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 ⇒ 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 $j$ ($j = 1, 2, \ldots, n_i$)

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

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

$\beta = p \times 1$ vector of regression coefficients

$\nu_i \sim N(0, \sigma^2_\nu)$ BS variance

$\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$ WS variance
Log-linear models for variances

BS variance \[ \sigma_{v_{ij}}^2 = \exp(u'_{ij}\alpha) \quad \text{or} \quad \log(\sigma_{v_{ij}}^2) = u'_{ij}\alpha \]

WS variance \[ \sigma_{\epsilon_{ij}}^2 = \exp(w'_{ij}\tau) \quad \text{or} \quad \log(\sigma_{\epsilon_{ij}}^2) = w'_{ij}\tau \]

- \( u_{ij} \) and \( w_{ij} \) include covariates (and 1)
- exp function ensures a positive multiplicative factor, and so resulting variances are positive
WS variance varies across subjects

\[ \sigma_{\epsilon_{ij}}^2 = \exp(w_i^T \tau + \omega_i) \quad \text{where} \quad \omega_i \sim N(0, \sigma_{\omega}^2) \]

\[ \log(\sigma_{\epsilon_{ij}}^2) = w_i^T \tau + \omega_i \]

- \( \omega_i \) are log-normal subject-specific perturbations of WS variance
- \( \omega_i \) are “scale” random effects - how does a subject differ in terms of the variation in their data
- \( \nu_i \) 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

\[
\begin{bmatrix}
\nu_i \\
\omega_i
\end{bmatrix} =
\begin{bmatrix}
\sigma_{vij} & 0 \\
\sigma_{v\omega}/\sigma_{vij} & \sqrt{\sigma_{\omega}^2 - \sigma_{v\omega}^2/\sigma_{vij}^2}
\end{bmatrix}
\begin{bmatrix}
\theta_{1i} \\
\theta_{2i}
\end{bmatrix} =
\begin{bmatrix}
s_{1ij} & 0 \\
\sigma_{v\omega}/\sigma_{vij} & \sigma_{\omega}
\end{bmatrix}
\begin{bmatrix}
\theta_{1i} \\
\theta_{2i}
\end{bmatrix}
\]

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

\[
y_{ij} = x'_{ij} \beta + \sigma_{vij} \theta_{1i} + \sigma_{eij} e_{ij}
\]

BS std dev \( \sigma_{vij} = s_{1ij} = \exp\left(\frac{1}{2} u'_{ij} \alpha\right) \)

WS std dev \( \sigma_{eij} = \exp\left(\frac{1}{2} w'_{ij} \tau + s_{2ij} \theta_{1i} + s_{3ij} \theta_{2i}\right) \)
• \( E(y_{ij}) = x'_{ij} \beta \)

• \( V(y_{ij}) = \exp(u'_{ij} \alpha) + \exp(w'_{ij} \tau + \frac{1}{2} \sigma^2) \)

  BS variance          WS variance

• \( C(y_{ij}, y_{ij}') = \sigma^2_{y_{ij}} = \exp(u'_{ij} \alpha) \) for \( j \neq j' \)

• \( r_{ij} = \frac{\exp(u'_{ij} \alpha)}{\exp(u'_{ij} \alpha) + \exp(w'_{ij} \tau + \frac{1}{2} \sigma^2)} \)

\( \Rightarrow \) ICC varies as a function of BS covariates \((\alpha)\), WS covariates \((\tau)\), and variance of random scale effects \((\sigma^2)\)
Estimation

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

$$
\mathbf{y}_i = X_i \beta + 1_i s_{1i} \theta_{1i} + \exp \left( \frac{1}{2} \left[ W_i \tau + 1_i s_{2i} \theta_{1i} + 1_i s_{3i} \theta_{2i} \right] \right) \mathbf{e}_i
$$

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

$$
h(\mathbf{y}_i) = \int \theta f(\mathbf{y}_i | \theta_i) g(\theta) \, d\theta
$$

The marginal log-likelihood from the sample of $N$ subjects

$$
\log L = \sum_i \log h(\mathbf{y}_i)
$$

- 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)
- \( \sum_{i}^{N} n_i = 14,105 \) 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 at all) to 10 (very much) scale
Subjects with smallest and largest estimated PA scale (-4.03 and 2.11)

- Scale = -4.03
  - Count distribution

- Scale = 2.11
  - Count distribution
Subject-level Independent Variables

<table>
<thead>
<tr>
<th></th>
<th>mean</th>
<th>std dev</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker</td>
<td>.508</td>
<td>.500</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>.449</td>
<td>.498</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

