Small study design: How to distinguish the signal from the noise

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WORKSHOP ON INNOVATIVE STUDY DESIGNS AND METHODS FOR DEVELOPING, TESTING AND IMPLEMENTING BEHAVIORAL INTERVENTIONS TO IMPROVE HEALTH

APRIL 2 - 3, 2014
6701 ROCKLEDGE DRIVE (ROCKLEDGE 2), ROOM 3087/3091
BETHESDA, MD 20892

Linear Mixed Effect (LME) or Multilevel (ML) Models for Repeated Measures (Laird & Ware, 1982; Bryk & Raudenbush, 1992)

Cushing, C. C., Walters, R. W., & Hoffman, L. (2013). Aggregated N-of-1 randomized controlled trials: Modern data analytics applied to a clinically valid method of intervention effectiveness. *Journal of Pediatric Psychology*, jst083.

Ferron, J. M., Bell, B. A., Hess, M. R., Rendina-Gobioff, G., & Hibbard, S. T. (2009). Making treatment effect inferences from multiple-baseline data: The utility of multilevel modeling approaches. *Behavior Research Methods, 41*(2), 372-384.

Ridenour, T. A., Pineo, T. Z., Molina, M. M. M., & Lich, K. H. (2013). Toward rigorous idiographic research in prevention science: Comparison between three analytic strategies for testing preventive intervention in very small samples. *Prevention science, 14*(3), 267-278.

Shadish, W. R., Kyse, E. N., & Rindskopf, D. M. (2013). Analyzing data from single-case designs using multilevel models: New applications and some agenda items for future research. *Psychological Methods, 18*(3), 385-405. doi: 10.1037/a0032964

LME models and very small N

Multilevel models points from the literature, so far only Ferron et al. 2009, 2010

- Estimate fixed treatment effects
  - Fixed effects were estimated without bias even when the sample size was as small as 4 cases and the series of repeated measurement varied from 10 to 30 (Ferron et al. 2009, 2010)

Contingency management pilot study

- Multiple-baseline single-case design (SCD)
- The cohorts consisted of 12 teens in two groups
- Each teen designated a parent or caregiver that was also enrolled
- All teens received contingency management (CM)
- The caregivers in Cohort 1 did not receive CM. They received praise instead

