Mood Changes Associated with Smoking in Adolescents: An Application of a Mixed-Effects Location Scale Model for Longitudinal Ecological Momentary Assessment (EMA) Data

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Ecological Momentary Assessment (EMA) data

aka experience sampling and diary methods

- Subjects provide frequent reports on events and experiences of their daily lives (*e.g.*, 30-40 responses per subject collected over the course of a week or so)

  electronic diaries: palm pilots, personal digital assistants (PDAs)

- Capture particulars of experience in a way not possible with more traditional designs
  e.g., allow investigation of phenomena as they happen over time

- Reports could be time-based, following a fixed-schedule, randomly triggered, event-triggered

- EMA reports might be repeated over several measurement waves

Data are rich and offer many modeling possibilities!

- person-level, wave-level, and occasion-level determinants of occasion-level responses ⇒ potential influence of context and/or environment
  e.g., subject response might vary when alone vs with others

- allows examination of why subjects differ in variability rather than just mean level
  - between-subjects variance
    e.g., subject heterogeneity could vary by gender or wave
  - within-subjects variance
    e.g., subject degree of stability could vary by gender or wave

Ecological Momentary Assessment (EMA) Study of Adolescent Smokers (Mermelstein)

- 461 adolescents (9th and 10th graders; 55% female); former and current smoking experimenters, and regular smokers
  - reported on a screening questionnaire 6-8 weeks prior to baseline that they had smoked at least one cigarette in their lifetime
  - 57.6% smoked at least one cigarette in the past month at baseline
  - 57% white, 20% hispanic, 16% black, and 7% of other race

- Carry PDA for a week, answer questions when randomly prompted (average = 30 answered prompts, range = 7 to 71), or event-record when smoking (mutually exclusive)

- baseline, 6-, 15-, and 24-month follow-ups

Interest: characterizing determinants of change in positive and negative affect associated with smoking events, especially across time

Mixed-effects location scale model

Hedeker, Mermelstein, Demirtas (2008). *Biometrics, 64*, 627-634

$$y_{ij} = \boldsymbol{x}'_{ij}\boldsymbol{\beta} + \upsilon_i + \epsilon_{ij}$$

$i = 1, 2, \ldots, N$ subjects $\quad j = 1, 2, \ldots, n_i$ occasions

$\upsilon_i \sim N(0, \sigma^2_\upsilon)$ BS variance $\sigma^2_{\upsilon_i} = \exp(\boldsymbol{u}'_i\boldsymbol{\alpha})$ or $\log(\sigma^2_{\upsilon_i}) = \boldsymbol{u}'_i\boldsymbol{\alpha}$

$\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$ WS variance $\sigma^2_{\epsilon_{ij}} = \exp(\boldsymbol{w}'_{ij}\boldsymbol{\tau})$ or $\log(\sigma^2_{\epsilon_{ij}}) = \boldsymbol{w}'_{ij}\boldsymbol{\tau}$

- $\boldsymbol{u}_i$ and $\boldsymbol{w}_{ij}$ include covariates (and $\mathbf{1}$)
- subscripts i and j on variances indicate that these change depending on covariates $\boldsymbol{u}_i$ and $\boldsymbol{w}_{ij}$ (and their coefficients) (number of parameters does not vary with i or j)
- exp function ensures a positive multiplicative factor, and so resulting variances are positive

WS variance varies across subjects

$$\sigma^2_{\epsilon_{ij}} = \exp(\boldsymbol{w}'_{ij}\boldsymbol{\tau} + \omega_i) \quad \text{where} \quad \omega_i \sim N(0, \sigma^2_\omega)$$

$$\log(\sigma^2_{\epsilon_{ij}}) = \boldsymbol{w}'_{ij}\boldsymbol{\tau} + \omega_i$$

- ω_i are log-normal subject-specific perturbations of WS variance
- ω_i are "scale" random effects - how does a subject differ in terms of the variation in their data
- υ_i are "location" random effects - how does a subject differ in terms of the mean of their data

$$\begin{bmatrix} \upsilon_i \\ \omega_i \end{bmatrix} \sim N\left\{ \begin{bmatrix} 0 \\ 0 \end{bmatrix} \begin{bmatrix} \sigma^2_\upsilon & \sigma_{\upsilon\omega} \\ \sigma_{\upsilon\omega} & \sigma^2_\omega \end{bmatrix} \right\}$$

