



PIECEWISE LINEAR MIXED EFFECTS MODELING

ROSENKRANZ LAB MEETING

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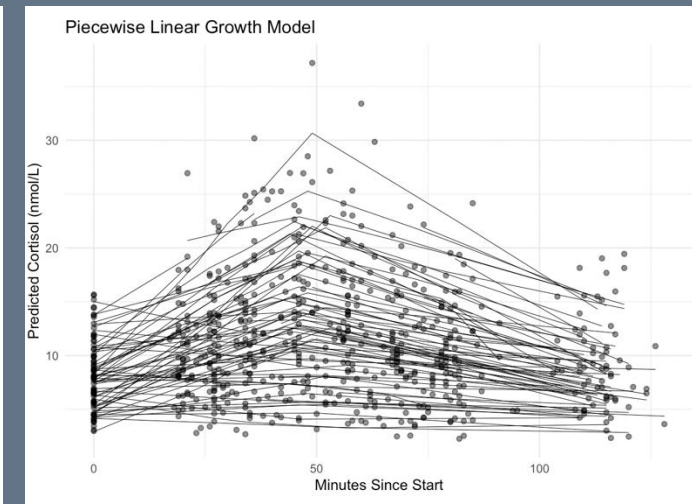
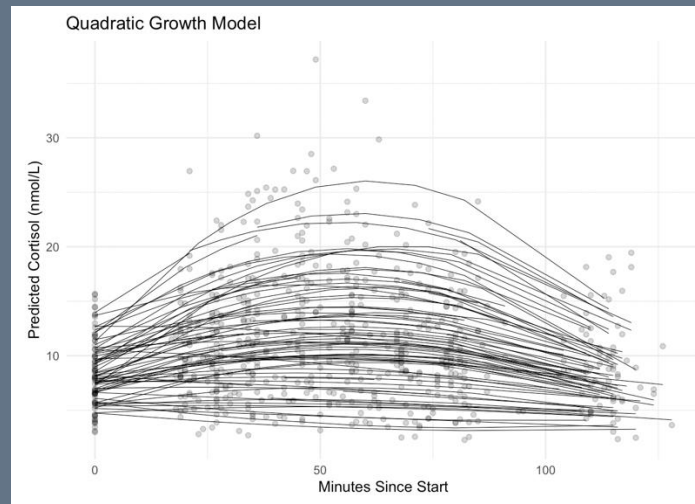
SPRING 2023

WHEN DO YOU NEED PIECEWISE?

- Data with different linear trends over different regions
 - x-y relationship is a continuous function with 2+ linear segments
- Clear break points (“knots”)
- Theoretically-motivated questions
 - Longitudinal data

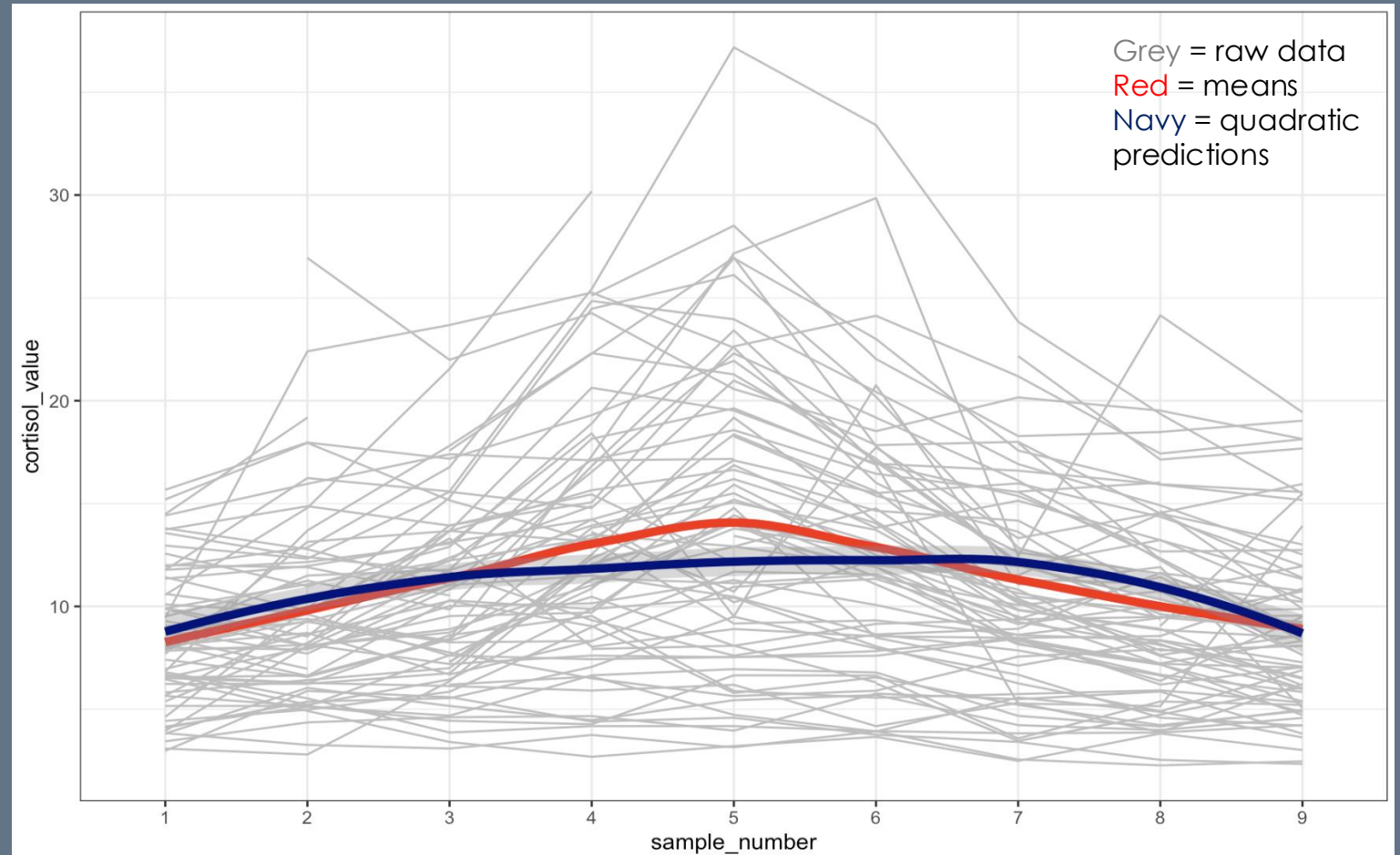
WHY PIECEWISE AND NOT POLYNOMIAL?

