



Integrative Data Analysis

ICDSS COVID Scholars Network

(11.18.2022)

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Overview

- ▶ What is Integrative Data Analysis (IDA)?
- ▶ When to use IDA?
- ▶ How to create commensurate measures in IDA?

- ▶ Worked Examples

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Typical Steps in IDA (v2.0)

1. Explicate theoretical question of interest
 2. Identify contributing data sets
 3. Create collaborative IDA evaluation team
 4. Develop pool of potential items
 5. Create logically harmonized data set
 6. Conduct psychometric harmonization
 7. Estimate optimal scores anchored to a common scale
 8. Transport scores to analyses for hypothesis testing
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Feasibility analysis

Teen G1 Dep

→

Early Adult G1 Dep

→

Teen G2 Dep

Central Hypothesis

► Intergenerational Transmission Question → Do parents' (G1) depressive disorders in their adolescence and early adulthood predict depressive disorders for adolescent offspring (G2)?

Core Studies

► Study 1 – In Indiana

► Study 2 – In Arizona

► Study 3 – In North Carolina

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Overlapping study design

STUDY	1980-1987 Adolescent G1	1990-1995 Early Adult G1	2010-2012 Adolescent G2
IN	G1: 10-13	G1: 20-23	G1: 40-43 G2: 6-18
AZ	G1: 10-12	G1: 26	G1: 46 G2: 10-15
NC	G1: 11-14 OR G1: 12-15	G1: 20-23	G1: 46 G2: 10-15 OR G1: 35-38 G2: 8-20

IDA Design: G1 = parents; G2 = children; age range assessed per year tabled (with options).

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Overlapping study design

STUDY	1980-1987 Adolescent G1	1990-1995 Early Adult G1	2010-2012 Adolescent G2
IN	G1: 10-13	G1: 20-23	G2: 6-18
AZ	G1: 10-12	G1: 26	G2: 10-15
NC	G1: 11-14	G1: 20-23	G2: 10-15

IDA Design: G1 = parents; G2 = children; age range assessed per year tabled (clean version).

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Overlapping measurement design

STUDY	1980-1987 Adolescent G1	1990-1995 Early Adult G1	2010-2012 Adolescent G2
IN	G1: 10-13 DEP ✓	G1: 20-23 DEP ✓	G2: 6-18 DEP ✓
AZ	G1: 10-12 DEP ✓	G1: 26 DEP ✓	G2: 10-15 DEP ✓
NC	G1: 11-14 DEP ✓	G1: 20-23 DEP ✓	G2: 10-15 DEP ✓

Do they have depression measures for targets in each assessment? YES

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Overlapping measurement design

STUDY	1980-1987 Adolescent G1	1990-1995 Early Adult G1	2010-2012 Adolescent G2
IN	G1: 10-13 DEP ✓ A,B	G1: 20-23 DEP ✓ A,B	G2: 6-18 DEP ✓ D
AZ	G1: 10-12 DEP ✓ B'	G1: 26 DEP ✓ B'	G2: 10-15 DEP ✓ D'
NC	G1: 11-14 DEP ✓ A'	G1: 20-23 DEP ✓ C	G2: 10-15 DEP ✓ D''

Measures: A, B (original and B' modified), C, D (original and modified two ways D' & D'')

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Develop pool of potential items

- ▶ Do not need same items for the same construct across studies
- ▶ Can have items that are
 - ▶ IDENTICAL ITEMS: identical across all studies
 - ▶ LOGICALLY HARMONIZED ITEMS: can be manually modified to be similar
 - ▶ UNIQUE ITEMS: available in subset of studies or cannot be logically harmonized
- ▶ Need some subset of *common items* to establish commensurate scale for underlying construct