Multilevel model of WS variance

$$\log(\sigma^2_{\epsilon_{ij}}) \;=\; \boldsymbol{w}'_{ij}\boldsymbol{\tau} + \omega_i$$

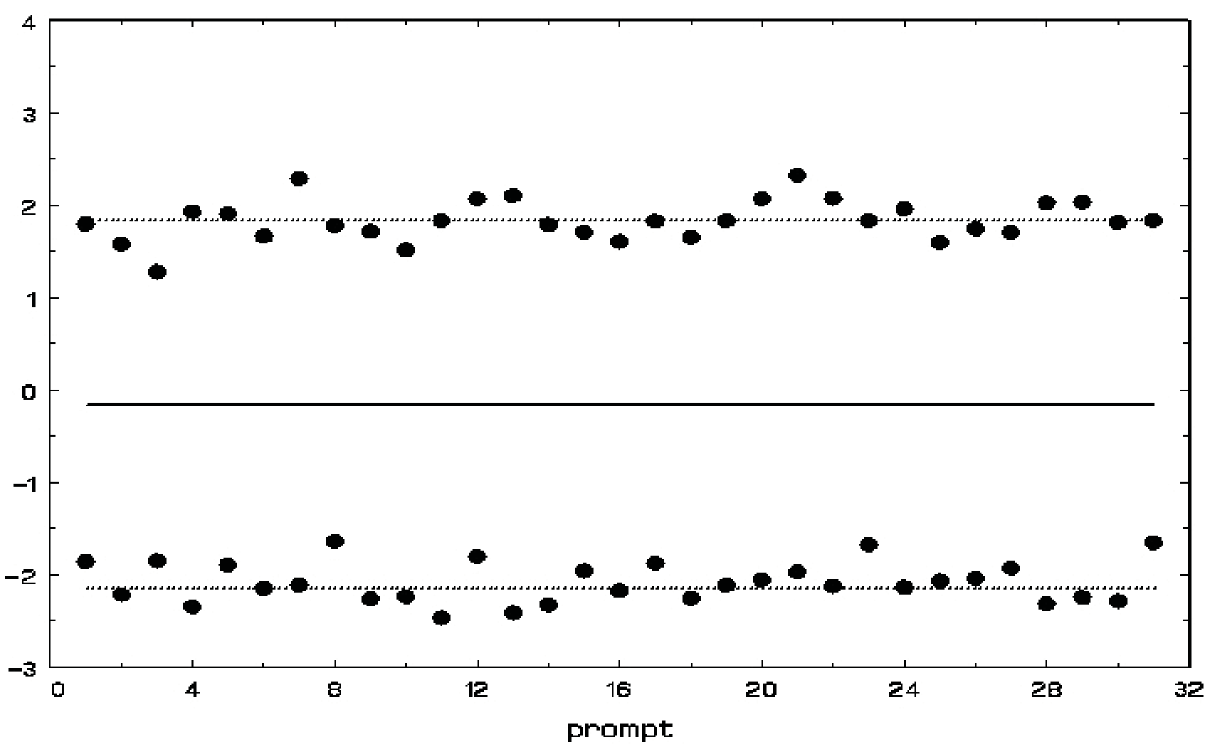
Why not use some summary statistic per subject (say, calculated subject standard deviation S_{y_i}) in a second-stage model?

