Mood Changes Associated with Smoking in Adolescents: Applications of Mixed-Effects Location Scale Models for Cross-Sectional and 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), smart phones

- 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

Data are rich and offer many modeling possibilities!

- person-level and occasion-level determinants of occasion-level responses $\Rightarrow$ 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 age
  - within-subjects variance
    e.g., subject degree of stability could vary by gender or age

Multilevel (mixed-effects regression) model for measurement y of subject i ($i = 1, 2, \ldots, N$) on occasion j ($j = 1, 2, \ldots, n_i$)

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

$\boldsymbol{x}_{ij} = p \times 1$ vector of regressors (including a column of ones)

$\boldsymbol{\beta} = p \times 1$ vector of regression coefficients

$\upsilon_i \sim N(0, \sigma_\upsilon^2)$ BS variance

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

Log-linear models for variances

$$\text{BS variance} \qquad \sigma^2_{\upsilon_{ij}} = \exp(\boldsymbol{u}'_{ij}\boldsymbol{\alpha}) \qquad \text{or} \quad \log(\sigma^2_{\upsilon_{ij}}) = \boldsymbol{u}'_{ij}\boldsymbol{\alpha}$$

$$\text{WS variance} \qquad \sigma^2_{\epsilon_{ij}} = \exp(\boldsymbol{w}'_{ij}\boldsymbol{\tau}) \qquad \text{or} \quad \log(\sigma^2_{\epsilon_{ij}}) = \boldsymbol{w}'_{ij}\boldsymbol{\tau}$$

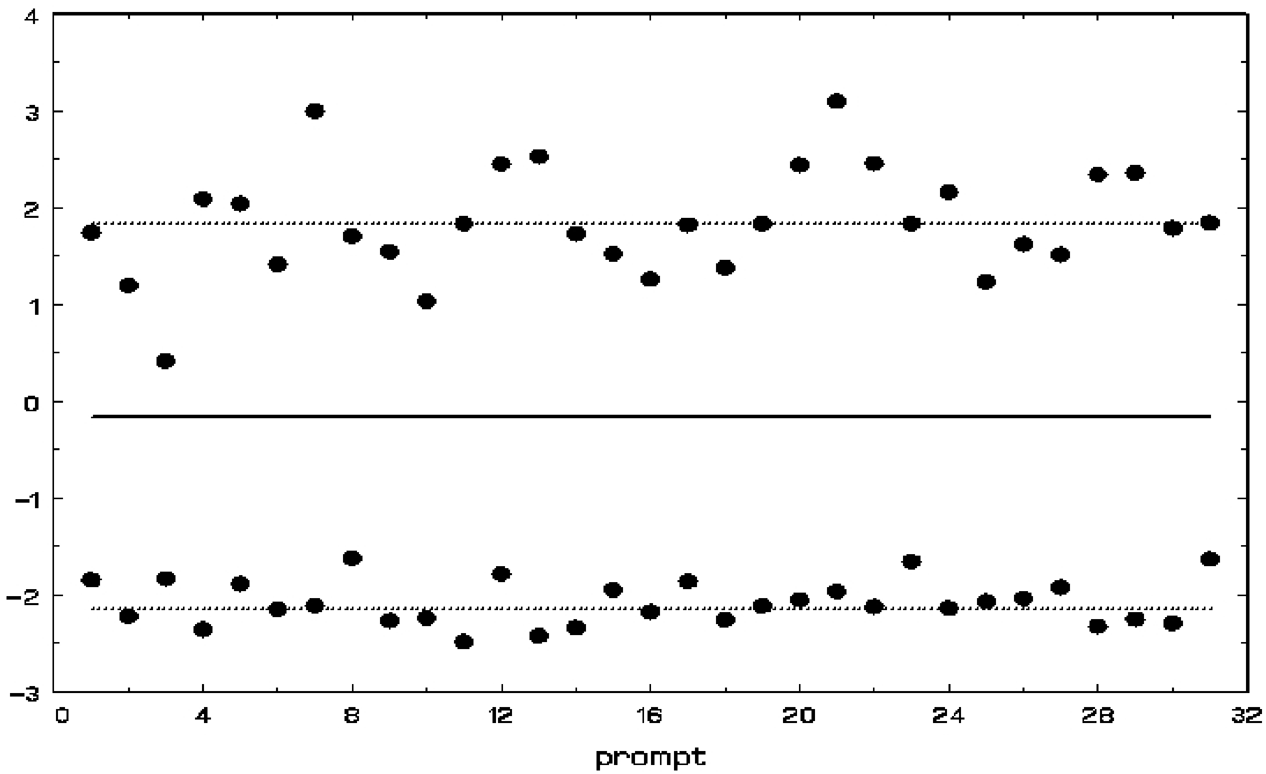
- $\boldsymbol{u}_{ij}$ and $\boldsymbol{w}_{ij}$ include covariates (and $\mathbf{1}$)
- exp function ensures a positive multiplicative factor, and so resulting variances are positive