Treatments conditions and expected outcomes

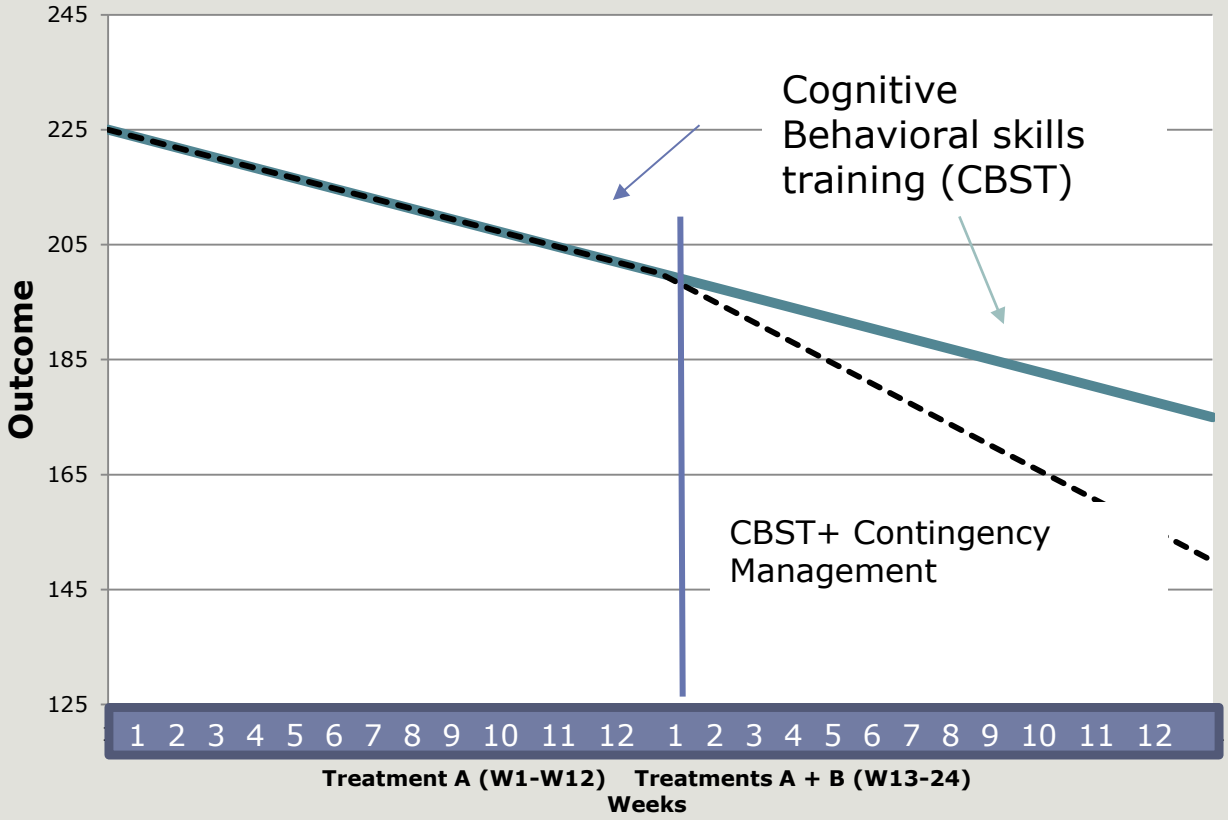


Figure 1. Expected outcomes in multiple-point baseline design

Linear piecewise regression

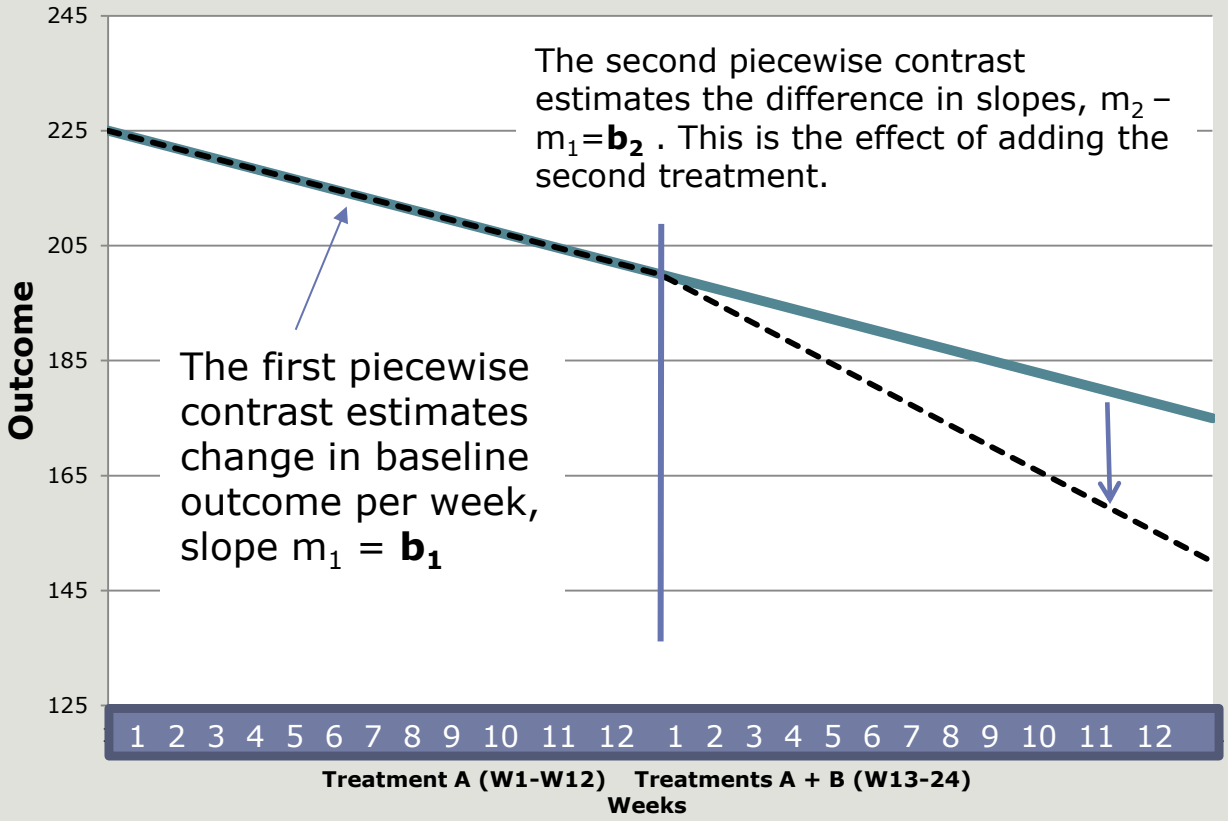


Figure 1. Expected outcomes in multiple-point baseline design

Linear piecewise equation

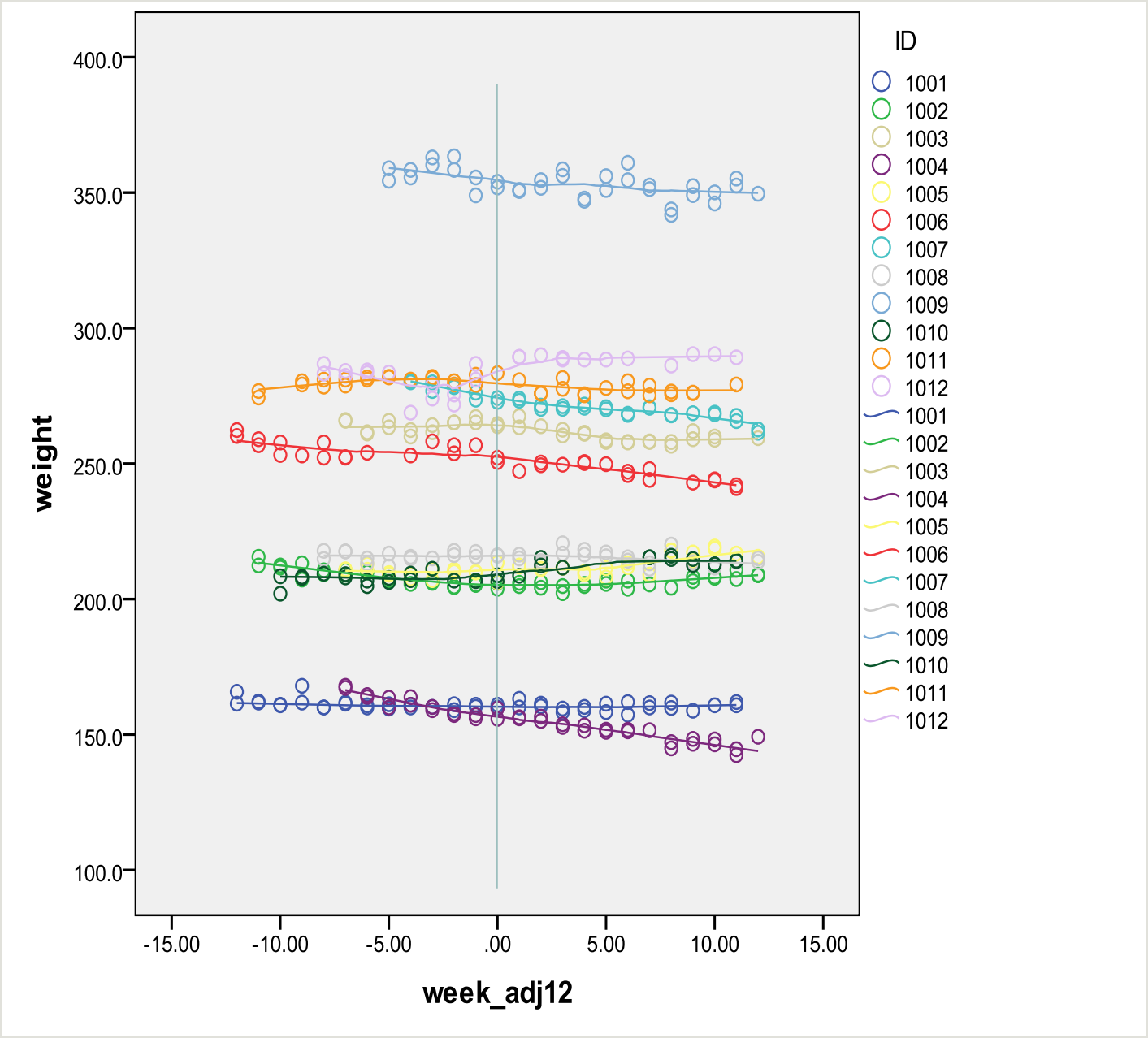
$$y_t = a + b_1 X_t + b_2 (X_t * T_t) + e_t$$

Where y_t is the outcome for a given participant at Week t, a is a constant (=1), X_i is intervention week centered at the start of CM and $X_t * T_t$ is the week by Treatment interaction.