$$S_{y_i} = \boldsymbol{x}'_i\boldsymbol{\beta} + \epsilon_i$$

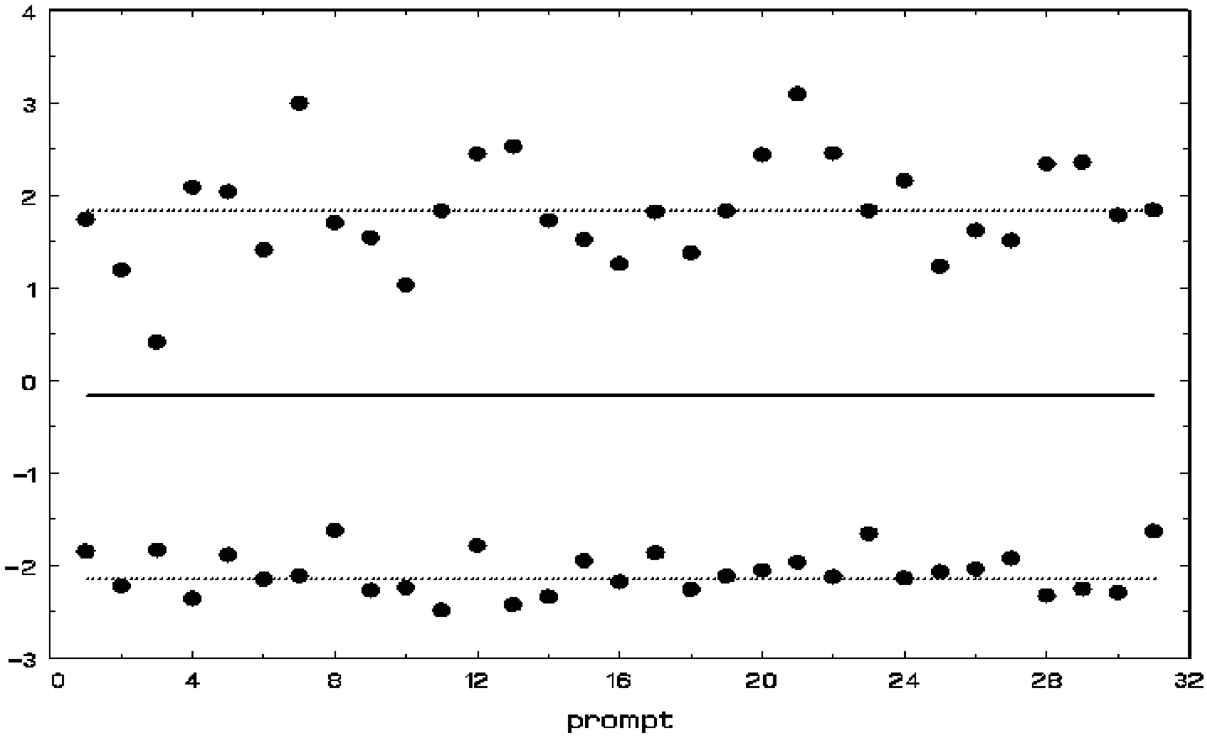
latter approach

- treats all standard deviations as if they are equally precise (but some might be based on 2 prompts or 40 prompts)
- does not recognize that these are estimated quantities (underestimation of sources of variation)
- does not allow occasion-varying predictors

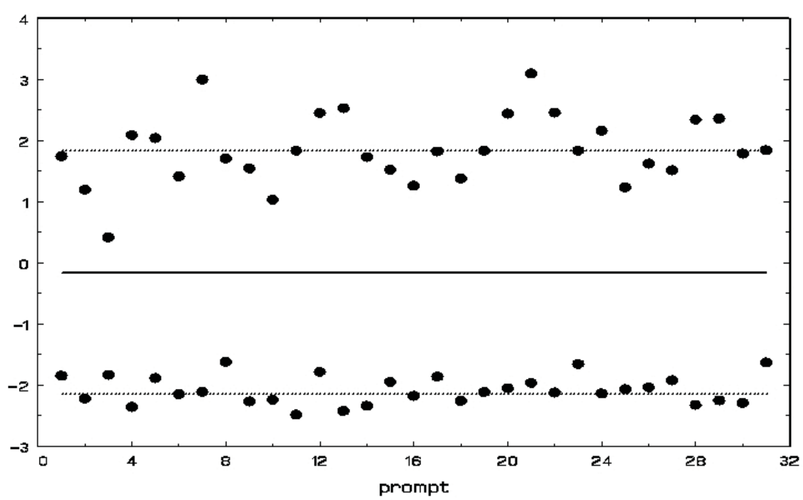
⇒ We use multilevel models for mean response, why not for variance?



