Two-stage and shared parameter mixed-effects location scale models for intensive longitudinal data

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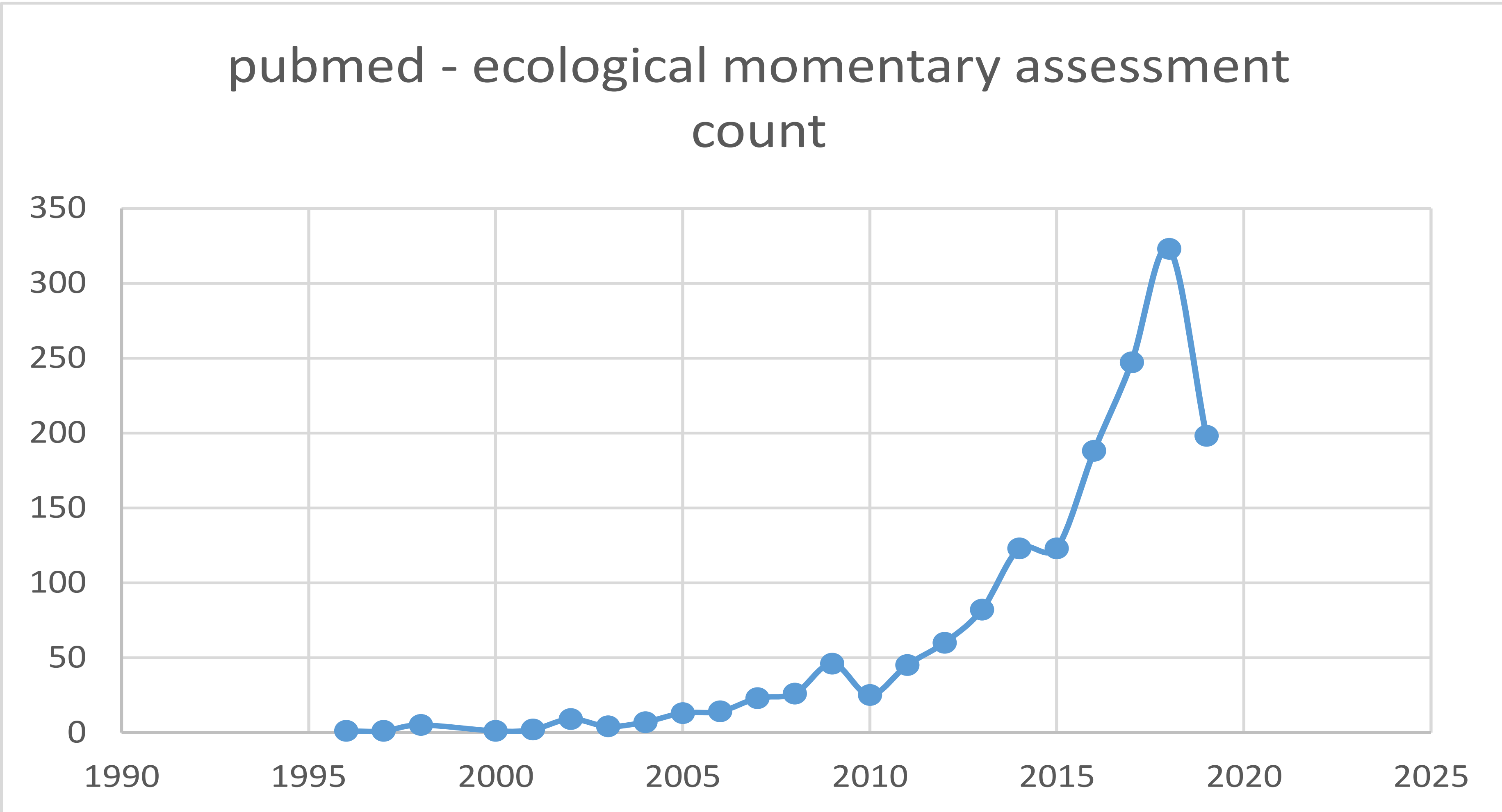
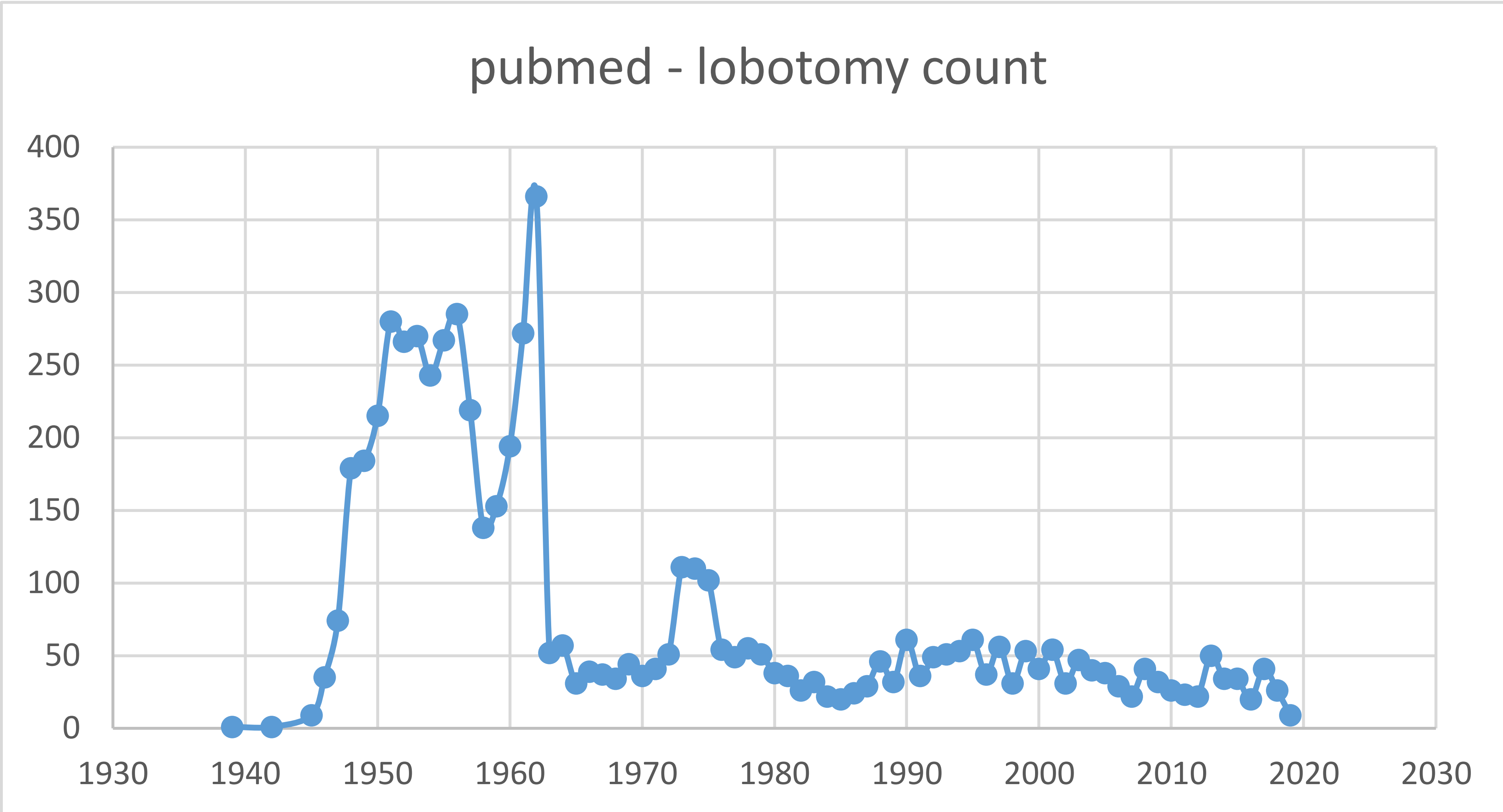
Ecological Momentary Assessment (EMA) data
experience sampling and diary methods, intensive longitudinal data

- 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


pubmed - ecological momentary assessment
count
350
300
250
200
150
100
50
0
1990
1995
2000
2005
2010
2015
2020
2025


pubmed - lobotomy count
400
350
300
250
200
150
100
50
0
1930
1940
1950
1960
1970
1980
1990
2000
2010
2020
2030

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 in addition to mean level
  - within-subjects (WS) variance
    e.g., subject degree of stability/inconsistency could vary by gender or age

Carroll (2003) Variances are not always nuisance parameters, *Biometrics*.

