32.9$, $p = .047$ (and AIC and BIC agree).

```
display "STATA Toeplitz (n=7 total bands, lag-6) R-only Model"
mixed severity , || subid: , noconstant reml nolog  ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(toeplitz6,t(week))
estat wcorrelation, covariance  // R matrix
estat wcorrelation              // RCORR matrix
estat ic                        // AIC and BIC
estimates store FitTP7          // Save for LRT
lrtest FitUN FitTP7             // TP7 worse than UN?
```

For Toeplitz in STATA, (*n*) indicates the number of bands NOT including the residual variance on the diagonal: just 6 covariances for the 7 occasions.

```
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
subid:               (empty) |  Interpretation is the same as SAS MIXED above
-----------------------------+------------------------------------------------
Residual: Toeplitz(6)        |
                        cov1 |   .7256645   .0900341      .549201     .902128   tot cov lag1
                        cov2 |   .6973526   .0899723     .5210101    .8736951   tot cov lag2
                        cov3 |   .6575993   .0900319       .48114    .8340586   tot cov lag3
                        cov4 |   .6393557   .0901891     .4625883    .8161231   tot cov lag4
                        cov5 |   .6368415     .09066     .4591512    .8145319   tot cov lag5
                        cov6 |   .6541479   .0917914       .47424    .8340558   tot cov lag6
                      var(e) |   .8103476    .090134     .6516181    1.007742   tot variance
------------------------------------------------------------------------------
```

```
print("R mmrm Toeplitz (n=7 total bands, lag-6) R-only Model")
TP7 = mmrm(data=Example4, formula=severity~1 + toep(Fweek|Fsubid), reml=TRUE)
print("Show results adding -2LL and RCORR matrix")
deviance(TP7); summary(TP7); cov2cor(TP7$cov)
```

```
Covariance:  Toeplitz (7 variance parameters)

Model selection criteria:
     AIC      BIC   logLik deviance
   940.0    959.7   -463.0    926.0

Coefficients:
            Estimate Std. Error       df t value Pr(>|t|)
(Intercept)   1.4884     0.0753 122.5000    19.8   <2e-16
```

```
Covariance estimate: → R matrix
      2     3     4     5     6     7     8
2 0.810 0.726 0.697 0.658 0.639 0.637 0.654
3 0.726 0.810 0.726 0.697 0.658 0.639 0.637
4 0.697 0.726 0.810 0.726 0.697 0.658 0.639
5 0.658 0.697 0.726 0.810 0.726 0.697 0.658
6 0.639 0.658 0.697 0.726 0.810 0.726 0.697
7 0.637 0.639 0.658 0.697 0.726 0.810 0.726
8 0.654 0.637 0.639 0.658 0.697 0.726 0.810
```

UN R matrix by comparison:

```
        2       3       4       5       6       7       8
2 0.74766 0.71901 0.68173 0.68075 0.61239 0.61821 0.63282
3 0.71901 0.82660 0.74284 0.74755 0.65714 0.66191 0.65410
4 0.68173 0.74284 0.83463 0.74985 0.65247 0.63899 0.61723
5 0.68075 0.74755 0.74985 0.83660 0.72929 0.72068 0.68058
6 0.61239 0.65714 0.65247 0.72929 0.82853 0.72810 0.73139
7 0.61821 0.66191 0.63899 0.72068 0.72810 0.79110 0.73527
8 0.63282 0.65410 0.61723 0.68058 0.73139 0.73527 0.84641
```

```
> cov2cor(TP7$cov) → RCORR matrix
        2       3       4       5       6       7       8
2 1.00000 0.89550 0.86056 0.81150 0.78898 0.78586 0.80723
3 0.89550 1.00000 0.89550 0.86056 0.81150 0.78898 0.78586
4 0.86056 0.89550 1.00000 0.89550 0.86056 0.81150 0.78898
5 0.81150 0.86056 0.89550 1.00000 0.89550 0.86056 0.81150
6 0.78898 0.81150 0.86056 0.89550 1.00000 0.89550 0.86056
7 0.78586 0.78898 0.81150 0.86056 0.89550 1.00000 0.89550
8 0.80723 0.78586 0.78898 0.81150 0.86056 0.89550 1.00000
```

```
print("LRT: Is TP7 worse than UN?")
devUNTP7 = deviance(TP7)-deviance(UN); devUNTP7                # difference in -2LL
dfUNTP7 = length(UN$jac_list)-length(TP7$jac_list); dfUNTP7    # difference in # parms
pchisq(devUNTP7, dfUNTP7, lower.tail=FALSE)                    # p-value for LRT
```

Could this be our model? But does it need to have heterogeneous total variances across weeks?

Heterogeneous Toeplitz(*n*) R-only Model: Unequal total variances and 6 lagged total correlations

```
TITLE1 "SAS Heterogeneous Toeplitz (n=7 total bands, lag-6) R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     REPEATED week / TYPE=TOEPH(7) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitTPH7; * Save for LRT;
RUN; TITLE1;
```

This model is not available directly in STATA MIXED as far as I can tell.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr Z	
Var(1)	SUBID	0.7346	0.09397	7.82	<.0001	Total variance at week 2
Var(2)	SUBID	0.8077	0.1016	7.95	<.0001	Total variance at week 3
Var(3)	SUBID	0.8665	0.1129	7.68	<.0001	Total variance at week 4
Var(4)	SUBID	0.8414	0.1115	7.55	<.0001	Total variance at week 5
Var(5)	SUBID	0.8781	0.1162	7.56	<.0001	Total variance at week 6
Var(6)	SUBID	0.7882	0.1030	7.65	<.0001	Total variance at week 7
Var(7)	SUBID	0.8416	0.1092	7.70	<.0001	Total variance at week 8
TOEPH(1)	SUBID	0.8979	0.01292	69.51	<.0001	Total correlation for t−1 (lag 1)
TOEPH(2)	SUBID	0.8644	0.01744	49.57	<.0001	Total correlation for t−2 (lag 2)
TOEPH(3)	SUBID	0.8153	0.02429	33.56	<.0001	Total correlation for t−3 (lag 3)
TOEPH(4)	SUBID	0.7923	0.02790	28.40	<.0001	Total correlation for t−4 (lag 4)
TOEPH(5)	SUBID	0.7865	0.03056	25.73	<.0001	Total correlation for t−5 (lag 5)
TOEPH(6)	SUBID	0.8053	0.03340	24.11	<.0001	Total correlation for t−6 (lag 6)

```
TITLE1 "Model comparison: did het variance help TP7?";
%FitTest(FitFewer=FitTP7, FitMore=FitTPH7); TITLE1;

Likelihood Ratio Test for FitToep7 vs. FitToep7H
             Neg2Log
  Name         Like     Parms     AIC      BIC     DevDiff   DFdiff     Pvalue
FitToep7       926.0      7     940.0    959.7       .          .         .
FitToep7H      921.5     13     947.5    984.1    4.54147       6     0.60381
```