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	Study A	Study B	Study C	Study D
Directions	These questions are about how you might have been feeling or acting. For each question, please check how you have been feeling or acting in the past year. If a sentence was not true about you, check NOT TRUE. If a sentence was only sometimes true, check SOMETIMES. If a sentence was true about you most of the time, check TRUE.	These questions are about how you might have been feeling or acting. For each question, please check how you have been feeling or acting in the past year. If a sentence was not true about you, check NOT TRUE. If a sentence was only sometimes true, check SOMETIMES. If a sentence was true about you most of the time, check TRUE.	These questions are about how you might have been feeling or acting. For each question please select how you have been feeling or acting in the past year. If a sentence was not true about you, select NO. If a sentence was true about you, select YES.	Please continue to answer these questions using the new response scale below. Remember, for each question, please select how you have been feeling or acting the past year. If a sentence was not true about you, select NOT AT ALL. If a sentence was true, select SEVERAL DAYS, MORE THAN HALF THE DAYS, or NEARLY EVERY DAY.
Response Scale	Not True (0), Sometimes (1), True (2), Refuse to answer (.)	Not True (0), Sometimes (1), True (2), Refuse to answer (.)	Yes (0), No (1), Refuse to answer (.)	Not at all (0), Several days (1), More than half the days (2), Nearly every day (3), Refuse to answer (.)
Item # (DEP)				
1	I felt miserable or unhappy	I felt miserable or unhappy	I felt miserable or unhappy	I felt depressed.
2	I didn't enjoy anything at all	I didn't enjoy anything at all	I didn't enjoy anything at all	I had little interest or pleasure in doing things

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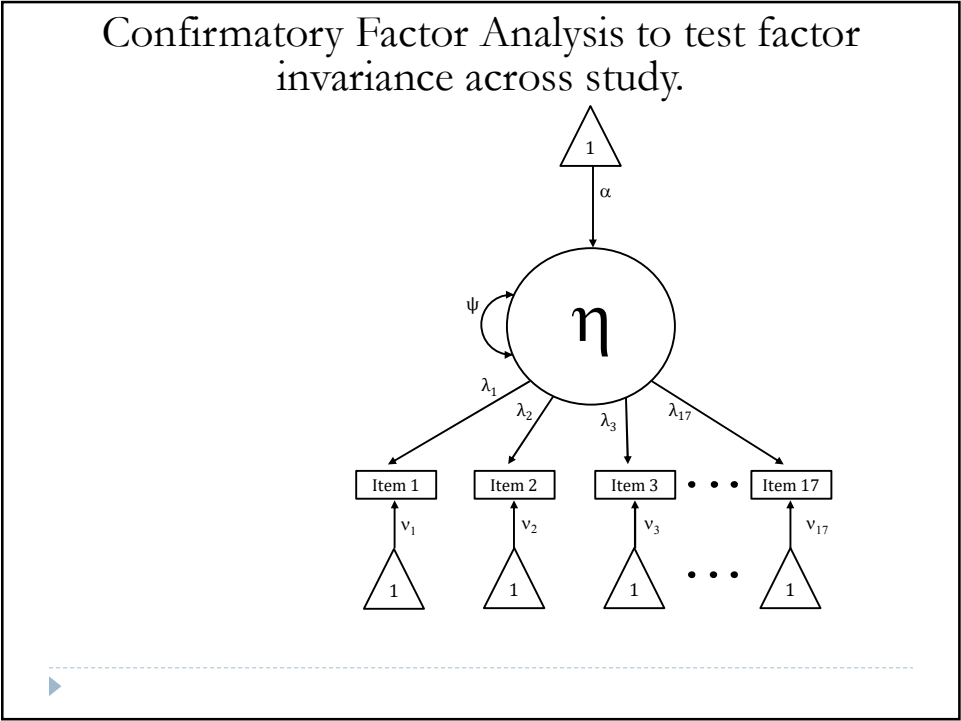
Example 2

- ▶ Motivating Question: Is parent distress related to child depression during the pandemic?
- ▶ Identify two studies with measures of both constructs with overlapping timeframes of assessment. Both are cross-sectional studies with similar but not identical measures of depression and parent distress.
- ▶ Create data use agreements and authorship guidelines to structure the cross study team.

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DEPRESSION	Study 1	
Directions	These questions are about how you might have been feeling or acting. For each question, please check how you have been feeling or acting in the past year. If a sentence was not true about you, check NOT TRUE. If a sentence was only sometimes true, check SOMETIMES. If a sentence was true about you most of the time, check TRUE.	These questions are about how you might have been feeling or acting. For each question, please check how you have been feeling or acting in the past year. If a sentence was not true about you, check NOT TRUE. If a sentence was only sometimes true, check SOMETIMES. If a sentence was true about you most of the time, check TRUE.
Response Scale	Not True (0), Sometimes (1), True (2), Refuse to answer (.)	Yes (0), No (1), Refuse to answer (.)
1	I felt miserable or unhappy	I felt miserable or unhappy
2	I didn't enjoy anything at all	I didn't enjoy anything at all
3	I felt so tired I just sat around and did nothing	I felt so tired I just sat around and did nothing
4	I was very restless	I felt so fidgety or restless
5	I felt I was no good any more	I felt I was no good any more
6	I cried a lot	I had crying spells.
7	I found it hard to think properly or concentrate	I found it hard to think properly or concentrate
8	I hated myself	I didn't like myself
9	I was a bad person	I felt bad about myself
10	I felt lonely	I felt lonely
11	I thought nobody really loved me	I thought nobody really loved me
12	I thought I could never be as good as other people	I did not feel like I was as good as other people
13	I did everything wrong	I thought my life had been a failure

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Motivating Example 3

► Question: Do children of parents with an alcohol use disorder show different trajectories of internalizing symptoms across time compared to children of parents without an alcohol use disorder?