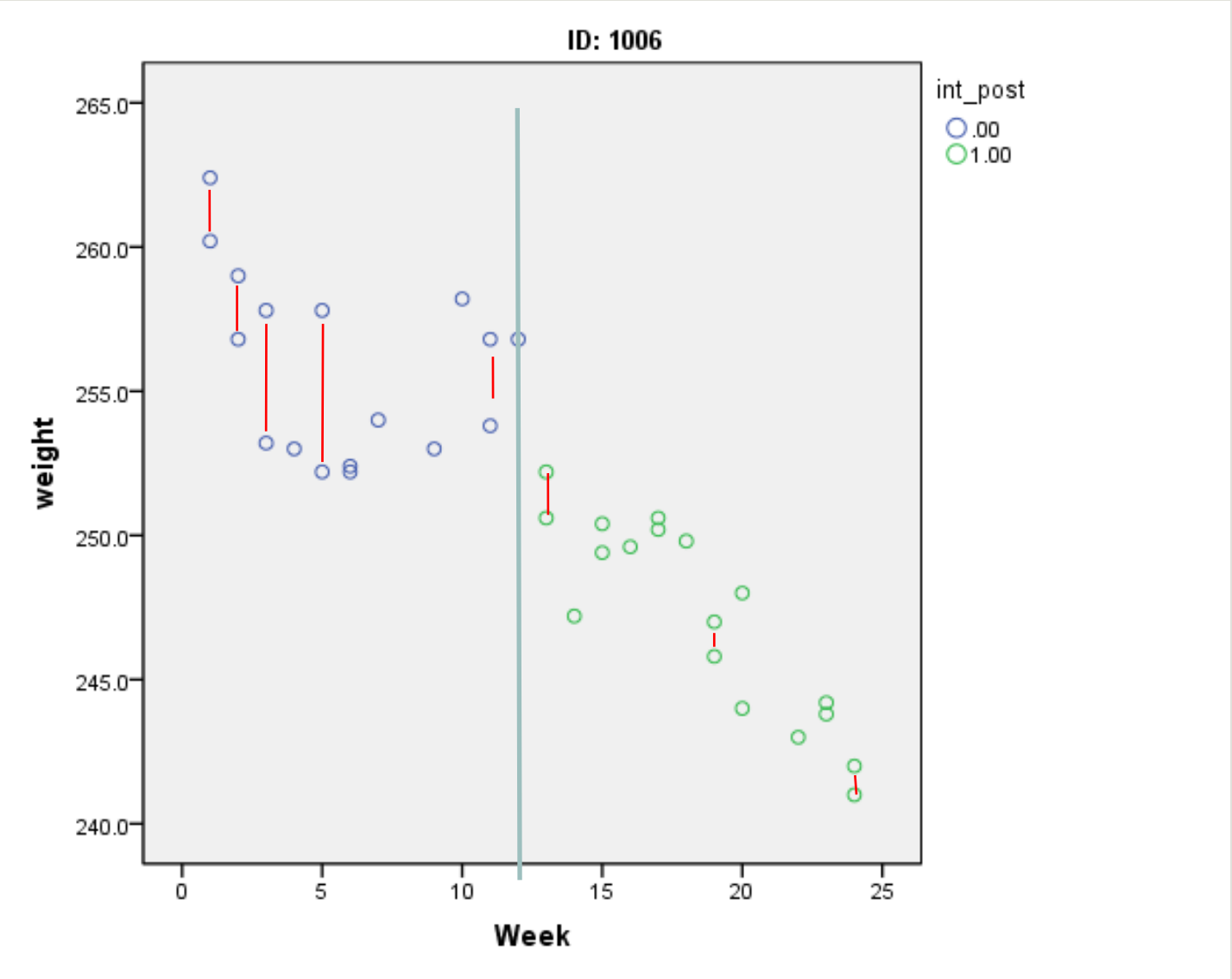
Note that T (A vs. A+B), treatment variable, is not in the equation. The omission of T forces the lines to meet at phase juncture. Inclusion of T would allow a discontinuity at the start of the post baseline follow-up