- Interpretation
 - *slope estimates at various stages; distinct “growth phases”*
 - *identify locations of meaningful change in slope*
 - Polynomial assumes **smooth trajectory**
- Piecewise allows you to examine how different “pieces” relate to other variables
- Avoid multicollinearity
- Piecewise with polynomial pieces



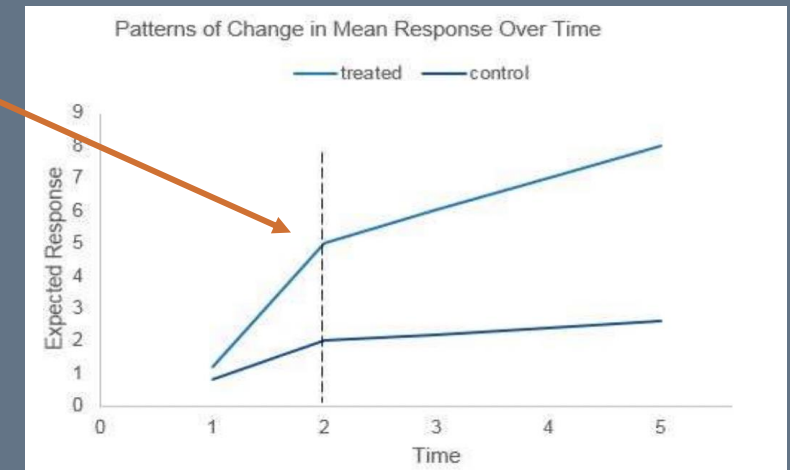
WHY PIECEWISE AND NOT POLYNOMIAL?

- Which fits better?



CHANGE POINTS (“KNOTS”)

- x-values where linear function slope changes
- Continuous or discontinuous
- Theory + Data:
 - is change point a known parameter?
 - estimate from data?
- R package SEGMENTED
 - *Determine change points to minimize SSE*



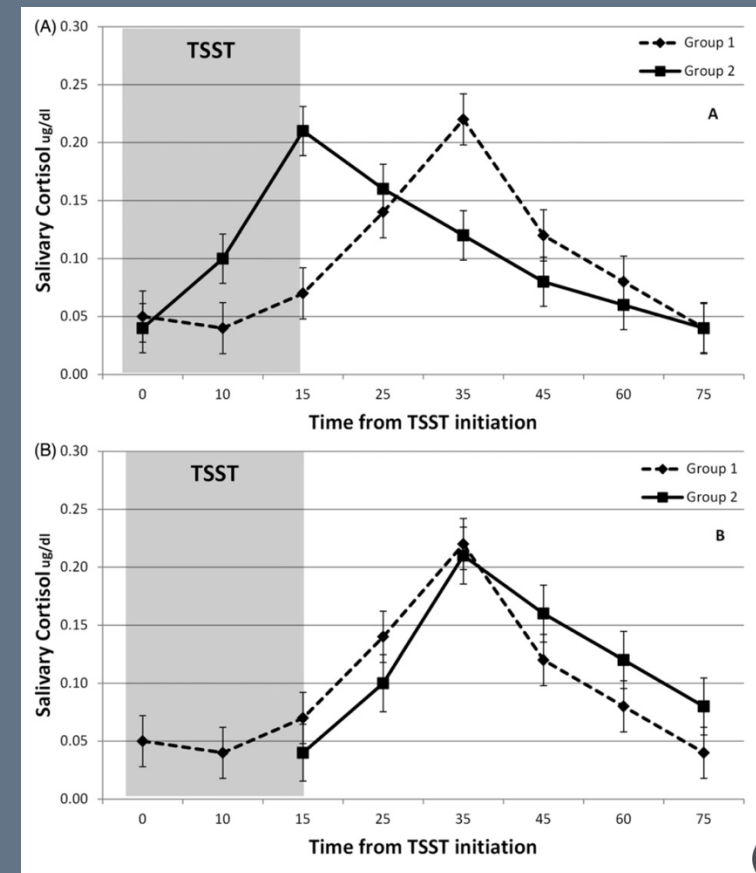
$$\begin{aligned} y &= \beta_{01} + \beta_1 x & \text{for } x \leq 2 \\ y &= \beta_{02} + \beta_2 x & \text{for } x \geq 2 \end{aligned}$$