- **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

  \[
  \text{PropSmk} = \frac{n_{\text{smk}}}{n_{\text{smk}} + n_{\text{random}}}
  \]
Model with Smoker and Psmk

\[ \text{PropSmk} = \frac{n_{\text{smk}}}{n_{\text{smk}} + n_{\text{random}}} \]

N=234 with \( n_{\text{smk}} > 0 \) (and \( \text{Smoker} = 1 \))

\( \text{min} = .014, \ 25\% \text{ quartile} = .05, \ \text{median} = .08, \ 75\% \text{ quartile} = .18 \)

\[ \text{Psmk} = \text{PropSmk} - \min(\text{PropSmk}) \]

Model: \( \text{Mood}_{ij} = \beta_0 + \beta_1 \text{Smoker} + \beta_2 \text{Psmk} + \ldots + \nu_i + \epsilon_{ij} \)

<table>
<thead>
<tr>
<th>subject</th>
<th>Smoker</th>
<th>Psmk</th>
<th>mean (with other covariates = 0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-smoker</td>
<td>0</td>
<td>0</td>
<td>( \beta_0 )</td>
</tr>
<tr>
<td>min smoker</td>
<td>1</td>
<td>0</td>
<td>( \beta_0 + \beta_1 )</td>
</tr>
<tr>
<td>light smoker</td>
<td>1</td>
<td>.05</td>
<td>( \beta_0 + \beta_1 + .036\beta_2 )</td>
</tr>
<tr>
<td>medium smoker</td>
<td>1</td>
<td>.08</td>
<td>( \beta_0 + \beta_1 + .066\beta_2 )</td>
</tr>
<tr>
<td>high smoker</td>
<td>1</td>
<td>.18</td>
<td>( \beta_0 + \beta_1 + .166\beta_2 )</td>
</tr>
</tbody>
</table>

\( \Rightarrow \) Piecewise linear mean model; same for BS & WS variance models
<table>
<thead>
<tr>
<th>parameter</th>
<th>Positive Affect</th>
<th></th>
<th>Negative Affect</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>estimate</td>
<td>se</td>
<td>p &lt;</td>
<td>estimate</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept $\beta_0$</td>
<td>6.740</td>
<td>.094</td>
<td>.001</td>
<td>3.607</td>
</tr>
<tr>
<td>Male $\beta_1$</td>
<td>.299</td>
<td>.114</td>
<td>.01</td>
<td>-.599</td>
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<tr>
<td>Smoker $\beta_2$</td>
<td>-.192</td>
<td>.141</td>
<td>.18</td>
<td>.462</td>
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<tr>
<td>PSmk $\beta_3$</td>
<td>.018</td>
<td>.742</td>
<td>.98</td>
<td>-1.530</td>
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<tr>
<td>WS variance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept $\tau_0$</td>
<td>.704</td>
<td>.059</td>
<td>.001</td>
<td>.820</td>
</tr>
<tr>
<td>Male $\tau_1$</td>
<td>-.272</td>
<td>.071</td>
<td>.001</td>
<td>-.444</td>
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<tr>
<td>Smoker $\tau_2$</td>
<td>.157</td>
<td>.086</td>
<td>.07</td>
<td>.407</td>
</tr>
<tr>
<td>PSmk $\tau_3$</td>
<td>-.693</td>
<td>.430</td>
<td>.11</td>
<td>-1.446</td>
</tr>
<tr>
<td>BS variance</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Intercept $\alpha_0$</td>
<td>.293</td>
<td>.102</td>
<td>.004</td>
<td>.800</td>
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<tr>
<td>Male $\alpha_1$</td>
<td>-.115</td>
<td>.123</td>
<td>.35</td>
<td>-.319</td>
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<tr>
<td>Smoker $\alpha_2$</td>
<td>.157</td>
<td>.149</td>
<td>.30</td>
<td>.183</td>
</tr>
<tr>
<td>PSmk $\alpha_3$</td>
<td>.370</td>
<td>.812</td>
<td>.65</td>
<td>-.657</td>
</tr>
<tr>
<td>Scale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BS variance of scale $\sigma_\omega^2$</td>
<td>.503</td>
<td>.038</td>
<td>.001</td>
<td>.893</td>
</tr>
<tr>
<td>covariance $\sigma_{v\omega}$</td>
<td>-.356</td>
<td>.047</td>
<td>.001</td>
<td>.647</td>
</tr>
</tbody>
</table>
• 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