Location random effects for two subjects



Location and scale random effects for two subjects



Model allows covariates to influence

- mean: level of solid line
- BS variance: dispersion of dotted lines
- WS variance: dispersion of points

additional random subject effects on: mean and WS variance

```
PROC NLMIXED GCONV=1e-12;

PARMS b0=.25 b1=-.5 b2=.3 alp0=1 alp1=0
      tau0=1 tau1=0 tau2=0 vs0=.05 cu0s0=0;

  z = b0 + b1*x1 + b2*x2 + u0;

  vu0 = EXP(alp0 + x2*alp1);

  vare = EXP(tau0 + x1*tau1 + x2*tau2 + s0);

MODEL y ~ NORMAL(z,vare);

RANDOM u0 s0 ~ NORMAL([0,0], [vu0,cu0s0,vs0])
SUBJECT=id;

RUN;
```


Longitudinal mixed-effects location scale model

$$y_{ij} = (\beta_0 + \upsilon_{0i}) + (\beta_1 + \upsilon_{1i})\texttt{Wave}_{ij} + \boldsymbol{x}'_{ij}\boldsymbol{\beta} + \epsilon_{ij}$$

$i = 1, 2, \ldots, N$ subjects $\quad j = 1, 2, \ldots, n_i$ occasions

BS variance

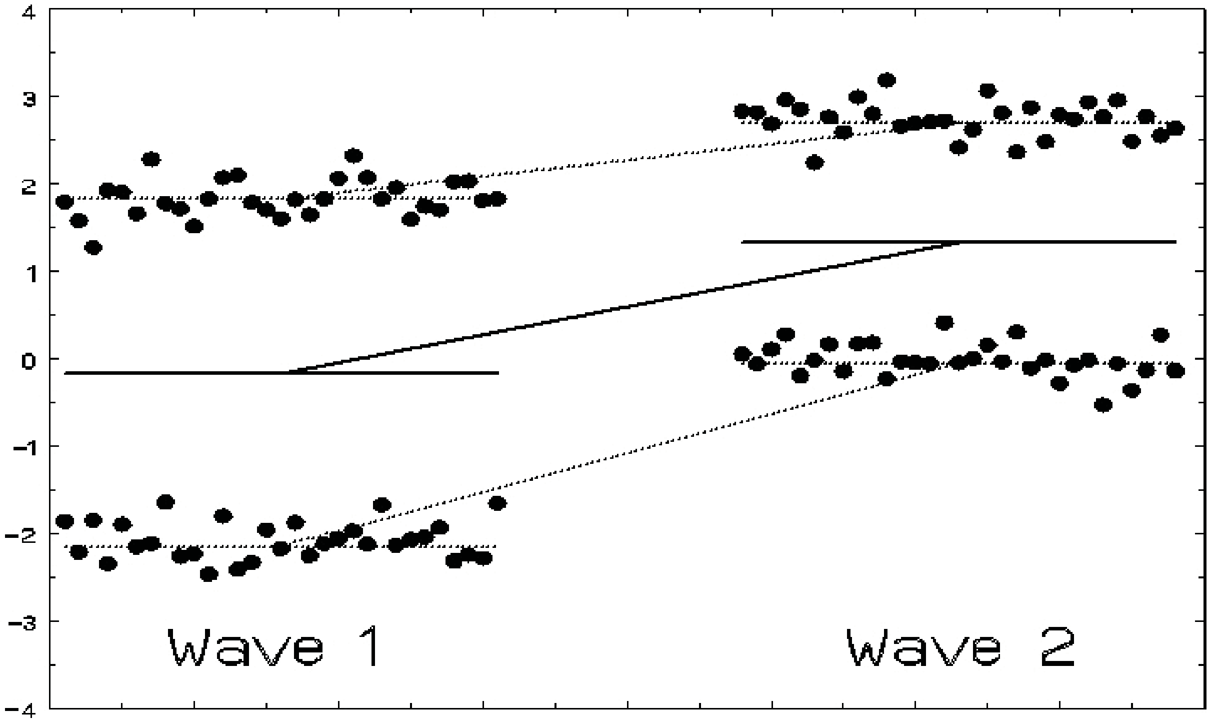
$$\begin{bmatrix} \upsilon_{0i} \\ \upsilon_{1i} \end{bmatrix} \sim N\left\{\begin{bmatrix} 0 \\ 0 \end{bmatrix}\begin{bmatrix} \sigma^2_{\upsilon_0} & \sigma_{\upsilon_0\upsilon_1} \\ \sigma_{\upsilon_0\upsilon_1} & \sigma^2_{\upsilon_1} \end{bmatrix}\right\}$$