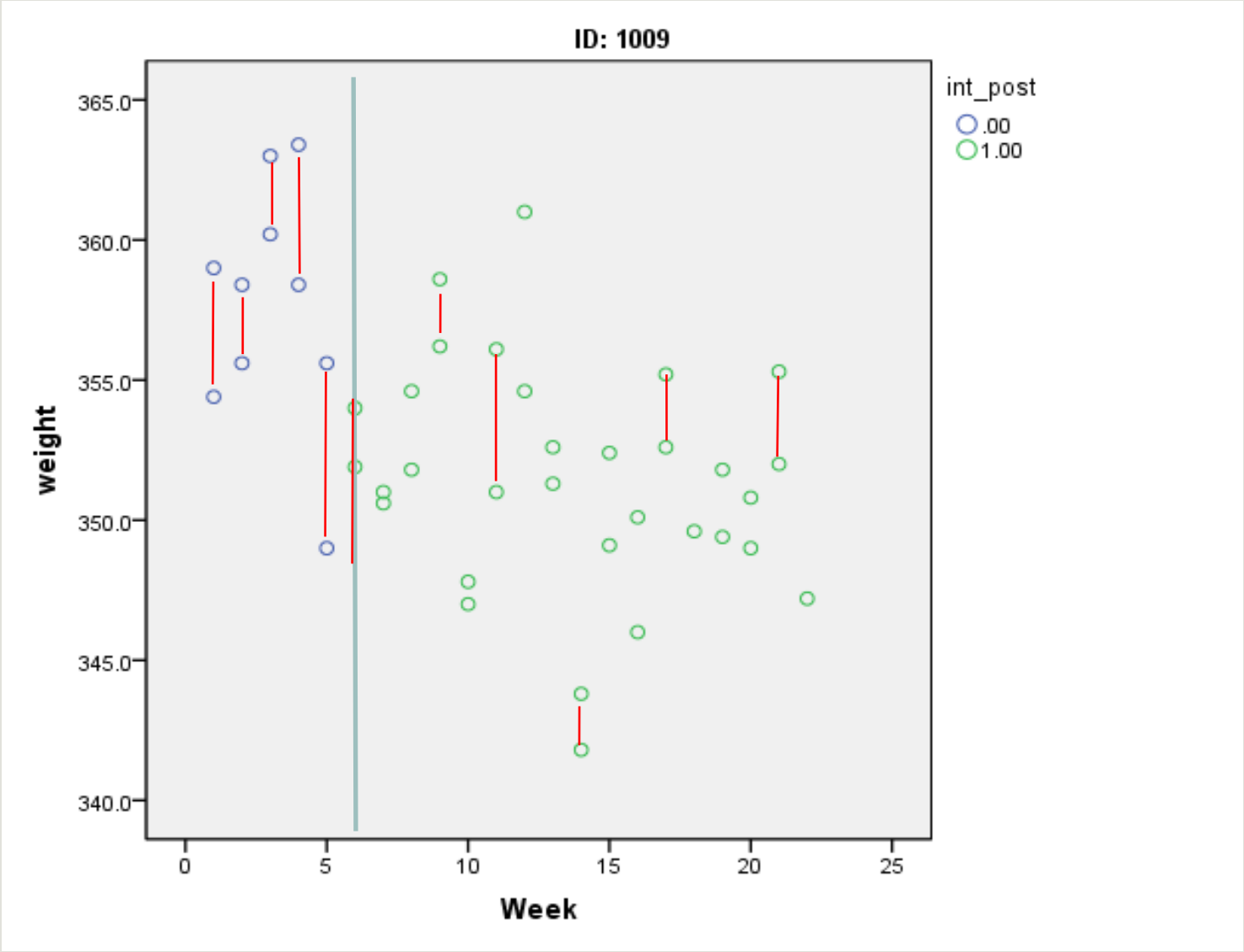
Contingency management pilot study

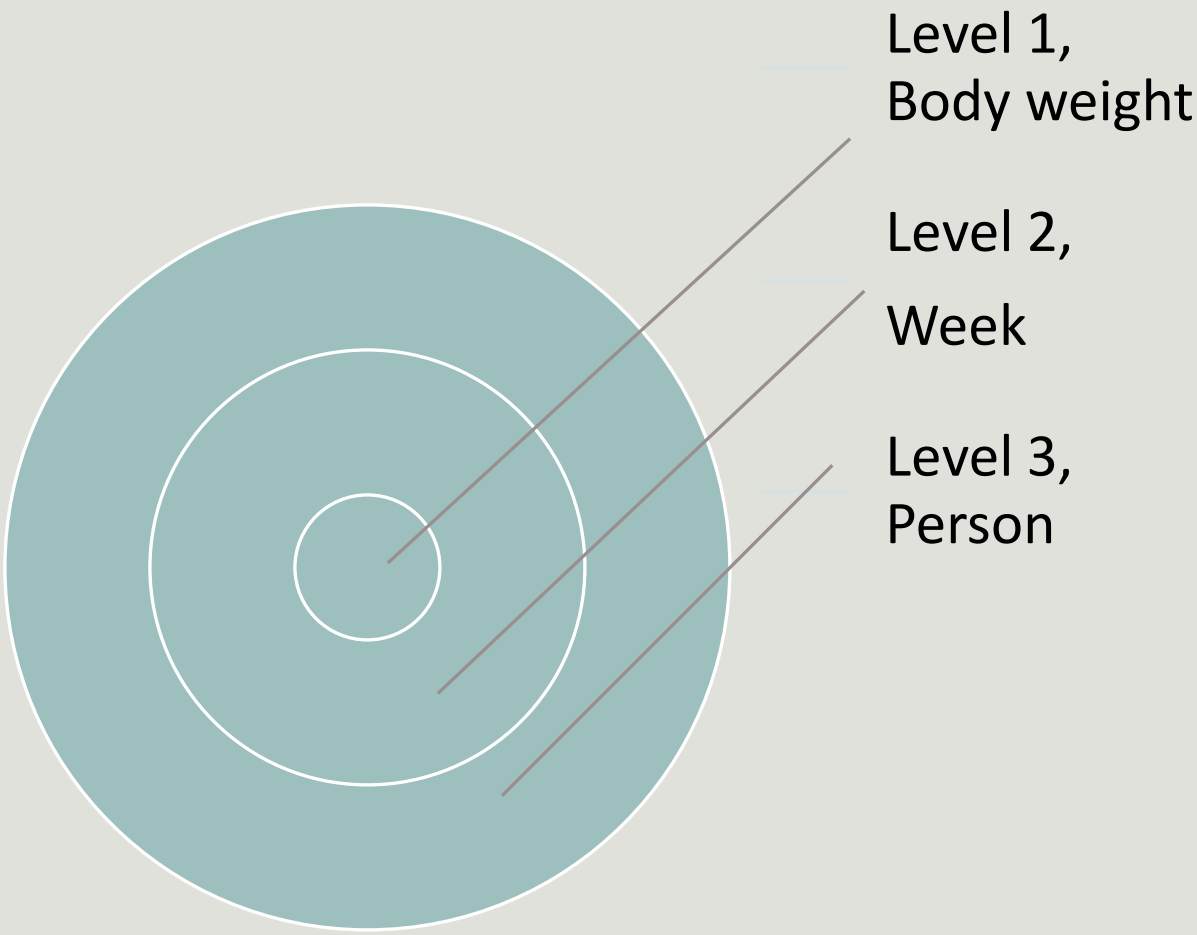
In addition to the primary hypothesis that weight loss would increase after introducing CM, we were also interested in differences in outcome due the Caregiver-Praise vs. Caregiver-CM condition, i.e., Cohort 1 vs. Cohort 2.