Relative to the homogeneous Toeplitz: $-2\Delta LL(6) = 4.5$, $p = .604$. Separate variances don't improve model fit (AIC and BIC agree).

The TOEPH(n) model also fits significantly worse than the UN(n) model, $-2\Delta LL(15) = 28.3$, $p = .020$.

```
TITLE1 "Model comparison: TPH7 now not worse than UN?";
%FitTest(FitFewer=FitTPH7, FitMore=FitUN);

Likelihood Ratio Test for FitToep7H vs. FitUN
             Neg2Log
Name           Like     Parms     AIC      BIC     DevDiff    Dfdiff     Pvalue
FitToep7H     921.5      13     947.5    984.1       .           .          .
FitUN         893.1      28     949.1   1028.1    28.3241       15     0.019626

print("R mmrm Heterogeneous Toeplitz (n=7 total bands, lag-6) R-only Model")
TPH7 = mmrm(data=Example4, formula=severity~1 + toeph(Fweek|Fsubid), reml=TRUE)
print("Show results adding -2LL and RCORR matrix")
deviance(TPH7); summary(TPH7); cov2cor(TPH7$cov)

Covariance:  heterogeneous Toeplitz (13 variance parameters)

Model selection criteria:
     AIC      BIC    logLik deviance
   947.5    984.1    -460.7    921.5

Coefficients:
            Estimate Std. Error       df t value Pr(>|t|)
(Intercept)   1.5204     0.0742 123.5000    20.5   <2e-16

Covariance estimate: → R matrix
      2     3     4     5     6     7     8
2 0.735 0.692 0.690 0.641 0.636 0.598 0.633
3 0.692 0.808 0.751 0.713 0.687 0.632 0.648
4 0.690 0.751 0.866 0.767 0.754 0.674 0.677
5 0.641 0.713 0.767 0.841 0.772 0.704 0.686
6 0.636 0.687 0.754 0.772 0.878 0.747 0.743
7 0.598 0.632 0.674 0.704 0.747 0.788 0.731
8 0.633 0.648 0.677 0.686 0.743 0.731 0.842
```

Total *covariances are unequal* within a time lag band (because the total variances are allowed to differ over weeks), but total *correlations are equal* within a time lag band.

```
> cov2cor(TPH7$cov)  → RCORR matrix
        2       3       4       5       6       7       8
2 1.00000 0.89793 0.86436 0.81524 0.79232 0.78651 0.80525
3 0.89793 1.00000 0.89793 0.86436 0.81524 0.79232 0.78651
4 0.86436 0.89793 1.00000 0.89793 0.86436 0.81524 0.79232
5 0.81524 0.86436 0.89793 1.00000 0.89793 0.86436 0.81524
6 0.79232 0.81524 0.86436 0.89793 1.00000 0.89793 0.86436
7 0.78651 0.79232 0.81524 0.86436 0.89793 1.00000 0.89793
8 0.80525 0.78651 0.79232 0.81524 0.86436 0.89793 1.00000

print("LRT: Is TPH7 better than TP7?")
devTPH7TP7 = deviance(TP7)-deviance(TPH7); devTPH7TP7                # difference in -2LL
dfTPH7TP7 = length(TPH7$jac_list)-length(TP7$jac_list); dfTPH7TP7  # difference in # parms
pchisq(devTPH7TP7, dfTPH7TP7, lower.tail=FALSE)                     # p-value for LRT

print("LRT: Is TPH7 worse than UN?")
devUNTPH7 = deviance(TPH7)-deviance(UN); devUNTPH7                # difference in -2LL
dfUNTPH7 = length(UN$jac_list)-length(TPH7$jac_list); dfUNTPH7  # difference in # parms
pchisq(devUNTPH7, dfUNTPH7, lower.tail=FALSE)                     # p-value for LR
```

Another set of possible models: Just as we'll see later in models for within-person change, models for within-person fluctuation can make use of a combination of the **G** matrix (for between-person random effects) and the **R** matrix (for within-person residuals) to recreate the total (marginal) variance–covariance matrix. Adding a random intercept variance in **G** removes the primary source of variance and covariance from the **R** matrix, such that it will be easier to find a model for what is left in **R**. To do so in R software, however, we have to switch to `lme` from the `nlme` package.

First, let's see the pattern of just the **residual** WP variances and covariances…

Random Intercept in G + UN(*n*−1) R Model → Have to eliminate last (lag6) covariance for the model to be identified because there is only one lag6 covariance (T1 with T7), so it is not separately estimable

```
TITLE1 "SAS Random Intercept + Unstructured(n-1) R Model";
TITLE2 "Equal to n-Order Unstructured R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=UN(6) R RCORR SUBJECT=subid;
RUN; TITLE1; TITLE2;
```

SAS now has a random statement that specifies the **G** matrix to have a random intercept variance.