WS variance $\epsilon_{ij} \sim N(0, \sigma^2_{\epsilon_{ij}})$

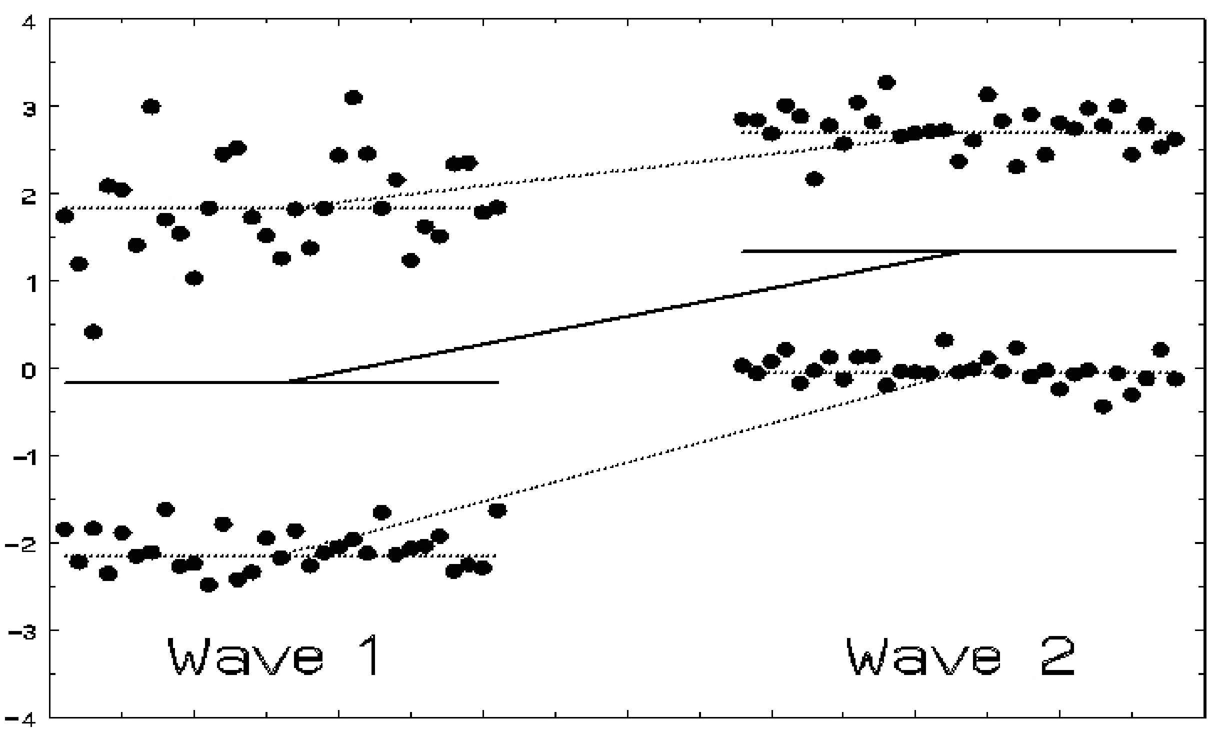
$$\sigma^2_{\epsilon_{ij}} = \exp(\boldsymbol{w}'_{ij}\boldsymbol{\tau} + \omega_i) \quad \text{where} \quad \omega_i \sim N(0, \sigma^2_\omega)$$

All random effects please rise!

$$\begin{bmatrix} \upsilon_{0i} \\ \upsilon_{1i} \\ \omega_i \end{bmatrix} \sim N\left\{\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}\begin{bmatrix} \sigma^2_{\upsilon_0} & \sigma_{\upsilon_0\upsilon_1} & \sigma_{\upsilon_0\omega} \\ \sigma_{\upsilon_0\upsilon_1} & \sigma^2_{\upsilon_1} & \sigma_{\upsilon_1\omega} \\ \sigma_{\upsilon_0\omega} & \sigma_{\upsilon_1\omega} & \sigma^2_\omega \end{bmatrix}\right\}$$



- population intercept and trend (solid line)
- random intercept and trend for 2 subjects (dotted lines)
- error variance is the same



- population intercept and trend (solid line)
- random intercept and trend for 2 subjects (dotted lines)
- error variance varies across time and subjects (random scale)

```
PROC NLMIXED GCONV=1e-12;

PARMS b0=.25 bWave=.5 t0=1 tWave=0
      vu0=1 vu1=.5 vs0=.05 cu0u1=0 cu0s0=0 cu1s0=0;

  z = (b0 + u0) + (bWave + u1)*Wave;

  vare = EXP(t0 + tWave*Wave + s0);

MODEL y ~ NORMAL(z,vare);

RANDOM u0 u1 s0 ~ NORMAL([0,0,0],
[vu0,cu0u1,vu1,cu0s0,cu1s0,vs0]) SUBJECT=id;

RUN;
```