Id = 1006 in red is shown on the next slide

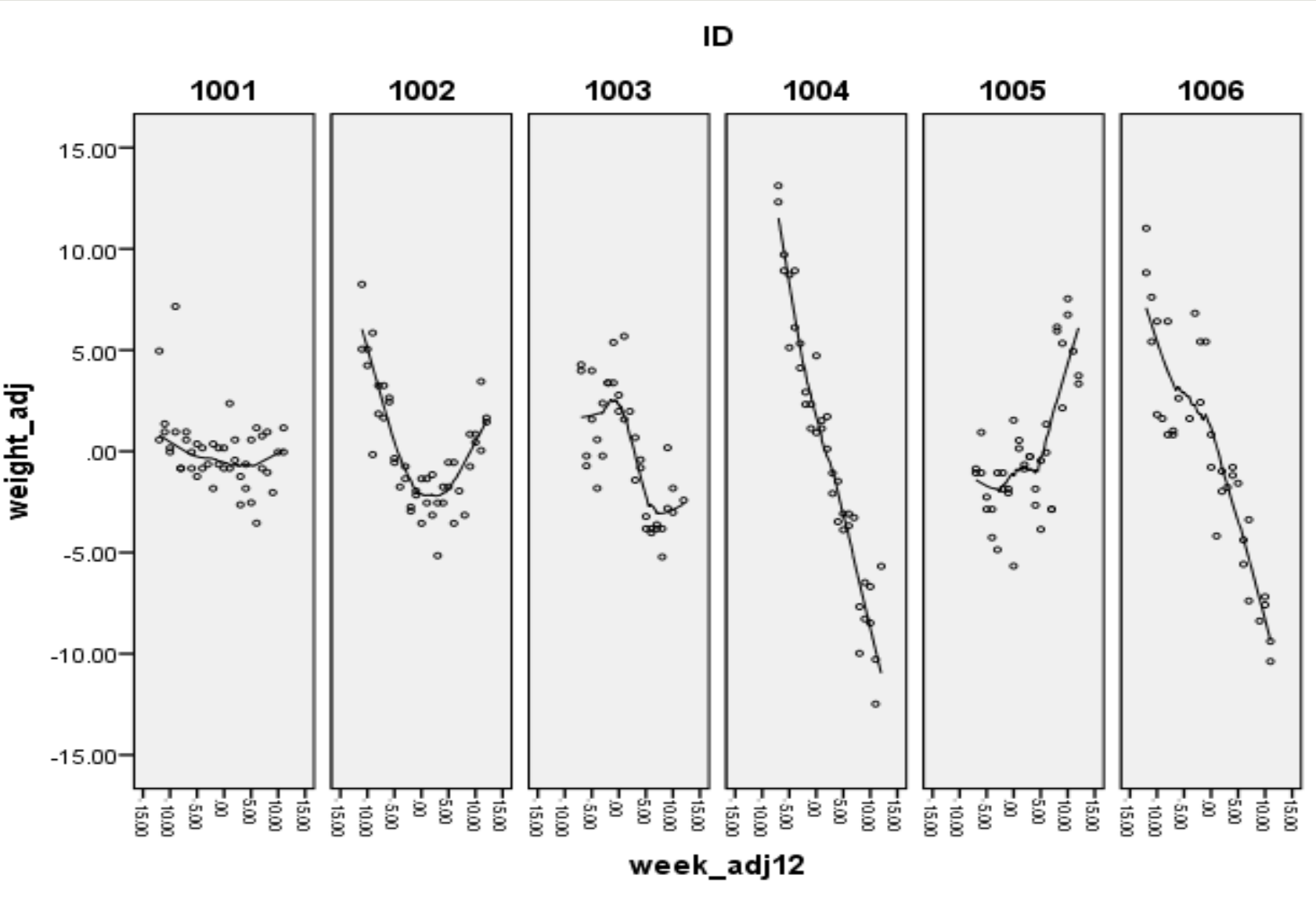

ID: 1006
int_post
.00
1.00
weight
265.0
260.0
255.0
250.0
245.0
240.0
0
5
10
15
20
25
Week


ID: 1009
int_post
.00
1.00
weight
365.0
360.0
355.0
350.0
345.0
340.0
0
5
10
15
20
25
Week