Submodel One: Mixed-effects location-scale model for measurement y of subject i ($i = 1, 2, \ldots, N$) on occasion j ($j = 1, 2, \ldots, n_i$)

$$y_{ij} \;=\; \boldsymbol{x}'_{ij}\boldsymbol{\beta} + \boldsymbol{z}'_{ij}\boldsymbol{\upsilon}_i + \epsilon_{ij}$$

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

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

$\boldsymbol{z}_{ij} = r \times 1$ vector of random effect variables (including a column of ones)

$\boldsymbol{\upsilon}_i \sim N(\mathbf{0}, \boldsymbol{\Sigma}_\upsilon)$ BS variance; how homogeneous/heterogeneous are subjects?

$\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$ WS variance; how consistent/erratic are the data within subjects?

Log-linear model for WS variance (exp function ensures a positive multiplicative factor, and so resulting variance is positive)

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

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

- ω_i are log-normal subject-specific perturbations of WS variance; "scale" random effects - how does a subject differ in terms of the variation in their data
- $\boldsymbol{\upsilon}_i$ are "location" random effects - how does a subject differ in terms of the mean of their data (e.g., intercepts and slopes)
- $\boldsymbol{\tau}^*$ are association parameters between location and scale

Submodel Two: Submodel One random subject effects (e.g., intercept υ_{0i}, slope υ_{1i}, scale ω_i) are shared, in addition to subject-level variables $\boldsymbol{x}_i$, as predictors of subject-level outcome $y_i^{(2)}$

$$y_i^{(2)} = \beta_0 + \beta_1 \upsilon_{0i} + \beta_2 \upsilon_{1i} + \beta_3 \omega_i + \boldsymbol{x}_i' \boldsymbol{\beta} + \varepsilon_i$$

- Can include interactions of random effects with each other and/or other subject-level variables $\boldsymbol{x}_i$ (e.g., location effect varies depending on erraticism/consistency of a subject)
- Submodel Two could be a logistic regression ($y_i^{(2)}$ is binary), proportional odds model ($y_i^{(2)}$ is ordinal), or Poisson regression ($y_i^{(2)}$ is a count)

SAS PROC NLMIXED - likelihood estimation for shared parameter location-scale mixed model (both models share random efffects `u0`, `u1`, `u2`)

```
PROC NLMIXED;
PARMS b0=.65 bEcig=-.05 t0=.405 tEcig=0
      v0=.37 v01=-.02 v1=.11  v02=0 v12=0 v2=.05
      a0=2.37 aCig=0 aEcig=0  aScale=0 vares=1;
lla=0;llb=0;   pi = arcos(-1);
if (ind eq 0) then do;
   mu = (b0 + u0) + (bEcig + u1)*Ecig ;
   vare = exp(t0 + tEcig*Ecig + u2);
   lla = log(1 / (SQRT(2*pi*vare))) + (-(outcome-mu)**2)/ (2*vare);
end;
if (ind eq 1) then do;
   mus = a0 + aCig*u0 + aEcig*u1 + aScale*u2;
   llb = log(1 / (SQRT(2*pi*vares))) + (-(outcome-mus)**2)/ (2*vares);
end;
ll = lla+llb;
MODEL outcome ~ GENERAL(ll);
RANDOM u0 u1 u2 ~ NORMAL([0,0,0], [v0,v01,v1,v02,v12,v2]) SUBJECT=id;
RUN;
```

Observational Study of Dual Users (Mermelstein)