Ecological Momentary Assessment (EMA) Study of Adolescent Smokers (Mermelstein)

- 461 adolescents (9th and 10th graders; 55% female); former and current smoking experimenters, and regular smokers
- Carry PDA for a week, answer questions when randomly prompted, or event-record when smoking (mutually exclusive)
- baseline, 6-, 15-, and 24-month follow-ups

Interest: characterizing determinants of change in positive and negative affect associated with smoking events, especially across time

$\Rightarrow$ analysis of 130 subjects with two or more waves, where at each wave subject had two or more smoking events

130 subjects with two or more waves
at each wave subject had two or more smoking events

- total of 3,388 smoking events
- 47, 39, and 44 subjects had data at two, three, and four waves, respectively
- number of subjects across waves: 116 (baseline), 91 (6 months), 92 (15 months), and 88 (24 months)
- average number of smoking events: 7.14 (range = 2 to 24), 7.65 (2 to 32), 9.97 (2 to 43), 10.76 (2 to 49) at the same four waves

Dependent Variables - mood reports for smoking events

- Positive Affect (`PA`) mood scale (5 items)
  before smoking I felt: happy, relaxed, cheerful, confident, accepted by others
- Negative Affect (`NA`) mood scale (5 items)
  before smoking I felt: sad, stressed, angry, frustrated, irritable
- items rated on 1 (not al all) to 10 (very much) scale
- also rated for "now after smoking: I feel"
- difference (now-before) is measure of reported mood change associated with smoking

Wave-stratified (model-based) descriptive results

$$y_{ij} = \beta_0 + \upsilon_i + \epsilon_{ij} \qquad (i = 1, \ldots, N \text{ subjects}, \quad j = 1, \ldots, n_i \text{ obs})$$

			Positive Affect			Negative Affect		
wave	N	$\Sigma_i n_i$	$\hat{\beta}_0$	$\hat{\sigma}^2_\upsilon$	$\hat{\sigma}^2_\epsilon$	$\hat{\beta}_0$	$\hat{\sigma}^2_\upsilon$	$\hat{\sigma}^2_\epsilon$
0	116	828	.730	.792	2.240	-.439	.902	2.495
1	91	696	.538	.371	2.020	-.445	.350	2.399
2.5	92	917	.353	.457	1.574	-.318	.380	1.771
4	88	947	.404	.243	1.460	-.391	.267	1.507

wave 0 = baseline, 1 = 6-month, 2.5 = 15-month, 4 = 24 month

Mixed Model for the (smoking-related) mood change y of subject i ($i = 1, 2, \ldots, N$ subjects) at occasion j ($j = 1, 2, \ldots, n_i$ smoking events):

$$\begin{aligned} y_{ij} &= (\beta_0 + \upsilon_{0i}) + (\beta_1 + \upsilon_{1i})\texttt{Wave}_j + \beta_2\texttt{Male}_i \\ &\quad + \beta_3\texttt{AvgSmk}_i + \beta_4\texttt{NumSmk}_{ij} + \epsilon_{ij} \end{aligned}$$

- $\texttt{Wave}_j$ (0=baseline, 1=6 months, 2.5=15 months, 4=24months)
- $\texttt{Male}_i$ (0=female, 1=male)
- Smoking level

  WS version $\texttt{NumSmk}_{ij}$ = per wave number of smoking events

  BS version $\texttt{AvgSmk}_i$ = subject average of $\texttt{NumSmk}_{ij}$

Random effects part of model

- υ_{0i} = subject i's mood at baseline
- υ_{1i} = change in subject i's mood over wave

$$\begin{bmatrix} \upsilon_{0i} \\ \upsilon_{1i} \end{bmatrix} \sim \mathcal{N}\left\{\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma^2_{\upsilon_0} & \sigma_{\upsilon_0\upsilon_1} \\ \sigma_{\upsilon_0\upsilon_1} & \sigma^2_{\upsilon_1} \end{bmatrix}\right\}$$

$\sigma^2_{\upsilon_0}$ = individual mood variation at baseline

$\sigma^2_{\upsilon_1}$ = individual mood variation in the slopes (or mood changes across waves)