The **V** matrix shows the combined (total, marginal) predicted matrix given by **R** (conditional) and **G**.

```
display "STATA Random Intercept + Unstructured(n-1) R Model"
display "Equal to n-Order Unstructured R-only Model"
mixed severity , || subid: , reml nolog ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(banded6,t(week))
display "-2LL = " e(ll)*-2          // Print -2LL for model
estat recovariance, relevel(subid) // G matrix
estat wcorrelation, covariance     // V matrix
estat wcorrelation                 // VCORR matrix
estat ic                           // AIC and BIC
```

In STATA, remove `noconstant` from the options to invoke the default random intercept variance.

```
# Cannot see how to fit UN6 R matrix
# using R lme (defaults to UN7)
```

The residual correlations in RCORR are minimal after removing the contribution of the random intercept variance, such that **R** may be able to have a simpler structure yet still fit well.

SAS Output (*STATA output is similar*):

Estimated R Matrix for SUBID 100 → WP residual (conditional) variances and covariances

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	**0.1148**	0.08620	0.04892	0.04793	-0.02044	-0.01461	
2	0.08620	**0.1938**	0.1100	0.1147	0.02429	0.02907	0.02126
3	0.04892	0.1100	**0.2018**	0.1170	0.01962	0.006156	-0.01561
4	0.04793	0.1147	0.1170	**0.2038**	0.09643	0.08783	0.04774
5	-0.02044	0.02429	0.01962	0.09643	**0.1957**	0.09523	0.09853
6	-0.01461	0.02907	0.006156	0.08783	0.09523	**0.1583**	0.1024
7		0.02126	-0.01561	0.04774	0.09853	0.1024	**0.2136**

Estimated R Correlation Matrix for SUBID 100 → WP residual (conditional) correlations

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.5778	0.3213	0.3133	-0.1364	-0.1084	
2	0.5778	1.0000	0.5563	0.5773	0.1247	0.1660	0.1045
3	0.3213	0.5563	1.0000	0.5771	0.09875	0.03445	-0.07519
4	0.3133	0.5773	0.5771	1.0000	0.4830	0.4891	0.2288
5	-0.1364	0.1247	0.09875	0.4830	1.0000	0.5412	0.4820
6	-0.1084	0.1660	0.03445	0.4891	0.5412	1.0000	0.5571
7		0.1045	-0.07519	0.2288	0.4820	0.5571	1.0000

```
Estimated G Matrix → BP random intercept variance
Row     Effect       subid        Col1
  1     Intercept    100        0.6328
```

> This random intercept variance exactly matches the last lag covariance (7,1) from the *n*-order UN **R**-only model.

```
Estimated V Matrix for SUBID 100 → TOTAL (marginal) variance and covariance (matches UN R-only)
Row        Col1        Col2        Col3        Col4        Col5        Col6        Col7
  1      0.7477      0.7190      0.6817      0.6807      0.6124      0.6182      0.6328
  2      0.7190      0.8266      0.7428      0.7475      0.6571      0.6619      0.6541
  3      0.6817      0.7428      0.8346      0.7498      0.6524      0.6390      0.6172
  4      0.6807      0.7475      0.7498      0.8366      0.7292      0.7206      0.6805
  5      0.6124      0.6571      0.6524      0.7292      0.8285      0.7280      0.7313
  6      0.6182      0.6619      0.6390      0.7206      0.7280      0.7911      0.7352
  7      0.6328      0.6541      0.6172      0.6805      0.7313      0.7352      0.8464

   Estimated V Correlation Matrix for SUBID 100 → TOTAL correlation (matches UN R-only RCORR)
Row        Col1        Col2        Col3        Col4        Col5        Col6        Col7
  1      1.0000      0.9146      0.8630      0.8608      0.7781      0.8038      0.7955
  2      0.9146      1.0000      0.8943      0.8989      0.7940      0.8185      0.7820
  3      0.8630      0.8943      1.0000      0.8974      0.7846      0.7864      0.7343
  4      0.8608      0.8989      0.8974      1.0000      0.8760      0.8859      0.8088
  5      0.7781      0.7940      0.7846      0.8760      1.0000      0.8993      0.8734
  6      0.8038      0.8185      0.7864      0.8859      0.8993      1.0000      0.8985
  7      0.7955      0.7820      0.7343      0.8088      0.8734      0.8985      1.0000

                              Information Criteria
Neg2LogLike     Parms       AIC       AICC       HQIC        BIC       CAIC
      893.1        28     949.1      951.3      981.2     1028.1     1056.1

                     Solution for Fixed Effects
                              Standard
Effect          Estimate       Error      DF    t Value    Pr > |t|
Intercept         1.5178     0.07429     122      20.43      <.0001
```

> In SAS using REML, only the parameters in the model for the variance count as "parms" listed here.

We can specify a model with constant residual variance (e-only) in the **R** matrix as our most simple baseline for what should be in **R**. Accordingly, our output now includes the **V** and **VCORR** matrices, which put **G** and **R** (or **GCORR** and **RCORR**, respectively) back together again. Thus, the structure we end up with in **V** after combining the random intercept variance and residual variance and covariance matrix is the **same compound symmetry as in an R-only model**.

Random Intercept in G + Diagonal R Model → Same as compound symmetry R-only model

```
TITLE1 "SAS Random Intercept + Diagonal R Model";
TITLE2 "Equal to Compound Symmetry R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=VC R RCORR SUBJECT=subid;
RUN; TITLE1; TITLE2;
```

> In SAS, VC = variance components as diagonal matrix

```
                      Covariance Parameter Estimates
                                          Standard          Z
Cov Parm     Subject     Estimate        Error          Value       Pr > Z
UN(1,1)      SUBID         0.6821      0.09020           7.56       <.0001   L2 Random intercept U0 variance
Week         SUBID         0.1306     0.007269          17.97       <.0001   L1 Residual e variance
```

```
display "STATA Random Intercept + Diagonal R Model"
display "Equal to Compound Symmetry R-only Model"
mixed severity , || subid: , reml nolog ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(independent,t(week))
display "-2LL = " e(ll)*-2          // Print -2LL for model
estat recovariance, relevel(subid) // G matrix
estat wcorrelation, covariance     // V matrix
estat wcorrelation                 // VCORR matrix
estat ic                           // AIC and BIC
estat icc                          // ICC
```