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



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

Standardize the random effects via the Cholesky factorization

$$\begin{bmatrix} \upsilon_i \\ \omega_i \end{bmatrix} = \begin{bmatrix} \sigma_{\upsilon_{ij}} & 0 \\ \sigma_{\upsilon\omega}/\sigma_{\upsilon_{ij}} & \sqrt{\sigma^2_\omega - \sigma^2_{\upsilon\omega}/\sigma^2_{\upsilon_{ij}}} \end{bmatrix} \begin{bmatrix} \theta_{1i} \\ \theta_{2i} \end{bmatrix} = \begin{bmatrix} s_{1ij} & 0 \\ s_{2ij} & s_{3ij} \end{bmatrix} \begin{bmatrix} \theta_{1i} \\ \theta_{2i} \end{bmatrix}$$

The model is now, with $\theta_{1i}, \theta_{2i}, e_{ij}$ all $N(0,1)$

$$y_{ij} = \boldsymbol{x}'_{ij}\boldsymbol{\beta} + \sigma_{\upsilon_{ij}}\theta_{1i} + \sigma_{\epsilon_{ij}} e_{ij}$$

$$\text{BS std dev} \qquad \sigma_{\upsilon_{ij}} \;=\; s_{1ij} \;=\; \exp\left(\frac{1}{2}\,\boldsymbol{u}'_{ij}\boldsymbol{\alpha}\right)$$

$$\text{WS std dev} \qquad \sigma_{\epsilon_{ij}} \;=\; \exp\left(\frac{1}{2}\,\left[\boldsymbol{w}'_{ij}\boldsymbol{\tau} + s_{2ij}\theta_{1i} + s_{3ij}\theta_{2i}\right]\right)$$

- $E(y_{ij}) = \boldsymbol{x}'_{ij}\boldsymbol{\beta}$

- $V(y_{ij}) \;=\; \exp(\boldsymbol{u}'_{ij}\boldsymbol{\alpha}) \;+\; \exp\left(\boldsymbol{w}'_{ij}\boldsymbol{\tau} + \frac{1}{2}\sigma^2_\omega\right)$

  BS variance WS variance

- $C(y_{ij}, y_{ij'}) \;=\; \sigma^2_{\upsilon_{ij}} \;=\; \exp\left(\boldsymbol{u}'_{ij}\boldsymbol{\alpha}\right)$ for $j \neq j'$

- $r_{ij} = \dfrac{\exp\left(\boldsymbol{u}'_{ij}\boldsymbol{\alpha}\right)}{\exp\left(\boldsymbol{u}'_{ij}\boldsymbol{\alpha}\right) + \exp\left(\boldsymbol{w}'_{ij}\boldsymbol{\tau} + \frac{1}{2}\sigma^2_\omega\right)}$

$\Rightarrow$ ICC varies as a function of BS covariates ($\boldsymbol{\alpha}$), WS covariates ($\boldsymbol{\tau}$), and variance of random scale effects (σ^2_ω)