$\sigma_{\upsilon_0\upsilon_1}$ = covariance of these two

Error variance model $\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$ WS variance

$$\sigma^2_{\epsilon_{ij}} = \exp(\tau_0 + \tau_1 \texttt{Wave}_j + \tau_2 \texttt{Male}_i + \tau_3 \texttt{AvgSmk}_i + \tau_4 \texttt{NumSmk}_{ij} + \omega_i)$$

or

$$\log(\sigma^2_{\epsilon_{ij}}) = \tau_0 + \tau_1 \texttt{Wave}_j + \tau_2 \texttt{Male}_i + \tau_3 \texttt{AvgSmk}_i + \tau_4 \texttt{NumSmk}_{ij} + \omega_i$$

log-linear model of within-subject variance, with subject-specific perturbation $\omega_i \sim N(0, \sigma^2_\omega)$

- WS variance follow a log-normal distribution at the subject level
- skewed nonnegative nature of log-normal makes it a reasonable choice for representing variances
- random scale effect ω_i allowed to be correlated with random intercept υ_{0i} and trend υ_{1i}

Smoking-related Positive and Negative Affect Change

estimates, standard errors (se), and p-values

Mean Model	Positive Affect est	se	$p <$	Negative Affect est	se	$p <$
Intercept β_0	.556	.084	.0001	-.305	.069	.0001
Wave β_1	-.062	.022	.006	.014	.020	.48
Male β_2	.113	.101	.27	-.132	.074	.077
AvgSmk β_3	-.073	.072	.32	-.043	.058	.46
NumSmk β_4	-.069	.035	.051	.071	.032	.029

Error Var Model	est	se	$p <$	est	se	$p <$
Intercept τ_0	.671	.107	.0001	.656	.152	.0001
Wave τ_1	-.122	.020	.0001	-.091	.022	.0001
Male τ_2	.234	.145	.11	.168	.215	.44
AvgSmk τ_3	-.222	.104	.035	-.191	.150	.21
NumSmk τ_4	-.100	.040	.014	-.228	.042	.0001

Smoking-related Positive and Negative Affect Change

estimates, standard errors (se), and p-values

Random effect (co)variances	Positive Affect est	se	$p <$	Negative Affect est	se	$p <$
Intercept $\sigma^2_{\upsilon_0}$	.297	.090	.001	.159	.068	.020
Wave $\sigma^2_{\upsilon_1}$	.013	.007	.079	.006	.005	.24
Scale σ^2_{ω}	.521	.085	.0001	1.26	.188	.0001
Int, Wave $\sigma_{\upsilon_0 \upsilon_1}$	-.040	.023	.086	-.025	.018	.19
Int, Scale $\sigma_{\upsilon_0 \omega}$	.186	.055	.001	-.191	.064	.004
Wave, Scale $\sigma_{\upsilon_1 \omega}$	-.023	.015	.14	-.002	.017	.89

Second or third thoughts?

- analysis treats observations (level-1) within subjects (level-2)

$$y_{ij} = (\beta_0 + \upsilon_{0i}) + (\beta_1 + \upsilon_{1i})\texttt{Wave}_j + \beta_2\texttt{Male}_i + \beta_3\texttt{AvgSmk}_i + \beta_4\texttt{NumSmk}_{ij} + \epsilon_{ij}$$

$$\sigma^2_{\epsilon_{ij}} = \exp(\tau_0 + \tau_1\texttt{Wave}_j + \tau_2\texttt{Male}_i + \tau_3\texttt{AvgSmk}_i + \tau_4\texttt{NumSmk}_{ij} + \omega_i)$$

- however, observations (level-1) are nested within waves (level-2) within subjects (level-3)
- model does include random subject wave effect (υ_{1i}), and allows mean and error variance to vary with wave (β_1 and τ_1)
- how bad is it to ignore the intermediate level as a random effect?