The `wcorrelation` option now refers to the **V** matrix instead of the **R**

```
print("R LME Random Intercept + Diagonal R Model")
RI = lme(data=Example4, method="REML", severity~1, random=~1|subid,
         correlation=NULL) # No correlation in R matrix
print("Show results adding -2LL and using residual DDF"); -2*logLik(RI); summary(RI)

'log Lik.' 1049.7 (df=3) → model -2LL

     AIC    BIC  logLik
  1055.7 1069.7 -524.86

Random effects:
 Formula: ~1 | subid
        (Intercept) Residual
StdDev:     0.82587  0.36143

Fixed effects:  severity ~ 1
             Value Std.Error  DF t-value p-value
(Intercept) 1.4767  0.075485 646  19.563       0

print("Show G, R, and V matrices for first person")
G=getVarCov(RI, individual="100", type="random.effects"); G

Random effects variance covariance matrix
            (Intercept)
(Intercept)     0.68206 → L2 Random intercept U0 variance

R=getVarCov(RI, individual="100", type="conditional"); R

Conditional variance covariance matrix
        1       2       3       4       5       6       7
1 0.13063 0.00000 0.00000 0.00000 0.00000 0.00000 0.00000
2 0.00000 0.13063 0.00000 0.00000 0.00000 0.00000 0.00000
3 0.00000 0.00000 0.13063 0.00000 0.00000 0.00000 0.00000
4 0.00000 0.00000 0.00000 0.13063 0.00000 0.00000 0.00000
5 0.00000 0.00000 0.00000 0.00000 0.13063 0.00000 0.00000
6 0.00000 0.00000 0.00000 0.00000 0.00000 0.13063 0.00000
7 0.00000 0.00000 0.00000 0.00000 0.00000 0.00000 0.13063

V=getVarCov(RI, individual="100", type="marginal"); V

Marginal variance covariance matrix
        1       2       3       4       5       6       7
1 0.81269 0.68206 0.68206 0.68206 0.68206 0.68206 0.68206
2 0.68206 0.81269 0.68206 0.68206 0.68206 0.68206 0.68206
3 0.68206 0.68206 0.81269 0.68206 0.68206 0.68206 0.68206
4 0.68206 0.68206 0.68206 0.81269 0.68206 0.68206 0.68206
5 0.68206 0.68206 0.68206 0.68206 0.81269 0.68206 0.68206
6 0.68206 0.68206 0.68206 0.68206 0.68206 0.81269 0.68206
7 0.68206 0.68206 0.68206 0.68206 0.68206 0.68206 0.81269
```

The intraclass correlation can be computed as:

$$\text{ICC} = \frac{0.6820}{0.6820 + 0.1306} = .8393$$

```
ICC=(V[[1]][2,1])/(V[[1]][1,1]); print("Show ICC"); ICC
[1] 0.83926
```

```
# Estimating UN model using gls in nlme to use for LRTs below
UN = gls(data=Example4, method="REML", model=severity~1,
         correlation=corSymm(form=~as.numeric(week1)|subid), # UN correlations
         weights=varIdent(form=~1|week1))                     # Het var by session

print("LRT: Is RI worse than UN?"); anova(UN,RI)

   Model df     AIC    BIC  logLik   Test L.Ratio p-value
UN     1 29  951.13 1085.8 -446.56
RI     2  3 1055.71 1069.7 -524.86 1 vs 2  156.59  <.0001
```

Next, we'll try **two types of residual correlations**: **AR1 and reduced-lag Toeplitz** (with residuals covariances or correlations only at lags 5, 4, 3, 2, and 1).

Random Intercept in G + AR1 R Model: only residuals have AR1 corr (equal residual variance)

```
TITLE1 "SAS Random Intercept + Auto-Regressive R Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=AR(1) R RCORR SUBJECT=subid;
* Use this version for unbalanced time;
     *REPEATED week / TYPE=SP(POW)(week) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitRIAR1; * Save for LRT;
RUN; TITLE1;
```

```
                  Covariance Parameter Estimates
                                    Standard        Z
Cov Parm     Subject     Estimate      Error    Value       Pr Z
UN(1,1)      SUBID         0.6350    0.09026     7.04     <.0001  L2 Random Intercept U0 variance
AR(1)        SUBID         0.5135    0.05179     9.92     <.0001  L1 Auto-regressive res cor in R
Residual                   0.1731    0.01777     9.74     <.0001  L1 Residual e variance
```

Adding the random intercept variance is a significant improvement over the **R**-only AR1, −2ΔLL(1) = 47.1, $p <$ 001, **indicating only the residuals need an AR1 correlation**.

```
TITLE1 "Model comparison: did random intercept help AR1?";
%FitTest(FitFewer=FitAR1, FitMore=FitRIAR1); TITLE1;

Likelihood Ratio Test for FitAR vs. FitARRI
          Neg2Log
 Name      Like       Parms        AIC        BIC    DevDiff     DFdiff       Pvalue
FitAR      990.9        2        994.9     1000.5       .           .             .
FitARRI    943.8        3        949.8      958.3    47.0541        1       6.9053E-12
```

```
TITLE1 "Model comparison: RI+AR1 not worse than UN?";
%FitTest(FitFewer=FitRIAR1, FitMore=FitUN); TITLE1;
```

AR+RI still fits worse than UN, −2ΔLL(25) = 50.7, $p <$ 002

```
Likelihood Ratio Test for FitAR1RI vs. FitUN
           Neg2Log
Name        Like       Parms        AIC        BIC    DevDiff     DFdiff        Pvalue
FitAR1RI    943.8        3        949.8      958.3       .           .        .
FitUN       893.1       28        949.1     1028.1    50.6930       25      .001748946
```

```
display "STATA Random Intercept + Auto-Regressive R Model"
mixed severity , || subid: , reml nolog ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(ar1,t(week))
display "-2LL = " e(ll)*-2           // Print -2LL for model
estat recovariance, relevel(subid)  // G matrix
estat wcorrelation, covariance      // V matrix
estat wcorrelation                  // VCORR matrix
estat ic                            // AIC and BIC
```