⇒ 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 at 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)

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

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

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

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 $\omega_i$ allowed to be correlated with random intercept $\nu_{0i}$ and trend $\nu_{1i}$
- 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 
vu0=.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, vwave,
              0, 0, 0, vwave,
              0, 0, 0, vwave,
              0, 0, 0, vwave,
              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

<table>
<thead>
<tr>
<th>Subject level</th>
<th>Wave level</th>
<th>parms</th>
<th>Positive Affect Deviance</th>
<th>AIC</th>
<th>Negative Affect Deviance</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Int, Wave</td>
<td>3</td>
<td></td>
<td>15916</td>
<td>15942</td>
<td>16526</td>
<td>16552</td>
</tr>
<tr>
<td>Int, Wave, Scale</td>
<td>6</td>
<td></td>
<td>14913</td>
<td>14945</td>
<td>15100</td>
<td>15132</td>
</tr>
<tr>
<td>Int</td>
<td>2</td>
<td></td>
<td>15906</td>
<td>15930</td>
<td>16504</td>
<td>16528</td>
</tr>
<tr>
<td>Int, Wave</td>
<td>4</td>
<td></td>
<td>15895</td>
<td>15923</td>
<td>Wave var goes to 0</td>
<td></td>
</tr>
<tr>
<td>Int, Scale</td>
<td>4</td>
<td></td>
<td>14900</td>
<td>14928</td>
<td>15090</td>
<td>15118</td>
</tr>
<tr>
<td>Int, Wave, Scale</td>
<td>7</td>
<td></td>
<td>Wave var goes to 0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Mean Model</th>
<th>Positive Affect</th>
<th></th>
<th>Negative Affect</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>est</td>
<td>se</td>
<td>$p &lt;$</td>
<td>est</td>
</tr>
<tr>
<td>Intercept $\beta_0$</td>
<td>.708</td>
<td>.106</td>
<td>.001</td>
<td>-.447</td>
</tr>
<tr>
<td>Wave $\beta_1$</td>
<td>-.020</td>
<td>.016</td>
<td>.22</td>
<td>.002</td>
</tr>
<tr>
<td>Male $\beta_2$</td>
<td>.119</td>
<td>.082</td>
<td>.15</td>
<td>-.057</td>
</tr>
<tr>
<td>AvgRate $\beta_3$</td>
<td>-.174</td>
<td>.059</td>
<td>.004</td>
<td>.083</td>
</tr>
<tr>
<td>DevRate $\beta_4$</td>
<td>-.081</td>
<td>.052</td>
<td>.12</td>
<td>.071</td>
</tr>
</tbody>
</table>

| Error Var Model     | est  | se  | $p <$ | est  | se  | $p <$ |
|---------------------|------------------|------------------|-----------------|-----------------|
|                     | est  | se  | $p <$ | est  | se  | $p <$ |
| Intercept $\tau_0$  | .893 | .174| .001  | 1.048| .211| .001 |
| Wave $\tau_1$      | -.158| .017| .001  | -.117| .018| .001 |
| Male $\tau_2$      | .218 | .156| .16   | .235 | .193| .22  |
| AvgRate $\tau_3$   | -.229| .107| .034  | -.361| .132| .007 |
| DevRate $\tau_4$   | -.314| .049| .001  | -.321| .055| .001 |
### 3-level Model of Smoking-related Positive and Negative Affect Change

<table>
<thead>
<tr>
<th>Random effect (co)variances</th>
<th>Positive Affect</th>
<th>Negative Affect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>est</td>
<td>se</td>
</tr>
<tr>
<td><strong>Subject level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept $\sigma^2_{\nu(3)}$</td>
<td>.130</td>
<td>.031</td>
</tr>
<tr>
<td>Scale $\sigma^2_\omega$</td>
<td>.780</td>
<td>.106</td>
</tr>
<tr>
<td>Int, Scale $\sigma_{\nu(3)}\omega$</td>
<td>.186</td>
<td>.040</td>
</tr>
<tr>
<td></td>
<td>($r = .59$)</td>
<td>($r = -.58$)</td>
</tr>
<tr>
<td><strong>Wave level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept $\sigma^2_{\nu(2)}$</td>
<td>.090</td>
<td>.021</td>
</tr>
</tbody>
</table>
Summary

• More applications where interest is on modeling variance


• Other kinds of outcomes, especially ordinal


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