- Ongoing observational study of "dual users" who are primarily combustible cigarette smokers who are "early" in their trial/uptake of e-cigarettes
- Goals: examine patterns and predictors of changes in tobacco use patterns (combustible/e-cigarette patterns), with an emphasis on subjective experience and contexts of use of products, over a 12 month time frame
  - EMA at multiple time points (random prompts, Cig & ECig events)
  - Biweekly reports of cigarette and e-cigarette use over the 12 months (after baseline EMA)
  - Extensive psychosocial and behavioral questionnaires at baseline and 12 months
  - Present data on 240 dual users who completed 12 months and provided at least 2 Cig and 2 ECig event reports during EMA

Outcomes - $N = 240$ subjects

- Submodel 1: satisfaction attributed to Cig & ECig events (EMA)
  - How satisfying was tobacco product used?
  - How pleasurable was tobacco product used?
  - each rated on 1 (not al all) to 10 (very much) scale
  - average = reported satisfaction attributed to cig & ecig use
  - 5339 cig events and 2510 ecig events (total = 7849 events)

- submodel 2: subject average of daily cigarette smoking rate (daily ecig rate) from biweekly reports (post-EMA)

- Shared parameter model concurrently models data from EMA (satisfaction from smoking/ecig events) and post-EMA (average biweekly cigarette smoking/ecig rate)
- Both models share random effects (intercept, slope, scale)
- Post-EMA data can influence estimation of random effects (variance-covariance matrix of random effects)
- Timewarp problem!
- Maybe better to fit two models separately in two stages

Stage 1 analysis - EMA Satisfaction ratings (N=240; 7849 events)

Variable	Estimate	Std Error	z-value	p-value
BETA (regression coefficients)				
Intercept	7.37402	0.09956	74.06853	0.00000
Ecig	0.09794	0.10264	0.95421	0.33998
Random (location) Effect Variances and Covariances (corr = 0.496)				
Intercept	2.51752	0.23670	10.63607	0.00000
Covariance12	-1.18002	0.18754	-6.29218	0.00000
Ecig	2.24915	0.21864	10.28713	0.00000
TAU (WS variance parameters: log-linear model)				
Intercept	0.33527	0.06862	4.88602	0.00000
Ecig	-0.12278	0.04475	-2.74375	0.00607
Random location effects on WS variance (log-linear model)				
Intercept	-0.37459	0.06678	-5.60945	0.00000
Ecig	0.02434	0.06876	0.35394	0.72338
Random scale standard deviation				
Std Dev	0.92704	0.04689	19.76850	0.00000

Stage 2 analysis

Stage 1 random subject effect estimates (e.g., intercept $\hat{\upsilon}_{0i}$, slope $\hat{\upsilon}_{1i}$, scale $\hat{\omega}_i$) and other subject-level variables $\boldsymbol{x}_i$ used as regressors to predict a Stage 2 subject-level outcome $y_i^{(2)}$

$$y_i^{(2)} = \beta_0 + \beta_1 \hat{\upsilon}_{0i} + \beta_2 \hat{\upsilon}_{1i} + \beta_3 \hat{\omega}_i + \boldsymbol{x}_i' \boldsymbol{\beta} + \varepsilon_i$$

Random subject effects are estimates with estimated uncertainty, "plausible value" replications of the the random effects are performed (Mislevy, 1991, *Psychometrika*); repeated samples from each subject's posterior distribution

Stage 2 analysis - N = 240 subjects - Average Daily Cig Rate

```
Descriptives
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 Dependent variable
                          mean         min         max     std dev
 ----------------------------------------------------------------
 sr_CigRate_mean        2.3363      0.1048      5.9161      1.1900


 Random Location and Scale EB mean estimates
                          mean         min         max     std dev
 ----------------------------------------------------------------
 Locat_1                0.0000     -2.5639      1.6546      0.9706
 Locat_2               -0.0000     -5.1979      3.4499      0.9170
 Scale                 -0.0000     -4.1966      1.7523      0.9481
```

Stage 2 analysis - averaged regression results from 500 plausible value replications of Stage 1 random effects