Options for unbalanced time are not available in STATA MIXED as far as I know

```
estimates store FitRIAR1            // Save for LRT
lrtest FitRIAR1 FitAR1              // RI+AR1 better than AR1?
lrtest FitUN FitRIAR1               // RI+AR1 worse than UN?

-----------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.    [95% Conf. Interval]
-----------------------------+-----------------------------------------------
subid: Identity              |
                  var(_cons) |    .634888    .0902351     .4805271    .8388346 L2 Rand int var
-----------------------------+-----------------------------------------------
Residual: AR(1)              |
                         rho |   .5135115    .0517865     .4050182    .6077446 L1 AR1 corr
                      var(e) |   .1730598    .0177741     .1415057    .2116503 L1 Res e var
-----------------------------------------------------------------------------

print("R LME Random Intercept + Auto-Regressive R Model")
RIAR1 = lme(data=Example4, method="REML", severity~1, random=~1|subid,
            correlation=(corAR1(form=~as.numeric(week1)|subid)))
# correlation=(corCAR1(form=~as.numeric(week1)|subid)) for unbalanced time
print("Show results adding -2LL and using residual DDF"); -2*logLik(RIAR1); summary(RIAR1)

'log Lik.' 943.82 (df=4) → Model -2LL

     AIC   BIC  logLik
  951.82 970.4 -471.91

Random effects:
 Formula: ~1 | subid
        (Intercept) Residual
StdDev:      0.7968    0.416

Correlation Structure: ARMA(1,0)
 Formula: ~as.numeric(week1) | subid
 Parameter estimate(s):
   Phi1
0.51351 → AR1 residual correlation in R

Fixed effects:  severity ~ 1
             Value Std.Error  DF t-value p-value
(Intercept) 1.4885  0.075149 646  19.807       0

print("Show G, R, RCORR, and V matrices for first person")
G=getVarCov(RIAR1, individual="100", type="random.effects"); G

Random effects variance covariance matrix
            (Intercept)
(Intercept)     0.63489 → Random intercept U0 variance

R=getVarCov(RIAR1, individual="100", type="conditional"); R

Conditional variance covariance matrix → R matrix
          1         2        3        4        5         6         7
1 0.1730600 0.0888680 0.045635 0.023434 0.012034 0.0061794 0.0031732
2 0.0888680 0.1730600 0.088868 0.045635 0.023434 0.0120340 0.0061794
3 0.0456350 0.0888680 0.173060 0.088868 0.045635 0.0234340 0.0120340
4 0.0234340 0.0456350 0.088868 0.173060 0.088868 0.0456350 0.0234340
5 0.0120340 0.0234340 0.045635 0.088868 0.173060 0.0888680 0.0456350
6 0.0061794 0.0120340 0.023434 0.045635 0.088868 0.1730600 0.0888680
7 0.0031732 0.0061794 0.012034 0.023434 0.045635 0.0888680 0.1730600
```

```
RCORR=corMatrix(RIAR1$modelStruct$corStruct)[[6]]; RCORR

         [,1]     [,2]     [,3]    [,4]     [,5]     [,6]     [,7]
[1,] 1.000000 0.513512 0.263694 0.13541 0.069535 0.035707 0.018336
[2,] 0.513512 1.000000 0.513512 0.26369 0.135410 0.069535 0.035707
[3,] 0.263694 0.513512 1.000000 0.51351 0.263694 0.135410 0.069535
[4,] 0.135410 0.263694 0.513512 1.00000 0.513512 0.263694 0.135410
[5,] 0.069535 0.135410 0.263694 0.51351 1.000000 0.513512 0.263694
[6,] 0.035707 0.069535 0.135410 0.26369 0.513512 1.000000 0.513512
[7,] 0.018336 0.035707 0.069535 0.13541 0.263694 0.513512 1.000000

V=getVarCov(RIAR1, individual="100", type="marginal"); V total matrix

Marginal variance covariance matrix
        1       2       3       4       5       6       7
1 0.80795 0.72376 0.68052 0.65832 0.64692 0.64107 0.63806
2 0.72376 0.80795 0.72376 0.68052 0.65832 0.64692 0.64107
3 0.68052 0.72376 0.80795 0.72376 0.68052 0.65832 0.64692
4 0.65832 0.68052 0.72376 0.80795 0.72376 0.68052 0.65832
5 0.64692 0.65832 0.68052 0.72376 0.80795 0.72376 0.68052
6 0.64107 0.64692 0.65832 0.68052 0.72376 0.80795 0.72376
7 0.63806 0.64107 0.64692 0.65832 0.68052 0.72376 0.80795

# Have to re-estimate AR1 using gls for LRT
# Estimating UN model using gls in nlme to use for LRTs below
AR1 = gls(data=Example4, method="REML", model=severity~1,
          correlation=corAR1(form=~as.numeric(week1)|subid)) # AR1 correlations

print("LRT: Is RIAR1 better than AR1?"); anova(RIAR1,AR1)

      Model df    AIC    BIC  logLik   Test L.Ratio p-value
RIAR1     1  4 951.82  970.4 -471.91
AR1       2  3 996.88 1010.8 -495.44 1 vs 2  47.054  <.0001

print("LRT: Is RIAR1 worse than UN?"); anova(UN,RIAR1)

      Model df    AIC    BIC  logLik   Test L.Ratio p-value
UN        1 29 951.13 1085.8 -446.56
RIAR1     2  4 951.82  970.4 -471.91 1 vs 2  50.693  0.0017
```