Estimation

Model for the $n_i \times 1$ vector of responses, $\boldsymbol{y}_i$, of subject i

$$\boldsymbol{y}_i = \boldsymbol{X}_i \boldsymbol{\beta} + \mathbf{1}_i \boldsymbol{s}_{1i} \theta_{1i} + \exp\left(\frac{1}{2}\left[\boldsymbol{W}_i \boldsymbol{\tau} + \mathbf{1}_i \boldsymbol{s}_{2i} \theta_{1i} + \mathbf{1}_i \boldsymbol{s}_{3i} \theta_{2i}\right]\right) \boldsymbol{e}_i$$

The marginal density of $\boldsymbol{y}_i$ in the population

$$h(\boldsymbol{y}_i) \;=\; \int_{\boldsymbol{\theta}} \; f(\boldsymbol{y}_i \mid \boldsymbol{\theta}_i) \; g(\boldsymbol{\theta}) \; d\boldsymbol{\theta}$$

The marginal log-likelihood from the sample of N subjects

$$\log L = \sum_{i}^{N} \log h(\boldsymbol{y}_i)$$

- SAS PROC NLMIXED (slow and must provide starting values)
- MIXREGLS freeware (faster and no starting values); also DLL is accessible via R

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

- 461 adolescents (9th and 10th graders); former and current smoking experimenters, and regular smokers

- Carry PDA for a week, answer questions when prompted

  average = 30 answered prompts (range = 7 to 71)

- $\Sigma_i^N n_i = 14,105$ total number of observations

Outcomes: positive and negative affect

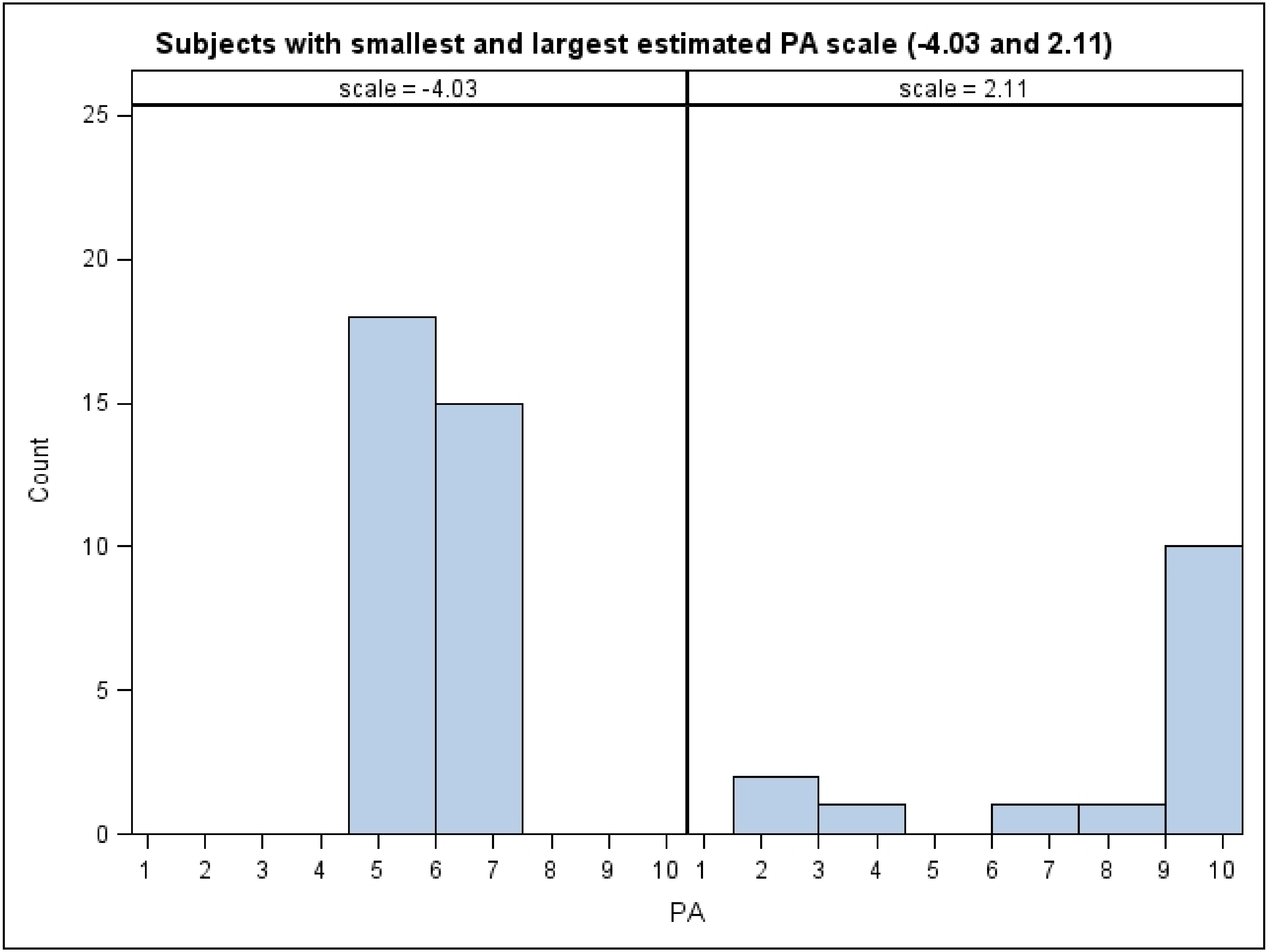
Interest: characterizing determinants of affect level, as well as BS and WS affect heterogeneity