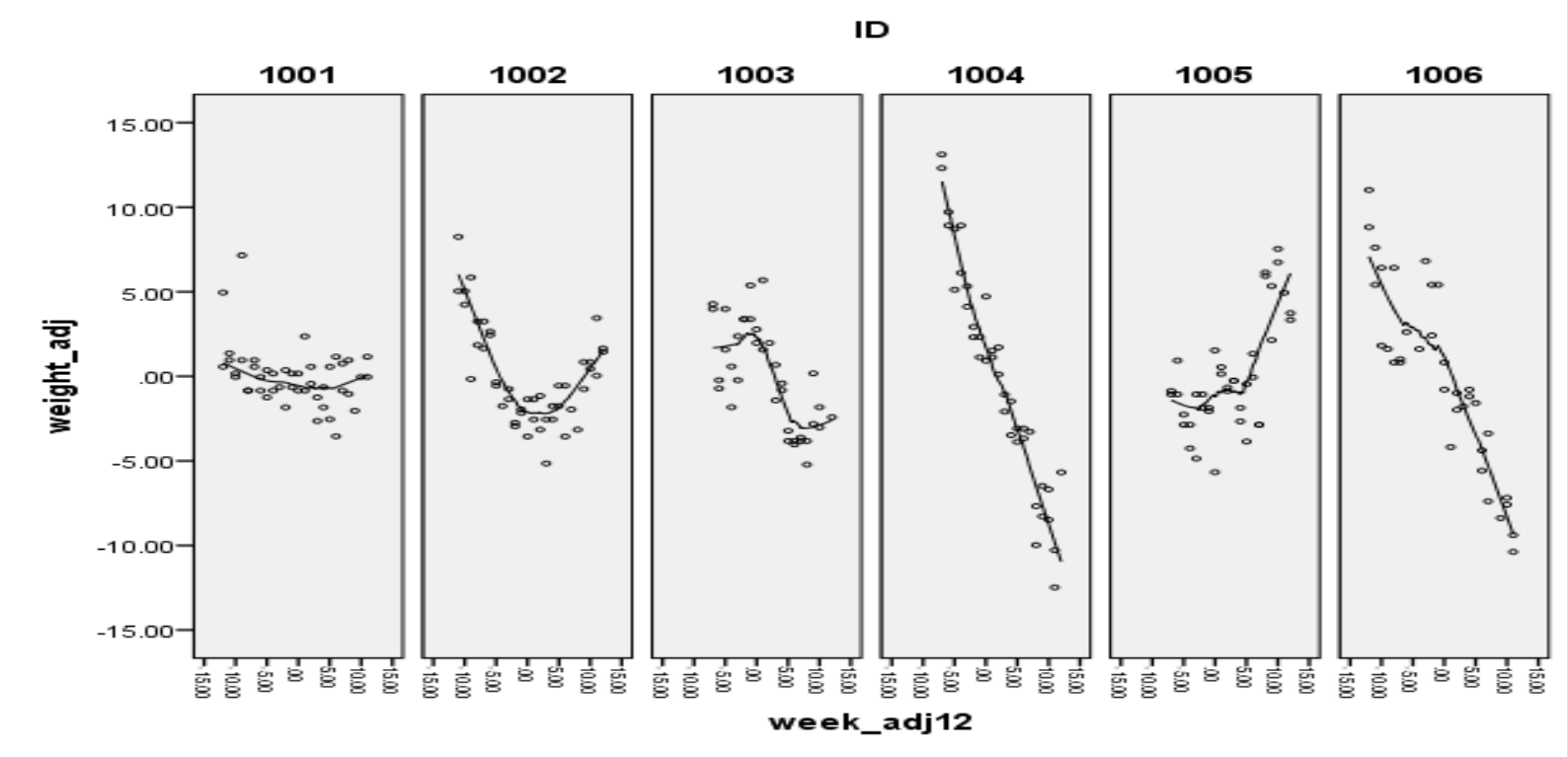

Level 1,
Body weight
Level 2,
Week
Level 3,
Person

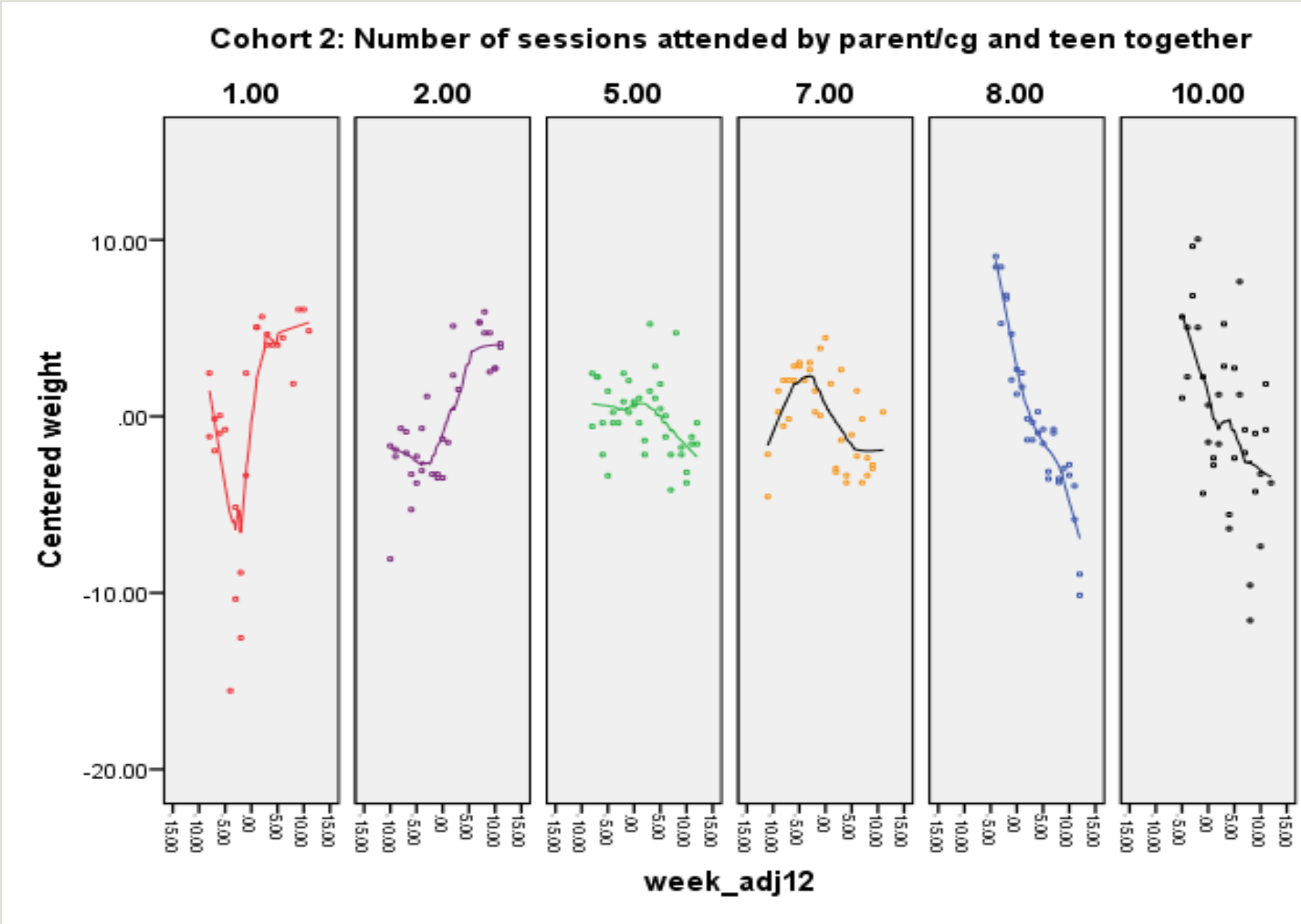
Estimates of Covariance Parameters[a]			
Parameter		Estimate	Std. Error
Residual (observations within weeks)		2.76	.27
Intercept [subject = Week * ID] (time)	Variance	16.58	1.64
Intercept [subject = ID] (individuals)	Variance	3162.32	1348.77
a. Dependent Variable: weight.			

Lesson: The twice weekly weights appears to contribute very little to the overall variability in the data, yet if you look at the individual scatter plots you can that slopes will move around depending on what weekly weights was used.

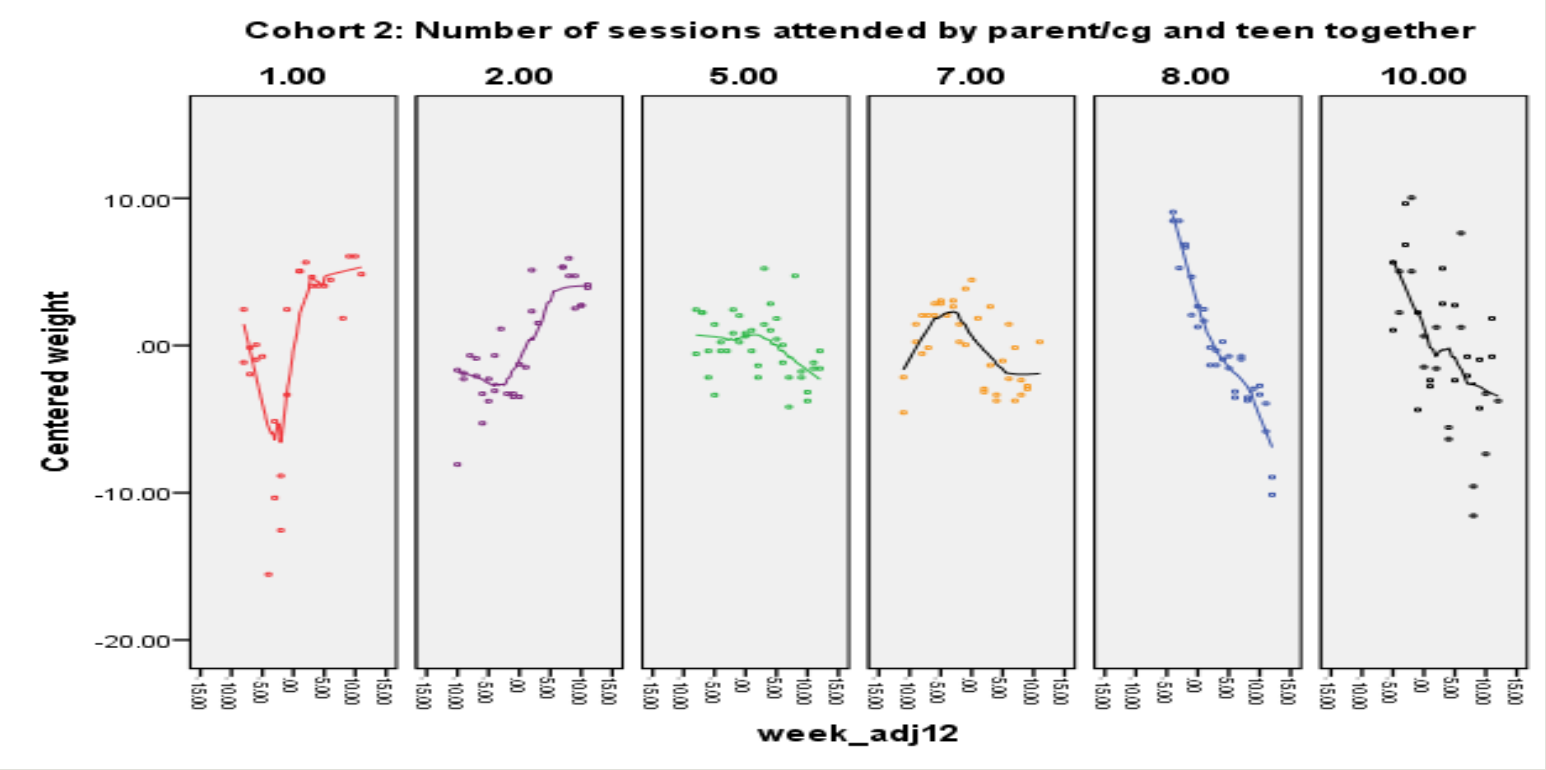

ID
1001
1002
1003
1004
1005
1006
weight_adj
15.00
10.00
5.00
.00
-5.00
-10.00
-15.00
week_adj12

Cohort 1 (parent praise) only the baseline trend was significant (b = -.25, p < .05), indicating that participants lost .25 pounds per week due to cognitive behavioral skills training during the baseline interval. Panels are arranged by number of sessions that teen and parent/cg attended together.