Multilevel representation ($i = 1, \ldots, N$ subjects; $j = 1, \ldots, n_i$ waves, min=2 and max = 4; $k = 1, \ldots, n_{ij}$ observations)

Level-1 within subjects, within waves

$$y_{ijk} = b_{0ij} + \epsilon_{ijk}$$

Level-2 within subjects, between waves

$$b_{0ij} = b_{0i} + b_{1i}\texttt{Wave}_{ij} \quad [+\upsilon_{0ij}]$$

Level-3 between subjects

$$b_{0i} = \beta_0 + \upsilon_{0i}$$
$$b_{1i} = \beta_1 + \upsilon_{1i}$$

$\Rightarrow$ without υ_{0ij}, assume each subject's means across time (b_{0ij}) follow a line without error (this error is treated as error variance)

3-level PROC NLMIXED code (thanks to Dale McLerran)

```
PROC NLMIXED GCONV=1e-12;

PARMS b0=.25 bWave=.5 t0=1 tWave=0
       vu0=1 vu1=.5 vs0=.05 vwave=.1
       cu0u1=0 cu0s0=0 cu1s0=0;

   z = (b0 + u0) + (bWave + u1)*Wave
        + d1*w1 + d2*w2 + d3*w3 + d4*w4;

   vare = EXP(t0 + tWave*Wave + s0);

MODEL y ~ NORMAL(z,vare);

RANDOM u0 u1 s0 d1 d2 d3 d4 ~ NORMAL([0,0,0,0,0,0,0],
        [vu0,cu0u1,vu1,cu0s0,cu1s0,vs0,
         0, 0, 0, vwave,
         0, 0, 0, 0, vwave,
         0, 0, 0, 0, 0, vwave,
         0, 0, 0, 0, 0, 0, vwave ]) SUBJECT=id;
```

where `w1, w2, w3, w4` are indicator variables (0,1) of the four waves

Random effect model comparisons

Subject	Wave		Positive Affect		Negative Affect	
level	level	parms	Deviance	AIC	Deviance	AIC
Int, Wave		3	11763	11789	11999	12025
Int, Wave, Scale		6	11246	11278	11154	11186
Int	Int	2	11756	11780	11997	12021
Int, Wave	Int	4	Int, Wave corr = -1			
Int, Scale	Int	4	*11228*	*11256*	*11150*	*11178*
Int, Wave, Scale	Int	7	Wave var goes to 0			

regressors = `Wave, Male, AvgSmk, NumSmk` in mean and error variance models

3-level Model of Smoking-related Positive and Negative Affect Change; estimates, standard errors (se), and p-values

	Positive Affect			Negative Affect		
Mean Model	est	se	$p <$	est	se	$p <$
Intercept β_0	.547	.078	.0001	-.339	.064	.0001
Wave β_1	-.059	.020	.005	.025	.017	.14
Male β_2	.112	.099	.27	-.114	.079	.15
AvgSmk β_3	-.111	.077	.16	.016	.063	.81
NumSmk β_4	-.042	.045	.36	.034	.039	.38
Error Var Model	est	se	$p <$	est	se	$p <$
Intercept τ_0	.654	.111	.0001	.650	.152	.0001
Wave τ_1	-.124	.020	.0001	-.095	.021	.0001
Male τ_2	.217	.151	.16	.166	.214	.44
AvgSmk τ_3	-.259	.107	.018	-.198	.145	.19
NumSmk τ_4	-.080	.040	.046	-.220	.042	.0001

3-level Model of Smoking-related Positive and Negative Affect Change; estimates, standard errors (se), and p-values

Random effect	Positive Affect			Negative Affect		
(co)variances	est	se	$p <$	est	se	$p <$
Subject level						
Intercept $\sigma^2_{\upsilon_{(3)}}$	.162	.041	.001	.082	.027	.004
Scale σ^2_{ω}	.560	.091	.0001	1.28	.188	.0001
Int, Scale $\sigma_{\upsilon_{(3)}\omega}$	.139	.041	.001	-.204	.048	.0001
	($r = .47$)			($r = -.63$)		
Wave level						
Intercept $\sigma^2_{\upsilon_{(2)}}$	.071	.024	.004	.033	.017	.06

Summary

- More applications for these mixed location scale models where interest is on modeling variance

- Random intercept and trend effects considered here; this could be generalized (*e.g.*, random coefficient models)

- Other kinds of outcomes, especially ordinal
  Hedeker, Demirtas, & Mermelstein (2009). A mixed ordinal location scale model for analysis of ecological momentary assessment (EMA) data. *Statistics and Its Interface, 2*, 391-402.

- Need a fair amount of BS and WS data, but modern data collection procedures are good for this

- Simulations with small datasets (*e.g.*, 20 subjects with 5 observations) often leads to non-convergence; this improves as numbers increase