Dependent Variables

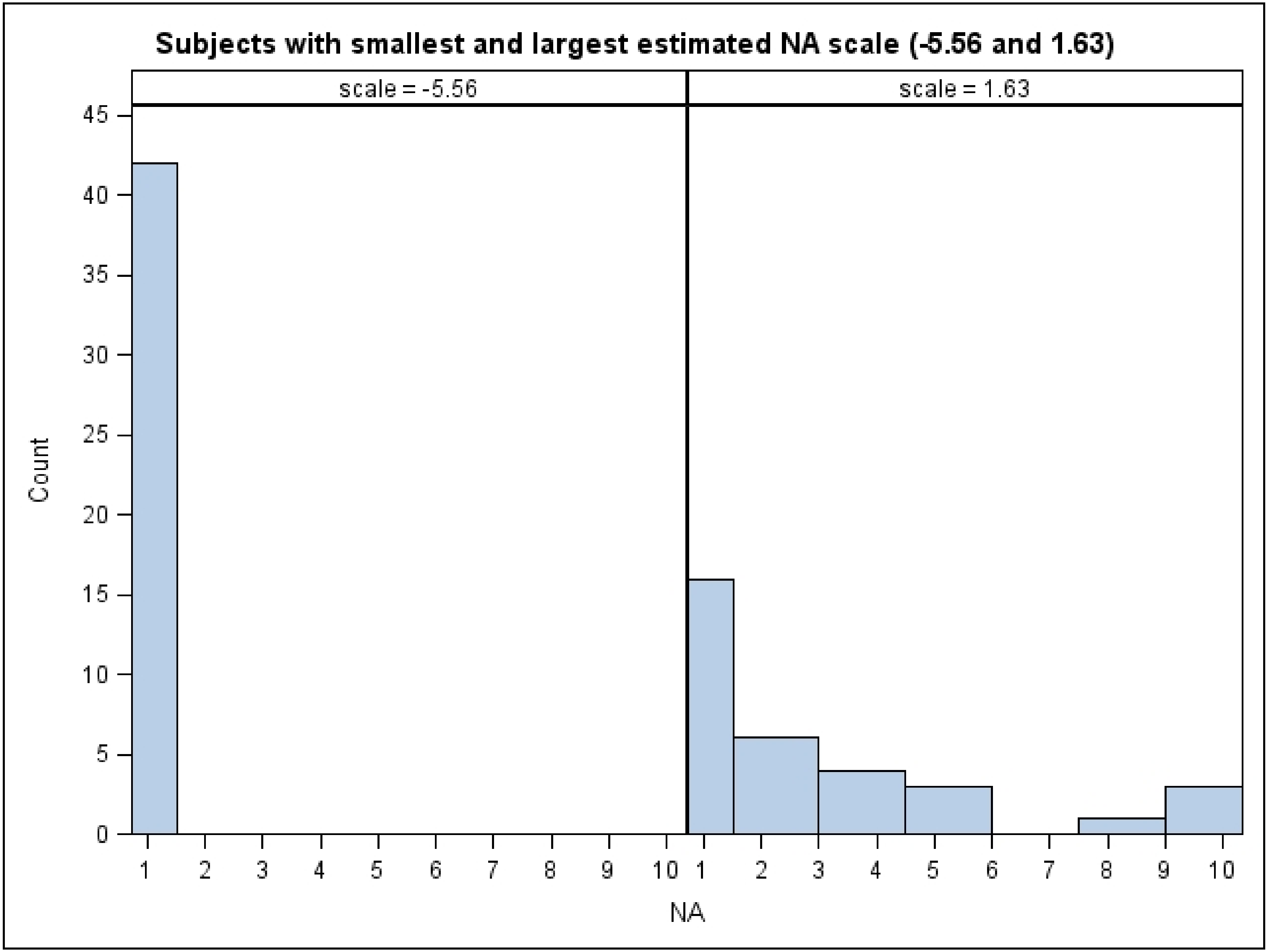
- Positive Affect mood scale (mean=6.797 and sd=1.935)
  - Before signal: I felt Happy
  - Before signal: I felt Relaxed
  - Before signal: I felt Cheerful
  - Before signal: I felt Confident
  - Before signal: I felt Accepted by Others