Variable	Estimate	Std Error	z-value	p-value
Intercept	2.33637	0.07343	31.81973	0.00000
Stage 1 Intercept	0.18206	0.07592	2.39790	0.01649
Stage 1 Slope	-0.31452	0.07893	-3.98476	0.00007
Stage 1 Scale	0.10463	0.07660	1.36601	0.17194
Residual Variance	1.26680	0.11773	10.76049	0.00000

$\Rightarrow$ higher levels of Stage 1 intercept (satisfaction from EMA smoking events) and lower levels of Stage 1 slope (satisfaction from EMA ecig relative to smoking events) lead to increased smoking rates

Stage 2 analysis - averaged regression results from 500 plausible value replications of Stage 1 random effects; controlling for baseline level of smoking dependency (`cigNDSSc`)

Variable	Estimate	Std Error	z-value	p-value
Intercept	2.36837	0.06845	34.60029	0.00000
cigNDSSc	0.62973	0.10599	5.94145	0.00000
Stage 1 Intercept	0.09163	0.07208	1.27135	0.20360
Stage 1 Slope	-0.28249	0.07397	-3.81908	0.00013
Stage 1 Scale	0.03892	0.07205	0.54023	0.58904
Residual Variance	1.10056	0.10174	10.81791	0.00000

$\Rightarrow$ higher levels of Stage 1 slope (satisfaction from EMA ecig relative to smoking events) lead to decreased smoking rates

Stage 2 analysis - N = 240 subjects - Average Daily ECig Rate

```
Descriptives
------------

 Dependent variable
                          mean         min         max     std dev
 ----------------------------------------------------------------
 sr_ECIGRate_mean       1.7402      0.0000      6.9725      1.1029


 Random Location and Scale EB mean estimates
                          mean         min         max     std dev
 ----------------------------------------------------------------
 Locat_1                0.0000     -2.5639      1.6546      0.9706
 Locat_2               -0.0000     -5.1979      3.4499      0.9170
 Scale                 -0.0000     -4.1966      1.7523      0.9481
```

Stage 2 analysis - averaged regression results from 500 plausible value replications of Stage 1 random effects

Variable	Estimate	Std Error	z-value	p-value
Intercept	1.74023	0.06938	25.08351	0.00000
Stage 1 Intercept	-0.14323	0.07282	-1.96676	0.04921
Stage 1 Slope	0.17843	0.07473	2.38754	0.01696
Stage 1 Scale	-0.12727	0.07290	-1.74573	0.08086
Residual.Variance	1.14158	0.10529	10.84252	0.00000

- lower levels of Stage 1 intercept (satisfaction from EMA smoking events) and higher levels of Stage 1 slope (satisfaction from EMA ecig relative to smoking events) lead to increased ECIG rates
- increased volatility of EMA reports leads to decreased ECIG rates

Stage 2 analysis - averaged regression results from 500 plausible value replications of Stage 1 random effects; controlling for baseline level of ECIG dependency (`EcigNDSSc`)

Variable	Estimate	Std Error	z-value	p-value
Intercept	1.74032	0.06676	26.06816	0.00000
ECigNDSSc	0.38619	0.08947	4.31648	0.00002
Stage 1 Intercept	-0.14264	0.06974	-2.04516	0.04084
Stage 1 Slope	0.14447	0.07246	1.99386	0.04617
Stage 1 Scale	-0.12460	0.07025	-1.77371	0.07611
Residual.Variance	1.05838	0.09746	10.85917	0.00000

- lower levels of Stage 1 intercept (satisfaction from EMA smoking events) and higher levels of Stage 1 slope (satisfaction from EMA ecig relative to smoking events) lead to increased ECIG rates
- increased volatility of EMA reports leads to decreased ECIG rates

Summary

- Joint shared parameter models are popular, but careful of time incompatibilities

- Two-stage approach can be more logically consistent

- Focus is on modeling Stage 1 intensive longitudinal data in terms of means (intercepts & slopes) and variance

- Stage 2 outcome is at subject level and predictors are Stage 1 random subject effects (and other subject variables)

- Freeware software program MixWILD automates the two-stage modeling, including random draws of plausible values of Stage 1 random effects: https://voices.uchicago.edu/hedeker/