Random Intercept in G with Toeplitz(6) in R Model (allows 5 lagged covariances; set last = 0)

```
TITLE1 "SAS Random Intercept + 5-Lag Toeplitz6 R Model";
TITLE2 "Equal to Toeplitz (n=7 total bands) R-only Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=TOEP(6) R RCORR SUBJECT=subid;
RUN; TITLE1; TITLE2;

display "STATA Random Intercept + 5-lag Toeplitz6 R Model"
display "Equal to Toeplitz (n=7 bands) R-only Model"
mixed severity , || subid: , reml nolog ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(toeplitz5,t(week))
display "-2LL = " e(ll)*-2         // Print -2LL for model
estat recovariance, relevel(subid) // G matrix
estat wcorrelation, covariance     // V matrix
estat wcorrelation,                // VCORR matrix
estat ic                           // AIC and BIC

# Toeplitz is not a pre-defined structure in R lme
```

SAS Output (*STATA output is very similar*):

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr Z	
UN(1,1)	SUBID	0.6541	0.09179	7.13	<.0001	**L2 Random intercept U0 variance**
TOEP(2)	SUBID	0.07152	0.02189	3.27	0.0011	**L1 Residual e covariance for t−1**
TOEP(3)	SUBID	0.04321	0.02130	2.03	0.0425	**L1 Residual e covariance for t−2**
TOEP(4)	SUBID	0.003458	0.02096	0.16	0.8690	**L1 Residual e covariance for t−3**
TOEP(5)	SUBID	-0.01479	0.01860	-0.80	0.4266	**L1 Residual e covariance for t−4**
TOEP(6)	SUBID	-0.01730	0.01487	-1.16	0.2444	**L1 Residual e covariance for t−5**
Residual		0.1562	0.02178	7.17	<.0001	**L1 Residual e var (equal over weeks)**

Estimated R Matrix for SUBID 100 → WP residual (conditional) variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	**0.1562**	0.07152	0.04321	0.003458	-0.01479	-0.01730	
2	0.07152	**0.1562**	0.07152	0.04321	0.003458	-0.01479	-0.01730
3	0.04321	0.07152	**0.1562**	0.07152	0.04321	0.003458	-0.01479
4	0.003458	0.04321	0.07152	**0.1562**	0.07152	0.04321	0.003458
5	-0.01479	0.003458	0.04321	0.07152	**0.1562**	0.07152	0.04321
6	-0.01730	-0.01479	0.003458	0.04321	0.07152	**0.1562**	0.07152
7		-0.01730	-0.01479	0.003458	0.04321	0.07152	**0.1562**

Estimated R Correlation Matrix for SUBID 100 → WP (conditional) residual correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.4579	0.2766	0.02214	-0.09467	-0.1108	
2	0.4579	1.0000	0.4579	0.2766	0.02214	-0.09467	-0.1108
3	0.2766	0.4579	1.0000	0.4579	0.2766	0.02214	-0.09467
4	0.02214	0.2766	0.4579	1.0000	0.4579	0.2766	0.02214
5	-0.09467	0.02214	0.2766	0.4579	1.0000	0.4579	0.2766
6	-0.1108	-0.09467	0.02214	0.2766	0.4579	1.0000	0.4579
7		-0.1108	-0.09467	0.02214	0.2766	0.4579	1.0000

Estimated G Matrix → BP random intercept variance

Row	Effect	subid	Col1
1	Intercept	100	0.6541

Estimated V Matrix for SUBID 100 → TOTAL (marginal) variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	0.8104	0.7257	0.6974	0.6576	0.6394	0.6368	0.6541
2	0.7257	0.8104	0.7257	0.6974	0.6576	0.6394	0.6368
3	0.6974	0.7257	0.8104	0.7257	0.6974	0.6576	0.6394
4	0.6576	0.6974	0.7257	0.8104	0.7257	0.6974	0.6576
5	0.6394	0.6576	0.6974	0.7257	0.8104	0.7257	0.6974
6	0.6368	0.6394	0.6576	0.6974	0.7257	0.8104	0.7257
7	0.6541	0.6368	0.6394	0.6576	0.6974	0.7257	0.8104

Estimated V Correlation Matrix for SUBID 100 → TOTAL (marginal) correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.8955	0.8606	0.8115	0.7890	0.7859	0.8072
2	0.8955	1.0000	0.8955	0.8606	0.8115	0.7890	0.7859
3	0.8606	0.8955	1.0000	0.8955	0.8606	0.8115	0.7890
4	0.8115	0.8606	0.8955	1.0000	0.8955	0.8606	0.8115
5	0.7890	0.8115	0.8606	0.8955	1.0000	0.8955	0.8606
6	0.7859	0.7890	0.8115	0.8606	0.8955	1.0000	0.8955
7	0.8072	0.7859	0.7890	0.8115	0.8606	0.8955	1.0000

```
                    Information Criteria
Neg2LogLike     Parms        AIC        AICC        HQIC         BIC        CAIC
      926.0         7      940.0       940.1       948.0       959.7       966.7

                  Solution for Fixed Effects
                        Standard
Effect        Estimate       Error       DF     t Value     Pr > |t|
Intercept       1.4884     0.07533      122       19.76       <.0001
```

This RI + TOEP(n−1) 5-lag model is equivalent to the Toeplitz(n) 6-lag model without the random intercept, as shown by the fit statistics. But this RI+5lag model has an interpretational advantage: rather than testing whether the total (marginal) lagged covariance (in **V**) is different than 0, it tests whether the residual (conditional) lagged covariance (in **R**) is different from 0 *after taking out individual differences in the (random) intercept*. It looks like only some of the lagged residual covariances are significant, so we can probably simplify the model without hurting fit.