- Negative Affect mood scale (mean=3.455 and sd=2.253)
  - Before signal: I felt Sad
  - Before signal: I felt Stressed
  - Before signal: I felt Angry
  - Before signal: I felt Frustrated
  - Before signal: I felt Irritable

⇒ items rated on 1 (not al all) to 10 (very much) scale



Subjects with smallest and largest estimated PA scale (-4.03 and 2.11)
scale = -4.03
scale = 2.11
Count
PA
0
5
10
15
20
25
1
2
3
4
5
6
7
8
9
10



Subjects with smallest and largest estimated NA scale (-5.56 and 1.63)
scale = -5.56
scale = 1.63
Count
0
5
10
15
20
25
30
35
40
45
1 2 3 4 5 6 7 8 9 10
1 2 3 4 5 6 7 8 9 10
NA

Subject-level Independent Variables

	mean	std dev	min	max
`Smoker`	.508	.500	0	1
`Male`	.449	.498	0	1

- `Smoker`: gave at least one report of a smoking event in the week of EMA measurement (about half of the subjects)

- `Male`: a bit more females than males in this sample

What about smoking?

- `Smoker` does not consider smoking level (just whether or not a subject provided at least one smoking event)

- 234 with smoking events: average=5, median=3, range = 1 to 42

- Perhaps, smoking level needs to be considered

- `PropSmk` = proportion of occasions (both random prompts and smoking events) that were smoking events

  `PropSmk` = n_smk / (n_smk + n_random)

Model with `Smoker` and `Psmk`

`PropSmk` = n_smk / (n_smk + n_random)

N=234 with n_smk > 0 (and `Smoker` = 1)

min = .014, 25% quartile = .05, median = .08, 75% quartile = .18

`Psmk` = `PropSmk` - min(`PropSmk`)