SIDE NOTE: VARIED CHANGE POINTS

- Is **person-specific timing of change point** of interest?
 - *e.g., onset of cognitive decline*
- Increase model flexibility (fit)
- Change point in random effects structure?
 - Bayesian approach (Brilleman et al., 2017, Epidemiology)
- What if both location *and* number of change points is unknown?

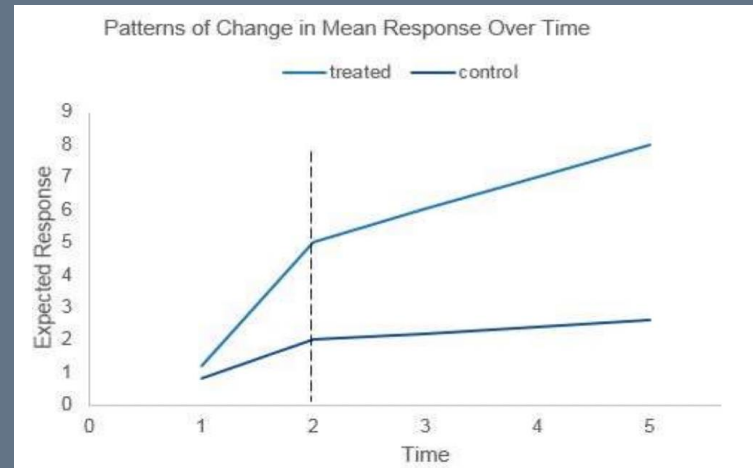
SIDE NOTE: VARIED CHANGE POINTS / LANDMARK REGISTRATION

- Control for individual/group difference in time latency of change points
- Example: groups do not differ in reactivity or recovery after adjusting for timing differences



THE MATH

- Continuous piecewise regression
 - 2+ equations
 - Equal at change points



$$y = \beta_{01} + \beta_1 x \quad \text{for } x \leq 0$$
$$y = \beta_{02} + \beta_2 x \quad \text{for } x \geq 0$$

$$\begin{aligned}\beta_{01} + \beta_1 * c &= \beta_{02} + \beta_2 * c \\ \beta_{01} + \beta_1 * c &= \beta_{02} + \beta_2 * c \\ \beta_{02} &= \beta_{01} + c(\beta_1 - \beta_2)\end{aligned}$$