Summary of sequential models taking out higher-lag covariances in SAS:

TOEP(5) → 4 lags only: REML −2LL = 927.2 AIC = 939.2 BIC = 956.2
TOEP(4) → 3 lags only: REML −2LL = 927.3 AIC = 937.3 BIC = 951.4 ← Best so far
TOEP(3) → 2 lags only: REML −2LL = 933.6 AIC = 941.6 BIC = 952.8

Random Intercept in G with Toeplitz(4) in R Model (allows 3 lagged covariances; sets others = 0)

```
TITLE1 "SAS Random Intercept + 3-Lag Toeplitz4 R Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=TOEP(4) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitRITP4; * Save for LRT;
RUN; TITLE1;

display "STATA Random Intercept + 3-lag Toeplitz4 R Model"
mixed severity , || subid: , reml nolog  ///
      dfmethod(satterthwaite) dftable(pvalue) residuals(toeplitz3,t(week))
display "-2LL = " e(ll)*-2          // Print -2LL for model
estat recovariance, relevel(subid) // G matrix
estat wcorrelation, covariance      // V matrix
estat wcorrelation                  // VCORR matrix
estat ic                            // AIC and BIC
estimates store FitRITP4            // Save for LRT
lrtest FitUN FitRITP4               // RI+TP4 worse than UN?
```

SAS Output:

Estimated R Matrix for SUBID 100 → WP residual (conditional) variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	**0.1702**	0.08576	0.05791	0.01872			
2	0.08576	**0.1702**	0.08576	0.05791	0.01872		
3	0.05791	0.08576	**0.1702**	0.08576	0.05791	0.01872	
4	0.01872	0.05791	0.08576	**0.1702**	0.08576	0.05791	0.01872
5		0.01872	0.05791	0.08576	**0.1702**	0.08576	0.05791
6			0.01872	0.05791	0.08576	**0.1702**	0.08576
7				0.01872	0.05791	0.08576	**0.1702**

Estimated R Correlation Matrix for SUBID 100 → WP residual (conditional) correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.5038	0.3402	0.1100			
2	0.5038	1.0000	0.5038	0.3402	0.1100		
3	0.3402	0.5038	1.0000	0.5038	0.3402	0.1100	
4	0.1100	0.3402	0.5038	1.0000	0.5038	0.3402	0.1100
5		0.1100	0.3402	0.5038	1.0000	0.5038	0.3402
6			0.1100	0.3402	0.5038	1.0000	0.5038
7				0.1100	0.3402	0.5038	1.0000

Estimated G Matrix → BP random intercept variance

Row	Effect	subid	Col1
1	Intercept	100	0.6395

Estimated V Matrix for SUBID 100 → TOTAL (marginal) variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	0.8097	0.7252	0.6974	0.6582	0.6395	0.6395	0.6395
2	0.7252	0.8097	0.7252	0.6974	0.6582	0.6395	0.6395
3	0.6974	0.7252	0.8097	0.7252	0.6974	0.6582	0.6395
4	0.6582	0.6974	0.7252	0.8097	0.7252	0.6974	0.6582
5	0.6395	0.6582	0.6974	0.7252	0.8097	0.7252	0.6974
6	0.6395	0.6395	0.6582	0.6974	0.7252	0.8097	0.7252
7	0.6395	0.6395	0.6395	0.6582	0.6974	0.7252	0.8097

Estimated V Correlation Matrix for SUBID 100 → TOTAL (marginal) correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.8957	0.8613	0.8129	0.7898	0.7898	0.7898
2	0.8957	1.0000	0.8957	0.8613	0.8129	0.7898	0.7898
3	0.8613	0.8957	1.0000	0.8957	0.8613	0.8129	0.7898
4	0.8129	0.8613	0.8957	1.0000	0.8957	0.8613	0.8129
5	0.7898	0.8129	0.8613	0.8957	1.0000	0.8957	0.8613
6	0.7898	0.7898	0.8129	0.8613	0.8957	1.0000	0.8957
7	0.7898	0.7898	0.7898	0.8129	0.8613	0.8957	1.0000

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr Z	
UN(1,1)	SUBID	0.6395	0.09004	7.10	<.0001	**L2 Random intercept U0 variance**
TOEP(2)	SUBID	0.08576	0.01267	6.77	<.0001	**L1 Residual e covariance for t–1**
TOEP(3)	SUBID	0.05791	0.009852	5.88	<.0001	**L1 Residual e covariance for t–2**
TOEP(4)	SUBID	0.01872	0.007469	2.51	0.0122	**L1 Residual e covariance for t–3**
Residual		0.1702	0.01401	12.15	<.0001	**L1 Residual e var (equal over weeks)**

Information Criteria

Neg2LogLike	Parms	AIC	AICC	HQIC	BIC	CAIC
927.3	5	937.3	937.4	943.1	951.4	956.4

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	1.4899	0.07528	122	19.79	<.0001

```
TITLE1 "Model comparison: RI+TP4 not worse than UN?";
%FitTest(FitFewer=FitRITP4, FitMore=FitUN);
```

This model is not worse than UN (just barely).

Likelihood Ratio Test for FitToep4RI vs. FitUN

Name	Neg2Log Like	Parms	AIC	BIC	DevDiff	DFdiff	Pvalue
FitToep4RI	927.3	5	937.3	951.4	.	.	.
FitUN	893.1	28	949.1	1028.1	**34.1944**	**23**	**0.062399**

One last thing to check: do the residual variances in **R** need to be heterogeneous?

Random Intercept in G with Heterogeneous Toeplitz(3) in R Model
(allows 3 lagged covariances; sets the others to 0, adds unequal residual variances across weeks)

```
TITLE1 "SAS Random Intercept + 3-Lag Heterogeneous Toeplitz4 R Model";
PROC MIXED DATA=work.Example4 COVTEST NOCLPRINT IC METHOD=REML;
     CLASS subid week;
     MODEL severity = / SOLUTION DDFM=Satterthwaite;
     RANDOM INTERCEPT / TYPE=UN V VCORR G SUBJECT=subid;
     REPEATED week / TYPE=TOEPH(4) R RCORR SUBJECT=subid;
     ODS OUTPUT InfoCrit=FitRITPH4; * Save for LRT;
RUN; TITLE1;
```

This model is only available directly in SAS MIXED as far as I can tell.