Model: $\texttt{Mood}_{ij} = \beta_0 + \beta_1 \texttt{Smoker} + \beta_2 \texttt{Psmk} + \ \ldots \ + \upsilon_i + \epsilon_{ij}$

subject	`Smoker`	`Psmk`	mean (with other covariates = 0)
non-smoker	0	0	β_0
min smoker	1	0	$\beta_0 + \beta_1$
light smoker	1	.05	$\beta_0 + \beta_1 + .036\beta_2$
medium smoker	1	.08	$\beta_0 + \beta_1 + .066\beta_2$
high smoker	1	.18	$\beta_0 + \beta_1 + .166\beta_2$

$\Rightarrow$ Piecewise linear mean model; same for BS & WS variance models

	Positive Affect			Negative Affect		
parameter	estimate	se	$p <$	estimate	se	$p <$
Mean						
Intercept β_0	6.740	.094	.001	3.607	.117	.001
`Male` β_1	.299	.114	.01	-.599	.135	.001
`Smoker` β_2	-.192	.141	.18	.462	.168	.007
`PSmk` β_3	.018	.742	.98	-1.530	.791	.054
WS variance						
Intercept τ_0	.704	.059	.001	.820	.077	.001
`Male` τ_1	-.272	.071	.001	-.444	.092	.001
`Smoker` τ_2	.157	.086	.07	.407	.112	.001
`Psmk` τ_3	-.693	.430	.11	-1.446	.554	.01
BS variance						
Intercept α_0	.293	.102	.004	.800	.100	.001
`Male` α_1	-.115	.123	.35	-.319	.115	.006
`Smoker` α_2	.157	.149	.30	.183	.135	.18
`Psmk` α_3	.370	.812	.65	-.657	.653	.31
Scale						
BS variance of scale σ^2_ω	.503	.038	.001	.893	.064	.001
covariance $\sigma_{\upsilon\,\omega}$	-.356	.047	.001	.647	.071	.001

- Analysis focused on one measurement wave and the effect of smoking level on mood variance from random prompts (between-subjects or cross-sectional effect)

- What about as subjects change their own level of smoking? (within-subjects or longitudinal effect)

- What about smoking-attributable change in mood? (mood responses from smoking events)

EMA Study of Adolescents (Mermelstein, NCI)

- 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-month, 15-month, 2-year, and 5-year follow-ups

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

$\Rightarrow$ analysis of 158 subjects with two or more waves, where at each wave subject had two or more smoking events

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

- total of 4,727 smoking events

- 65, 30, 33, 30 subjects had data at two, three, four and five waves

- number of subjects across waves:
  126 (baseline), 93 (6 mo), 95 (15 mo), 101 (2 yr), and 87 (5 yr)

- average number of smoking events across waves:
  6.90 (range = 2 to 42)
  7.53 (2 to 32)
  9.74 (2 to 43)
  10.14 (2 to 49)
  13.90 (2 to 64)

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
- `PA` mood change averages = .75, .54, .34, .41, .41 across waves
- `NA` mood change averages = -.46, -.45, -.33, -.44, -.32 across waves

3-level Mixed Model for the mood change y_{ijk} of

- subject i ($i = 1, 2, \ldots, N$ subjects)
- wave j ($j = 1, 2, \ldots, n_i$)
- occasion k ($k = 1, 2, \ldots, n_{ij}$ smoking events)