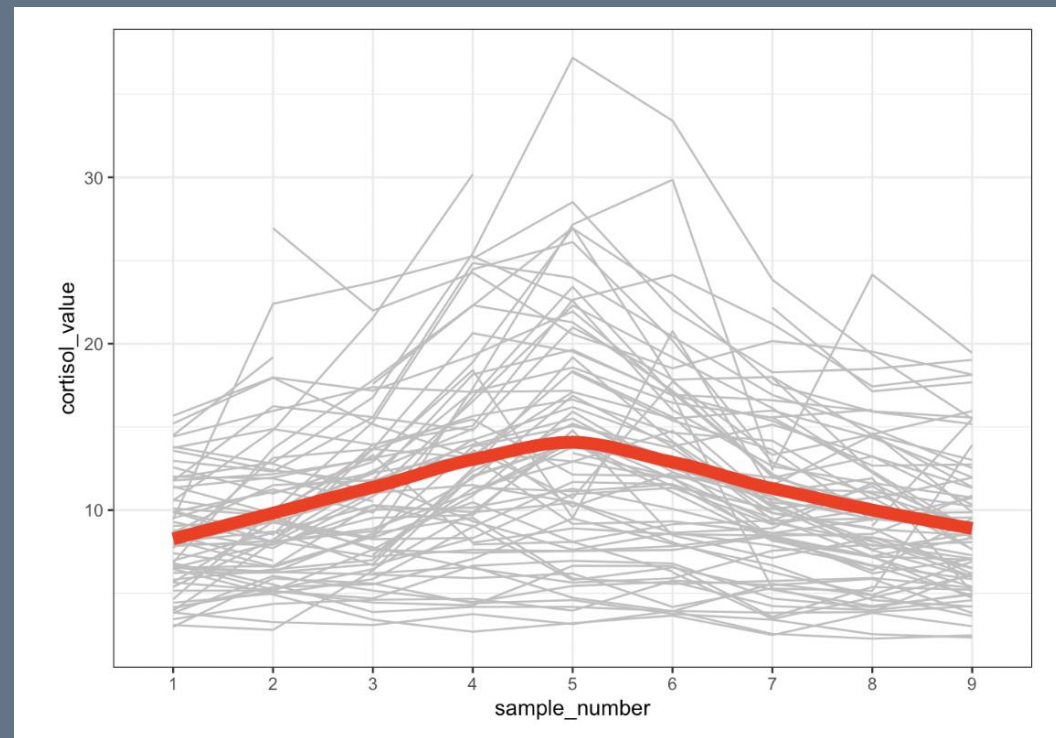
THE MATH

$$y(x) = \begin{cases} \beta_0^1 + \beta_1^1(x - b_1) + e^1 & b_1 \leq x \leq b_2 \\ \beta_0^2 + \beta_1^2(x - b_2) + e^2 & b_2 < x \leq b_3 \\ \vdots & \vdots \\ \beta_0^{n-1} + \beta_1^{n-1}(x - b_{n-1}) + e^{n-1} & b_{n-1} < x \leq b_n \end{cases}$$

- $b_1 = x$ location of first break
- $b_2 = x$ location of second break point
- $b_n = x$ location of n^{th} break point

PIECEWISE LMEMS

EXAMPLE



EXAMPLE: DATA

Dummy Code Contrast

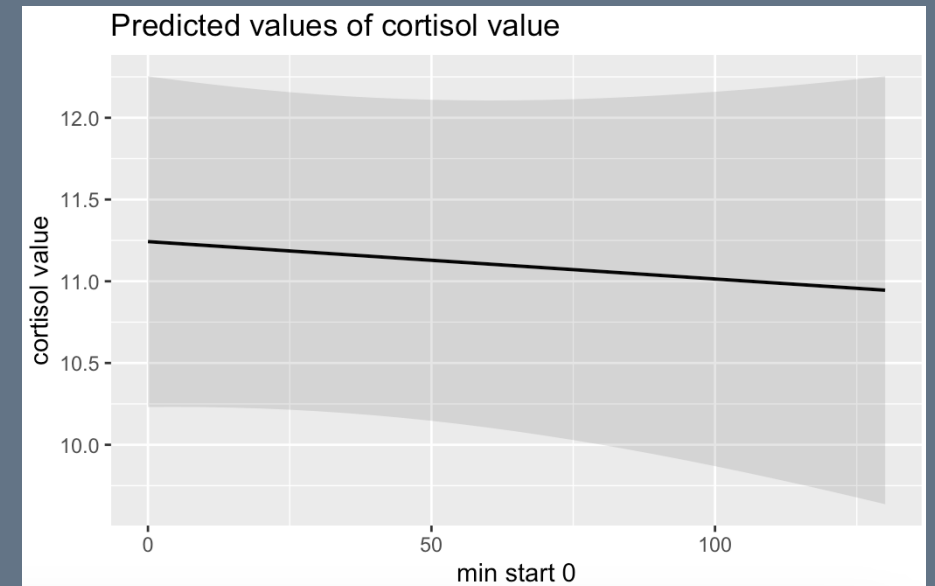
- $x_{i2} = 0$ for $x_{i1} < k$
- $x_{i2} = 1$ for $x_{i1} > k$

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 (x_{i1} - k) x_{i2} + \epsilon_i$$

subid	sample_num	time_to_peak_mean	reac	recov	cortisol_value
1001	1	-48	-48	0	15.2
1001	2	-26	-26	0	17.95
1001	3	-18	-18	0	15.16
1001	4	-11	-11	0	13.19
1001	5	0	0	0	9.17
1001	6	11	0	11	9.32
1001	7	22	0	22	8.62
1001	8	33	0	33	9.44
1001	9	65	0	65	10.73
1002	1	-48	-48	0	6.62
1002	2	-26	-26	0	6.28
1002	3	-18	-18	0	6.13
1002	4	-11	-11	0	5.91
1002	5	0	0	0	6.19
1002	6	11	0	11	4.18
1002	7	22	0	22	5.31
1002	8	33	0	33	3.9
1002	9	65	0	65	6.23
1003	1	-48	-48	0	10.57
1003	2	-26	-26	0	14.79
1003	3	-18	-18	0	21.55
1003	4	-11	-11	0	30.18
1003	5	0	0	0	NA
1003	6	11	0	11	25.32
1003	7	22	0	22	NA
1003	8	33	0	33	14.65
1003	9	65	0	65	9.88
1004	1	-48	-48	0	9.04

EXAMPLE: MODEL

- Linear growth (not piecewise):
`lmer(cortisol ~ time + (1 + time | subid), data)`