Cohort 2: Number of sessions attended by parent/cg and teen together
1.00
2.00
5.00
7.00
8.00
10.00
Centered weight
10.00
.00
-10.00
-20.00
15.00
10.00
5.00
.00
5.00
10.00
15.00
week_adj12

Cohort 2 (CM for parent/cg+teen) There was a significant drop in weight over the post-baseline interval but this depended on the number of sessions that parents/cg attended together. Panels are arranged by number of sessions that teen and parent/cg attended together. The estimated weight loss due to CM was 1.15 pounds per week.



Thank you

QUESTIONS?

Discussion Points

AS TIME PERMITS

STRONG FEATURES OF DESIGNS THAT HAVE A WITHIN-PERSON TREATMENT FACTOR

A NEW KIND OF DESIGN OR DIFFERENT ANALYSES OF THE SINGLE CASE DESIGN?

AGGREGATION: HOW DOES IT WORK?

Matyas, T. A., & Greenwood, K. M. (1990). Visual analysis of single-case time series: effects of variability, serial dependence, and magnitude of intervention effects. *Journal of Applied Behavior Analysis, 23(3), 341-351.*

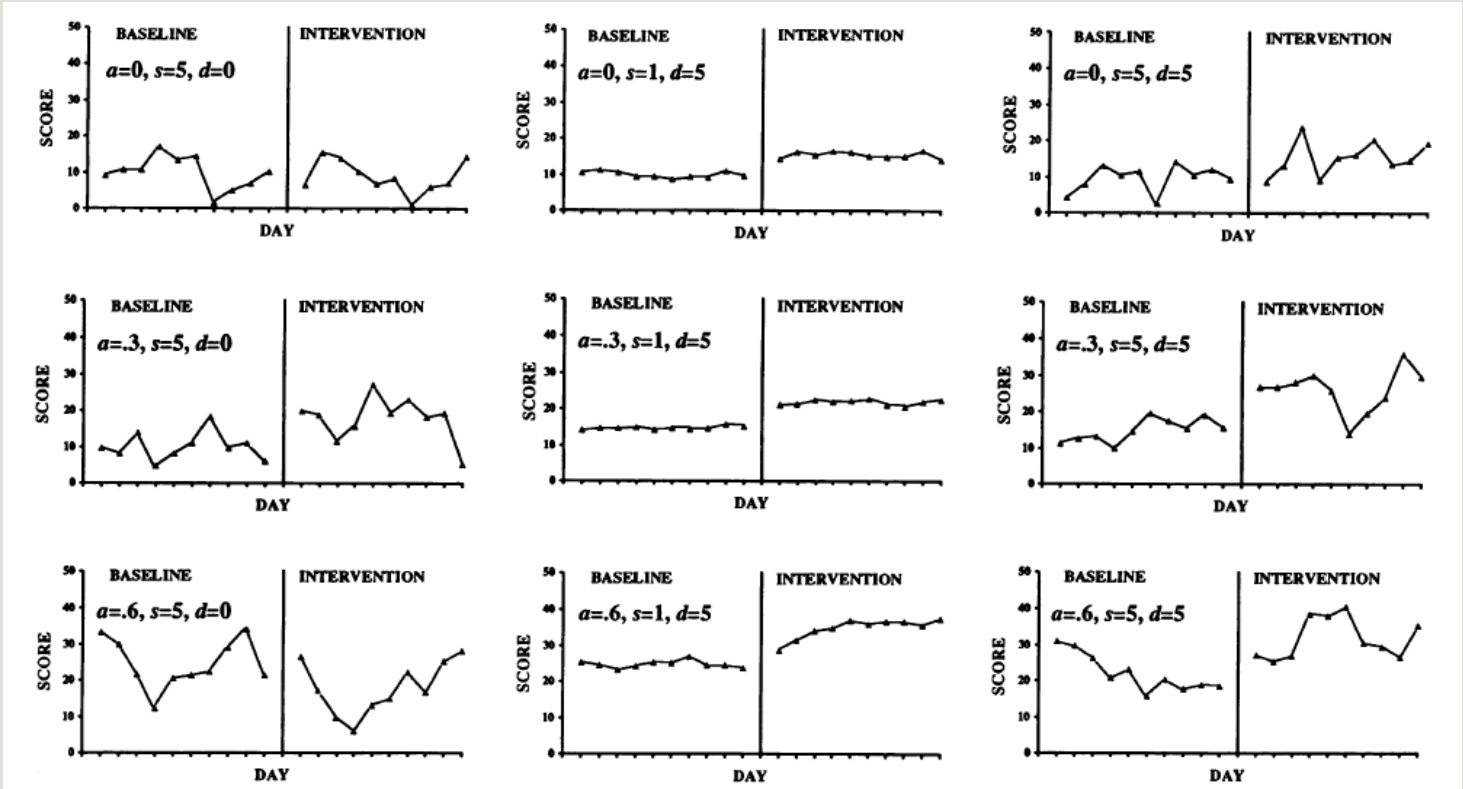
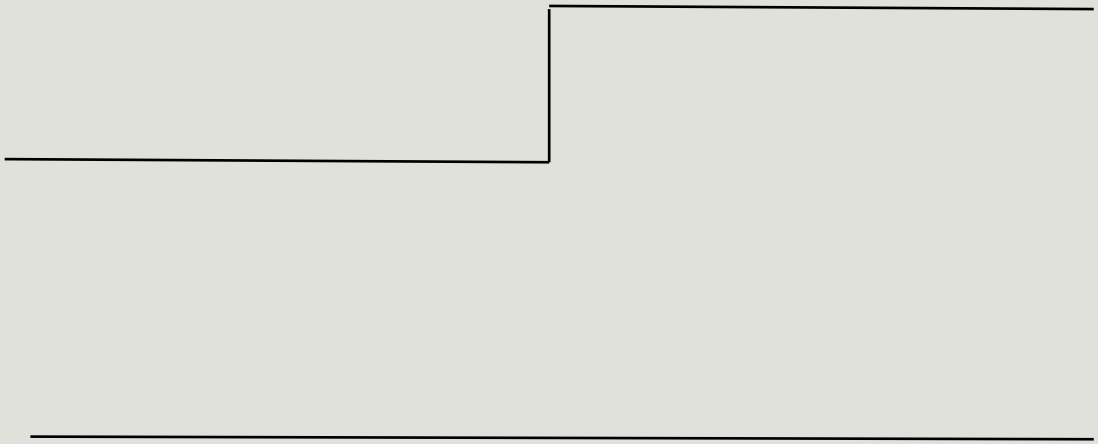
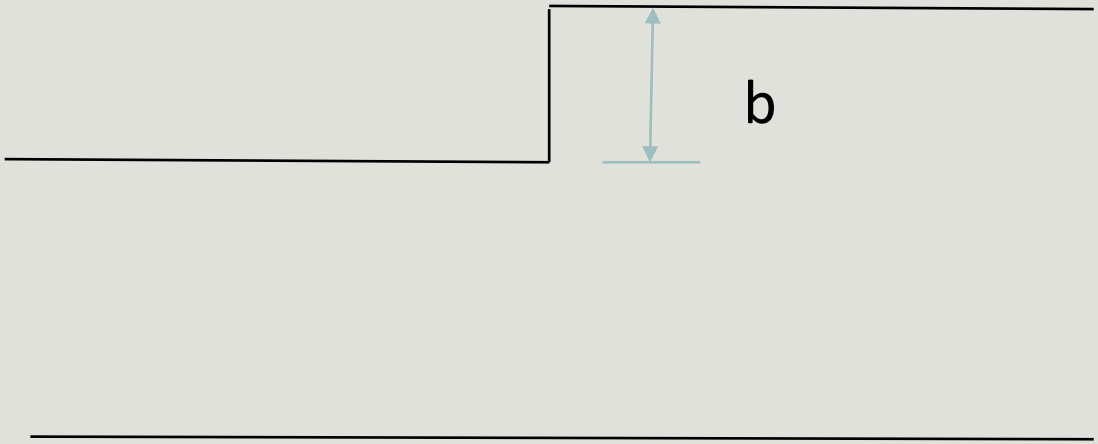