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

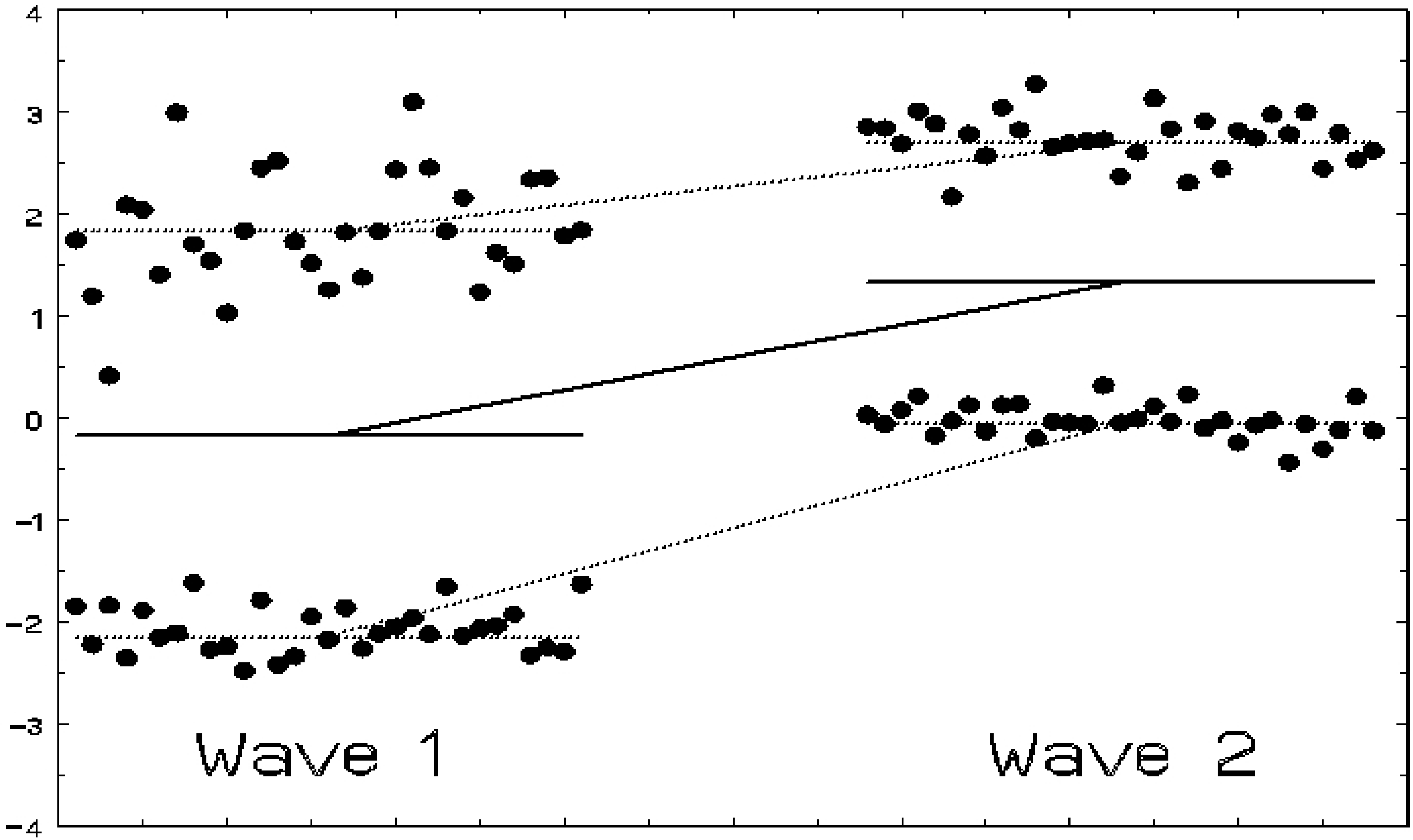
- $\texttt{Wave}_j$ (0=baseline, .5=6 mos, 1.25=15 mos, 2=2yrs, 5=5yrs)
- $\texttt{Male}_i$ (0=female, 1=male)
- Smoking level
  - * $\texttt{SmkRate}_{ij}$ = per wave daily smoking rate (ln units)
  - * BS version $\texttt{AvgRate}_i$ = subject average of $\texttt{SmkRate}_{ij}$
  - * WS version $\texttt{DevRate}_{ij} = (\texttt{SmkRate}_{ij} - \texttt{AvgRate}_i)$ = per wave deviation in the daily smoking rate

Error variance model $\epsilon_{ijk} \sim N(0, \sigma_\epsilon^2)$ WS variance

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

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

- 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}



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

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 + d5*w5;