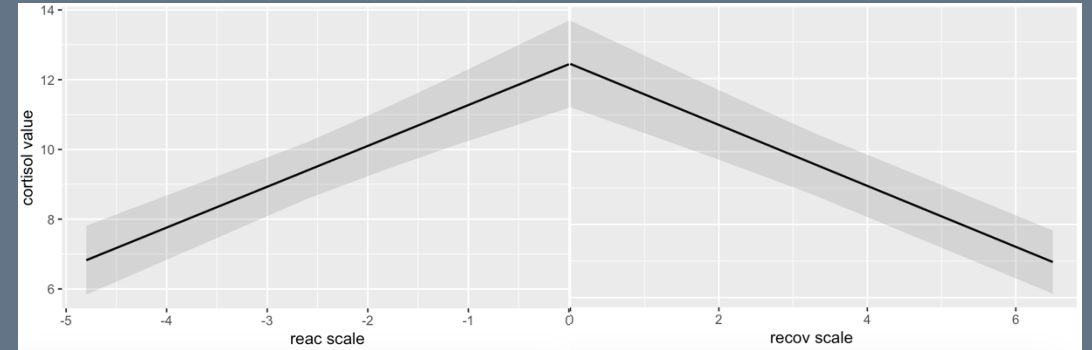


EXAMPLE: MODEL

- Piecewise linear growth:

`lmer(cortisol ~ time1 + time2 + (1 + time1 + time2 | subid), data)`

`= lmer(cortisol ~ reac + recov + (1 + reac + recov | subid), data)`



Level-1: $Cort_{ij} = \beta_{0j} + \beta_{1j}reac_{ij} + \beta_{2j}recov_{ij} + \epsilon_{ij}$

Level-2:

$$\beta_{0j} = \gamma_{00} + e_{0j}$$

= group avg peak cortisol

$$\beta_{1j} = \gamma_{10} + e_{1j}$$

= effect of reactivity on cortisol

$$\beta_{2j} = \gamma_{20} + e_{2j}$$

= effect of recovery on cortisol

$$Cort_{ij} = \gamma_{00} + e_{0j} + (\gamma_{10} + e_{1j}) * reac_{ij} + (\gamma_{20} + e_{2j}) * recov_{ij} + \epsilon_{ij}$$

by-subj random intercept

by-subj random slopes

residual error

Model: $\text{lmer}(\text{cortisol} \sim \text{reac} + \text{recov} + (1 + \text{reac} + \text{recov} \mid \text{subid}), \text{data})$

EXAMPLE: OUTPUT

- Random Effects:
 - int: betw-subj variance in average peak cortisol
 - reac: betw-subj variance of reactivity slope
 - recov: betw-subj variance of recovery slope
- Fixed Effects:
 - int: average cortisol at peak
 - reac: slope of increase in cort before peak
 - recov: slope of decrease in cort after peak

REML criterion at convergence: 3323.8

Scaled residuals:

Min	1Q	Median	3Q	Max
-3.2765	-0.4739	-0.0076	0.4554	3.4436

Random effects:

Groups	Name	Variance	Std.Dev.	Corr
subid	(Intercept)	40.0834	6.3311	
	reac_scale	1.6474	1.2835	0.84
	recov_scale	0.4604	0.6786	-0.86 -0.85
	Residual	5.7301	2.3938	

Number of obs: 639, groups: subid, 77

Fixed effects:

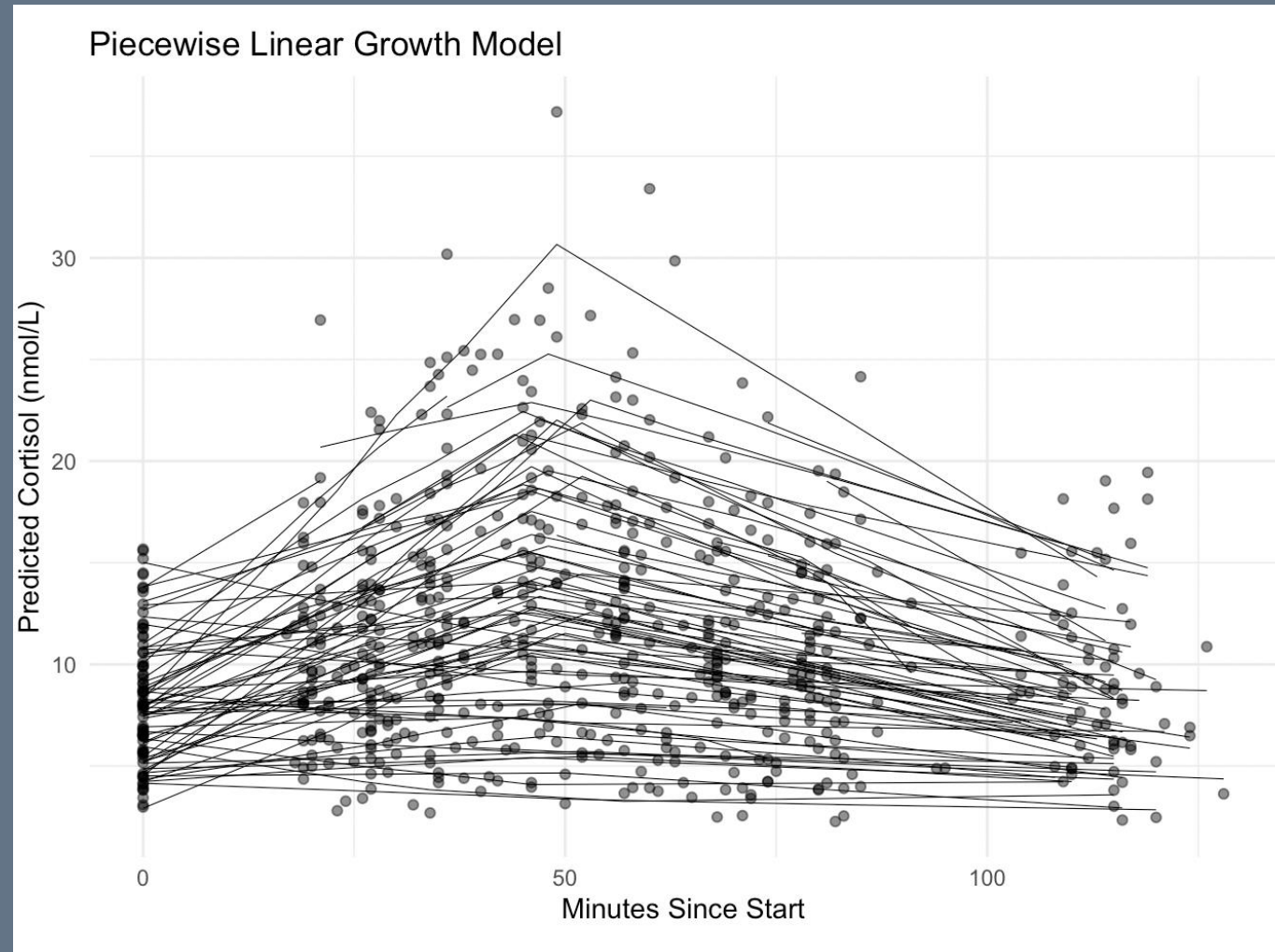
	Estimate	Std. Error	df	t value	Pr(> t)
(Intercept)	13.6996	0.7409	75.1920	18.489	< 2e-16 ***
reac_scale	1.1708	0.1632	74.6427	7.176	4.43e-10 ***
recov_scale	-0.8349	0.0931	74.8453	-8.968	1.75e-13 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:

	(Intr)	rc_scl
reac_scale	0.803	
recov_scale	-0.783	-0.753

EXAMPLE



MORE COMPLEX MODELS

- How does each piece relate to other variables?
 - *e.g., do those with higher life stress recover more slowly from acute stress?*

MORE COMPLEX MODELS: MATH

Q: does lifetime stress moderate cortisol reactivity and/or recovery from acute stress?

Level-1: $Cort_{ij} = \beta_{0j} + \beta_{1j}reac_{ij} + \beta_{2j}recov_{ij} + \epsilon_{ij}$

Level-2:

$$\beta_{0j} = \gamma_{00} + \gamma_{01}stress_j + e_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11}stress_j + e_{1j}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}stress_j + e_{2j}$$

γ_{00} : group avg peak cortisol and

γ_{01} : main effect of stress on cortisol (peak)

γ_{10} : main effect of reactivity on cortisol and

γ_{11} : interaction between reac and stress

γ_{20} : main effect of recovery on cortisol and

γ_{21} : interaction between recov and stress

$$Cort_{ij} = \gamma_{00} + \gamma_{01}stress_j + e_{0j} + (\gamma_{10} + \gamma_{11}stress_j + e_{1j}) * reac_{ij} + (\gamma_{20} + \gamma_{21}stress_j + e_{2j}) * recov_{ij} + \epsilon_{ij}$$

by-subj random intercept

by-subj random slopes

residual error

MORE COMPLEX MODELS: R

```
lmer(cortisol ~ reac*stress + recov*stress + (1 + reac + recov | id))
```

Random effects:

Groups	Name	Variance	Std.Dev.	Corr
subid	(Intercept)	40.6154	6.3730	
	reac_scale	1.6111	1.2693	0.84
	recov_scale	0.4541	0.6738	-0.87 -0.90
Residual		5.8873	2.4264	