SAS Output:

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr Z	
UN(1,1)	SUBID	0.6503	0.09069	7.17	<.0001	L2 Random intercept U0 variance
Var(1)	SUBID	0.1261	0.02255	5.59	<.0001	L1 Residual e Variance at week 1
Var(2)	SUBID	0.1462	0.02283	6.41	<.0001	L1 Residual e Variance at week 2
Var(3)	SUBID	0.2261	0.03247	6.96	<.0001	L1 Residual e Variance at week 3
Var(4)	SUBID	0.1416	0.02442	5.80	<.0001	L1 Residual e Variance at week 4
Var(5)	SUBID	0.2180	0.03228	6.75	<.0001	L1 Residual e Variance at week 5
Var(6)	SUBID	0.1494	0.02411	6.20	<.0001	L1 Residual e Variance at week 6
Var(7)	SUBID	0.1868	0.02890	6.47	<.0001	L1 Residual e Variance at week 7
TOEPH(1)	SUBID	0.5115	0.03899	13.12	<.0001	L1 Residual e correlation for t-1
TOEPH(2)	SUBID	0.3566	0.03764	9.48	<.0001	L1 Residual e correlation for t-2
TOEPH(3)	SUBID	0.1112	0.04115	2.70	0.0069	L1 Residual 3 correlation for t-3

Estimated R Matrix for SUBID 100 → WP (conditional) residual variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	**0.1261**	0.06946	0.06022	0.01485			
2	0.06946	**0.1462**	0.09301	0.05131	0.01985		
3	0.06022	0.09301	**0.2261**	0.09152	0.07918	0.02044	
4	0.01485	0.05131	0.09152	**0.1416**	0.08986	0.05187	0.01808
5		0.01985	0.07918	0.08986	**0.2180**	0.09231	0.07197
6			0.02044	0.05187	0.09231	**0.1494**	0.08546
7				0.01808	0.07197	0.08546	**0.1868**

Estimated R Correlation Matrix for SUBID 100 → WP (conditional) residual correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.5115	0.3566	0.1112			
2	0.5115	1.0000	0.5115	0.3566	0.1112		
3	0.3566	0.5115	1.0000	0.5115	0.3566	0.1112	
4	0.1112	0.3566	0.5115	1.0000	0.5115	0.3566	0.1112
5		0.1112	0.3566	0.5115	1.0000	0.5115	0.3566
6			0.1112	0.3566	0.5115	1.0000	0.5115
7				0.1112	0.3566	0.5115	1.0000

Estimated G Matrix → BP random intercept variance

Row	Effect	subid	Col1
1	Intercept	100	0.6503

Below: residual *covariances are unequal* within a time lag band (because the residual variances are allowed to differ over weeks), but the residual *correlations are equal* within a band.

Estimated V Matrix for SUBID 100 → TOTAL (marginal) variance and covariance

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	**0.7764**	0.7198	0.7105	0.6652	0.6503	0.6503	0.6503
2	0.7198	**0.7965**	0.7433	0.7016	0.6701	0.6503	0.6503
3	0.7105	0.7433	**0.8764**	0.7418	0.7295	0.6707	0.6503
4	0.6652	0.7016	0.7418	**0.7919**	0.7402	0.7022	0.6684
5	0.6503	0.6701	0.7295	0.7402	**0.8683**	0.7426	0.7223
7	0.6503	0.6503	0.6503	0.6684	0.7223	0.7358	**0.8371**

Estimated V Correlation Matrix for SUBID 100 → TOTAL (marginal) correlation

Row	Col1	Col2	Col3	Col4	Col5	Col6	Col7
1	1.0000	0.9153	0.8614	0.8483	0.7920	0.8253	0.8066
2	0.9153	1.0000	0.8896	0.8834	0.8058	0.8148	0.7964
3	0.8614	0.8896	1.0000	0.8905	0.8362	0.8012	0.7592
4	0.8483	0.8834	0.8905	1.0000	0.8926	0.8824	0.8209
5	0.7920	0.8058	0.8362	0.8926	1.0000	0.8912	0.8472
6	0.8253	0.8148	0.8012	0.8824	0.8912	1.0000	0.8992
7	0.8066	0.7964	0.7592	0.8209	0.8472	0.8992	1.0000

Information Criteria

Neg2LogLike	Parms	AIC	AICC	HQIC	BIC	CAIC
910.0	11	932.0	932.3	944.6	963.0	974.0

```
TITLE1 "Model comparison: did het variance help RI+TP4?";
%FitTest(FitFewer=FitRITP4, FitMore=FitRITPH4); TITLE1;
```

Likelihood Ratio Test for FitToep3RI vs. FitToep3HRI

Name	Neg2Log Like	Parms	AIC	BIC	DevDiff	DFdiff	Pvalue
FitToep4RI	927.3	5	937.3	951.4	.	.	.
FitToep4HRI	910.0	11	932.0	963.0	**17.3234**	**6**	**.008165240**

Adding separate residual variances improves fit, $-2\Delta LL(6) = 17.3$, $p = .008$, although BIC disagrees.

```
TITLE1 "Model comparison: RI+TOEP4H now not worse than UN?";
%FitTest(FitFewer=FitRITPH4, FitMore=FitUN); TITLE1;
```

Likelihood Ratio Test for FitToep3HRI vs. FitUN

Name	Neg2Log Like	Parms	AIC	BIC	DevDiff	DFdiff	Pvalue
FitToep3HRI	910.0	11	932.0	963.0	.	.	.
FitUN	893.1	28	949.1	1028.1	**16.8710**	**17**	**0.46314**

The model now fits not worse than UN, $-2\Delta LL(17) = 16.8$, $p = .463$. We win! But this fit should be re-checked after adding predictors.

A results section for these analyses (that are not of substantive interest) would be just a few sentences:

To ensure accurate standard errors for all fixed effects, the adequacy of fit of the variance–covariance model across all occasions was first evaluated using likelihood ratio tests (i.e., the χ^2 for the $-2LL$ difference between nested models given degrees of freedom equal to the number of additional model parameters). All models were estimated in SAS MIXED 9.4 using residual maximum likelihood. To maximize power, we sought to reduce the number of estimated parameters by examining alternative models. Fortunately, we found a more parsimonious model that showed no decrease in fit, $-2\Delta LL(17) = 16.8$, $p = .463$, which included a random intercept variance, separate residual variances per occasion, and Toeplitz residual correlations for outcomes 1, 2, and 3 weeks apart.