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

MODEL y ~ NORMAL(z,vare);

RANDOM u0 u1 s0 d1 d2 d3 d4 d5 ~ NORMAL([0,0,0,0,0,0,0,0],
        [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,
         0, 0, 0, 0, 0, 0, 0, vwave ]) SUBJECT=id;
```

where `w1, w2, w3, w4, w5` are indicator variables (0,1) of the five waves

Random effect model comparisons

Subject level	Wave level	parms	Positive Affect Deviance	Positive Affect AIC	Negative Affect Deviance	Negative Affect AIC
Int, Wave		3	15916	15942	16526	16552
Int, Wave, Scale		6	14913	14945	15100	15132
Int	Int	2	15906	15930	16504	16528
Int, Wave	Int	4	15895	15923	Wave var goes to 0	
Int, Scale	Int	4	*14900*	*14928*	*15090*	*15118*
Int, Wave, Scale	Int	7	Wave var goes to 0			

regressors = `Wave, Male, AvgRate, DevRate` 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	.708	.106	.001	-.447	.091	.001
Wave β_1	-.020	.016	.22	.002	.013	.90
Male β_2	.119	.082	.15	-.057	.069	.41
AvgRate β_3	-.174	.059	.004	.083	.050	.10
DevRate β_4	-.081	.052	.12	.071	.039	.08

Error Var Model	est	se	$p <$	est	se	$p <$
Intercept τ_0	.893	.174	.001	1.048	.211	.001
Wave τ_1	-.158	.017	.001	-.117	.018	.001
Male τ_2	.218	.156	.16	.235	.193	.22
AvgRate τ_3	-.229	.107	.034	-.361	.132	.007
DevRate τ_4	-.314	.049	.001	-.321	.055	.001

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 $\sigma^2_{\upsilon_{(3)}}$	.130	.031	.001	.084	.023	.001
Scale σ^2_{ω}	.780	.106	.001	1.28	.166	.001
Int, Scale $\sigma_{\upsilon_{(3)}\omega}$	.186	.040	.001	-.189	.041	.001
	$(r = .59)$			$(r = -.58)$		
Wave level						
Intercept $\sigma^2_{\upsilon_{(2)}}$	.090	.021	.001	.028	.012	.022

Summary

- More applications where interest is on modeling variance

  Hedeker D., Mermelstein R.J., & Demirtas H. (2008). An application of a mixed-effects location scale model for analysis of Ecological Momentary Assessment (EMA) data. *Biometrics, 64*, 627-634.

  Hedeker D., Mermelstein R.J., & Demirtas H. (2012). Modeling between- and within-subject variance in EMA data using mixed-effects location scale models. *Statistics in Medicine, 31*, 3328-3336.

  Hedeker D. & Mermelstein R.J. (2012). Mood changes associated with smoking in adolescents: An application of a mixed-effects location scale model for longitudinal EMA data. In G. R. Hancock & J. Harring (Eds.), *Advances in Longitudinal Methods in the Social and Behavioral Sciences* (pp. 59-79). Information Age Publishing, Charlotte, NC.

  Hedeker D. (in press). MIXREGLS: A program for mixed-effects location scale analysis. *Journal of Statistical Software.*

  Li X. & Hedeker D. (2012). A three-level mixed-effects location scale model with an application to Ecological Momentary Assessment (EMA) data. *Statistics in Medicine, 31*, 3192-3210.

- Other kinds of outcomes, especially ordinal

  Hedeker D., Demirtas H., & Mermelstein R.J. (2009). A mixed ordinal location scale model for analysis of Ecological Momentary Assessment (EMA) data. *Statistics and Its Interface, 2*, 391-402.

  Hedeker D. & Mermelstein R.J. (2013). A location scale Item Response Theory (IRT) model for analysis of ordinal questionnaire data. Annual meeting of the Eastern North American Region (ENAR) of the International Biometric Society, Orlando, FL.

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