Figure 1. Nine of the AB panels used as stimuli. Information about the statistical properties (a = amount of serial dependence, s = random variability, d = magnitude of intervention effect) has been superimposed on each graph and was not presented to subjects. Subjects were instructed that the ordinate represented the client's response score, but the precise response was not described.



LIMITATIONS AND CHALLENGES OF LME MODELING OF SCD


b

Subject specific design matrix

Design Matrix Codes: The coded variables are shown in Table 1. T_i is coded 0 for Treatment A and 1 for Treatment A+B. X_i is coded 0 at the start of the A+B intervention; it is numbered consecutively forward and backward from that point.

Note: because LME modeling allows each person to have their own design matrix, the design allows a different number of trials for each participant.

Table 1. Design Matrix: Linear Piecewise Regression, 5 baseline and 6 treatment sessions

Tx	T	Week	X	X*T
A	0	1	-5	0
A	0	2	-4	0
A	0	3	-3	0
A	0	4	-2	0
A	0	5	-1	0
A+B	1	6	0	0
A+B	1	7	1	1
A+B	1	8	2	2
A+B	1	9	3	3
A+B	1	10	4	4
A+B	1	11	5	5

Subject specific design matrix

Design Matrix: Linear Piecewise Regression, 3 baseline and 3 treatment sessions				
Tx	T	Week	X	X*T
A	0	1	-3	0
A	0	2	-2	0
A	0	3	-1	0
A+B	1	4	0	0
A+B	1	5	1	1
A+B	1	6	2	2

Efficacy trajectory with treatment exposure heterogeneity

The efficacy trajectory, dotted line, is the trajectory expected when all treatments are received. The red trajectory shows the drop in weight for due to A alone or A+B depending on if treatment was received as intended or not.

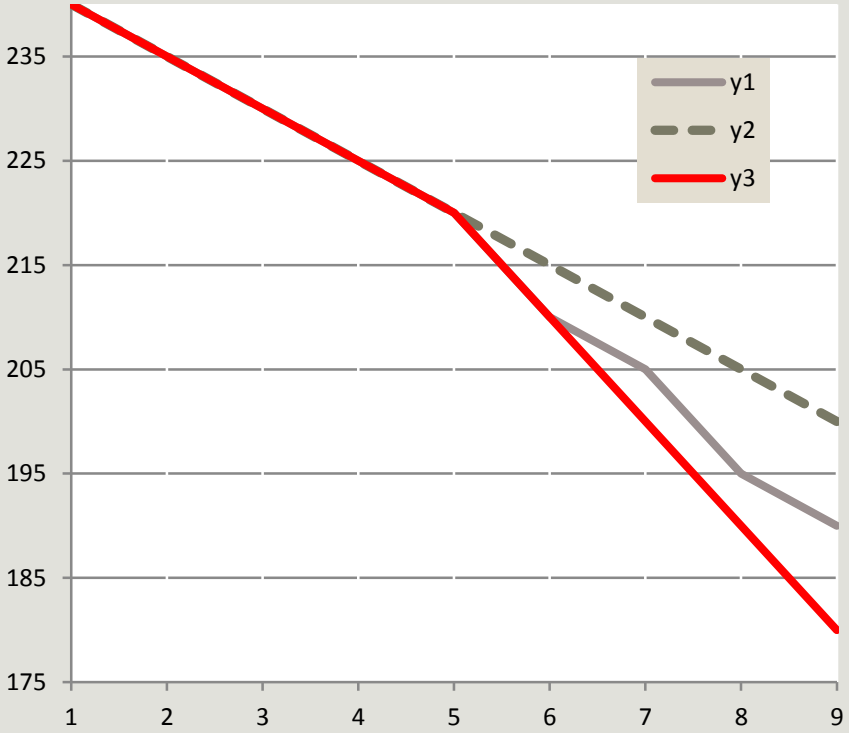


Figure 2. Predicted A+B treatment trajectory with partial adherence (dose), red line = y1.

$$y_{hi} = a + b_1 X_{hi} + b_2 U_{hi} + e_{hi}$$

Table 2.Coding U_h for participants noncompliant at Sessions 2 and 4.

Treatment	Week	a	X	S#	Adherence	T	X*T	U	y1	y2	y3
A	1	1	-4		0	0	0	0	240	240	240
A	2	1	-3		0	0	0	0	235	235	235
A	3	1	-2		0	0	0	0	230	230	230
A	4	1	-1		0	0	0	0	225	225	225
A+B start	5	1	0	1	1	1	0	0	220	220	220
A+B	6	1	1	2	0	1	1	1	210	215	210
A+B	7	1	2	3	1	1	2	1	205	210	200
A+B	8	1	3	4	0	1	3	2	195	205	190
A+B	9	1	4	5	0	1	4	2	190	200	180