Number of obs: 546, groups: subid, 66

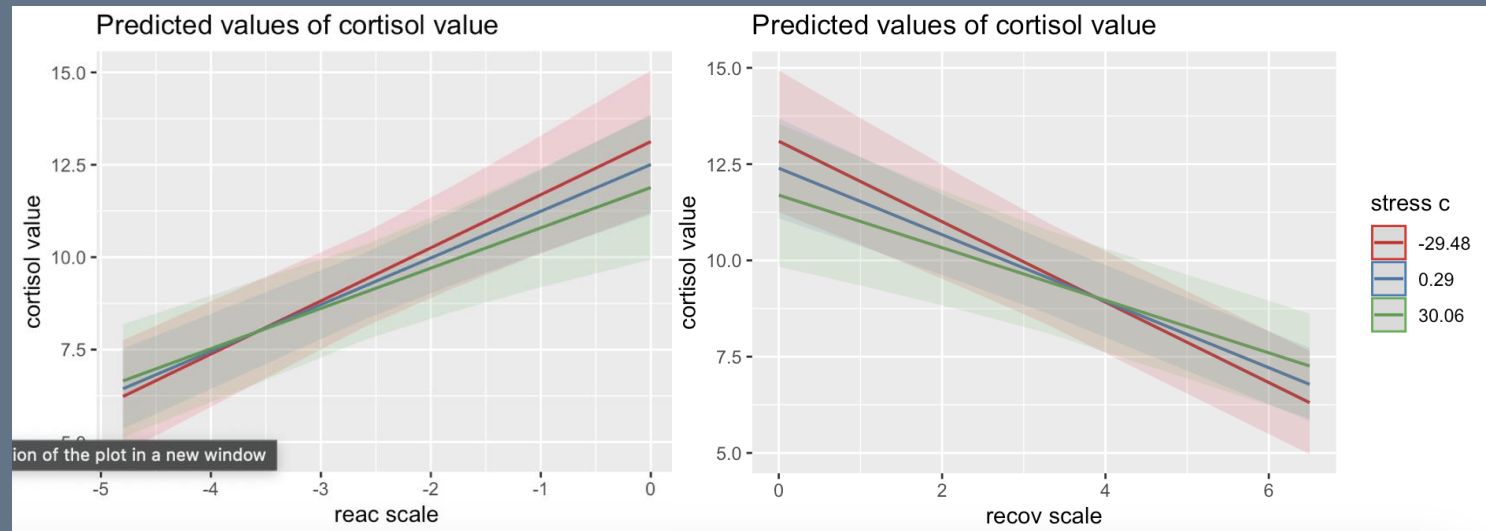
Fixed effects:

	Estimate	Std. Error	df	t value	Pr(> t)
(Intercept)	13.810321	0.805874	63.511361	17.137	< 2e-16 ***
reac_scale	1.265459	0.174957	62.199578	7.233	8.35e-10 ***
stress_c	-0.029991	0.027514	63.285098	-1.090	0.2798
recov_scale	-0.865245	0.100524	62.872620	-8.607	3.16e-12 ***
reac_scale:stress_c	-0.005826	0.005926	60.779749	-0.983	0.3294
stress_c:recov_scale	0.006075	0.003421	62.226329	1.776	0.0807 .

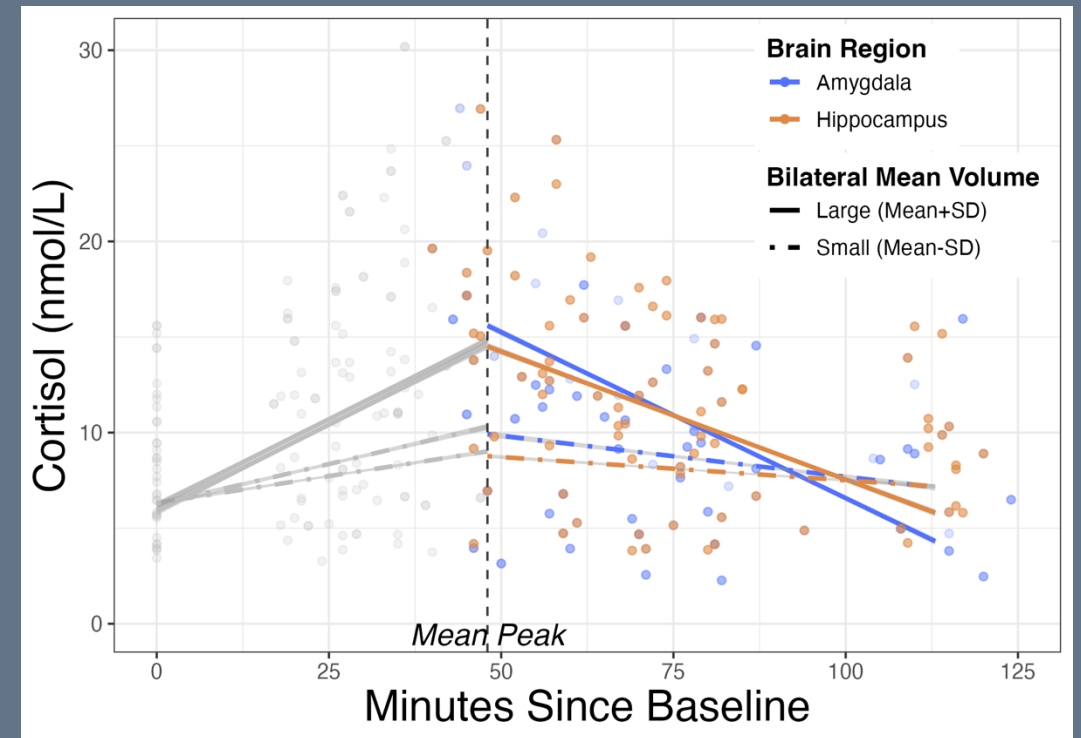
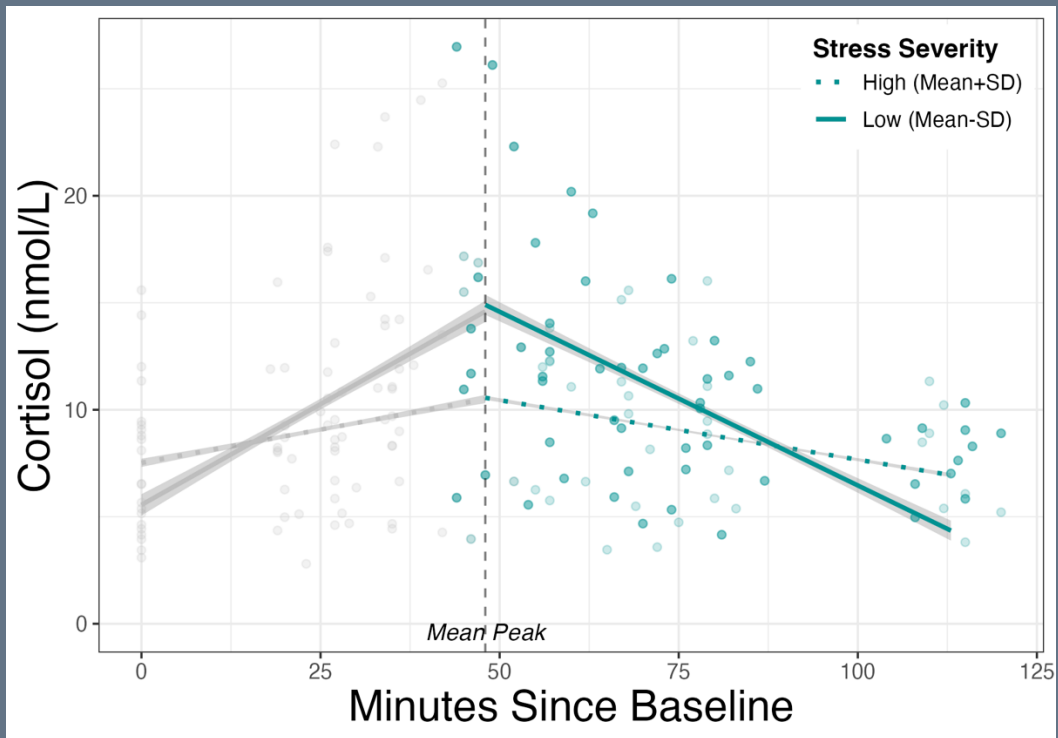
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:

	(Intr)	rc_scl	strss_	rcv_sc	rc_s:_
reac_scale	0.799				
stress_c	0.001	0.001			
recov_scale	-0.789	-0.789	-0.002		
rc_scl:str_	0.001	0.001	0.804	-0.003	
strss_c:rc_	-0.002	-0.003	-0.791	0.005	-0.795



MORE COMPLEX MODELS: VISUALS



EVEN MORE COMPLEX MODELS: R

```
lmer(cortisol_value ~  
      reac*(age + sex + race + icv + stress + amygd + hpc) +  
      recov*(age + sex + race + icv + stress + amygd + hpc) +  
      (1 + reac + recov | id))
```

Convergence... 🤪

- Scale reac/recov by a factor of 10
- Use different optimizers
- *etc.*

Psychological Methods
2018, Vol. 23, No. 3, 389–411

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1082-989X/18/\$12.00 <http://dx.doi.org/10.1037/met0000159>

Linear Mixed-Effects Models and the Analysis of Nonindependent Data:
A Unified Framework to Analyze Categorical and Continuous Independent
Variables that Vary Within-Subjects and/or Within-Items

Markus Brauer and John J. Curtin
University of Wisconsin-Madison

REMAINING QUESTIONS / FUTURE

- Piece trajectories re functional neuroimaging
 - Subject-specific slope estimates
- Significant relationships between pieces
 - e.g., is reactivity steeper than recovery?

RESOURCES

- Daniel Martin [tutorial](#) – *R code plus cool plots*
- Huang, 2015 [tutorial](#) – *in SAS but helpful mathematical explanations*
- [Penn State tutorial](#)
- Info/code on [random change points](#)

CORTISOL-SPECIFIC STUDIES (THANKS, CLAIRE!)

- Bendezú, J. J., Loughlin-Presnal, J. E., & Wadsworth, M. E. (2019). Attachment Security Moderates Effects of Uncontrollable Stress on Preadolescent Hypothalamic–Pituitary–Adrenal Axis Responses: Evidence of Regulatory Fit. *Clinical Psychological Science*, 7(6), 1355–1371. <https://doi.org/10.1177/2167702619854747>
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- Fiksdal, A., Hanlin, L., Kuras, Y., Gianferante, D., Chen, X., Thoma, M. V., & Rohleder, N. (2019). Associations between symptoms of depression and anxiety and cortisol responses to and recovery from acute stress. *Psychoneuroendocrinology*, 102, 44–52. <https://doi.org/10.1016/j.psyneuen.2018.11.035>
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- Ji, J., Negri, S., Kim, H., & Susman, E. J. (2016). A study of cortisol reactivity and recovery among young adolescents: Heterogeneity and longitudinal stability and change. *Developmental Psychobiology*, 58(3), 283–302. <https://doi.org/10.1002/dev.21369>
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