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The Cross Study

Investigators: Hussong, Curran, Bauer
NIDA R01-DA015398; R01-DA034636-01A1

Three landmark studies of children of alcoholic parents & controls

- Michigan Longitudinal Study (MLS; PI: Zucker)
- Adolescent and Family Development Project (AFDP; PI: Chassin)
- Alcohol and Health Behavior Project (AHBP; PI: Sher)

► 17

Hussong et al. for NIDA STTR 9/16/2014

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Integrated Sample for Model Fitting

	MLS (n=641)	AFDP (n=846)	AHBP (n=485)	Pooled Repeated Measures Sample (n=1972)
Age	15.24(3.12)	21.17(7.05)	22.79(4.77)	19.81(6.21)
% Male	71.0	52.4	47.2	57.2
% COA	76.0	50.4	48.7	58.3
% Minority	2.3	30.3	6.2	15.3
% Parent ASP	14.8	9.6	7.8	11.0
%Parent Depression	24.6	16.8	36.3	25.0
Parent Education	2.59(1.18)	3.09(1.13)	3.62(1.14)	3.05(1.21)

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Pool of Available Items

- ▶ 33 binary self-report items assessing presence or absence of internalizing symptomatology ages 11-35
 - ▶ some from Brief Symptom Inventory (BSI)
 - ▶ some from Child Behavior Check List (CBCL)
 - ▶ some items share content across BSI and CBCL
- ▶ Variations in item coverage across studies
 - ▶ MLS: all items administered
 - ▶ AFDP: subset of CBCL items administered
 - ▶ AHBP: all BSI items administered
- ▶ Subset of common items in all studies allow for linking and unique items within-study increase score precision
- ▶ Preliminary EFAs identified 17 items defining *depression*

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Understanding your data

- ▶ Draw a calibration sample
- ▶ Look at means over age within study for each item and pooled across study
- ▶ Look at within study exploratory factor analysis and pooled across study

Why?

- ▶ Are there items that show a different pattern over age or do the items 'travel together'?
- ▶ Are endorsement rates high enough to include the item to look at study effects?
- ▶ How many factors (or dimensions) underlie the set of items?

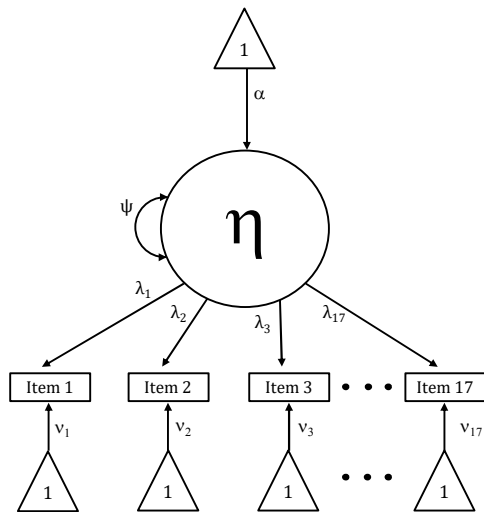
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EFA Results for 17 Depression Items

Item Description	Loading (se)	Intercept (se)
1. Lonely	2.53 (.17)	-0.74 (.09)
2. Cries a lot	1.52 (.12)	-1.60 (.10)
3. Fears will behave badly	1.33 (.17)	-1.61 (.13)
4. Have to be perfect	1.16 (.09)	-0.04 (.07)
5. No one loves me	2.50 (.21)	-3.26 (.21)
6. Worthless/inferior	2.85 (.21)	-2.98 (.19)
7. Prefers being alone	0.96 (.13)	-0.52 (.10)
8. Feel guilty	1.70 (.11)	-1.70 (.09)
9. Is secretive	1.51 (.17)	0.31 (.11)
10. Is underactive	1.11 (.14)	-0.76 (.10)
11. Unhappy/ sad/depressed	2.61 (.20)	-0.67 (.10)
12. Worried	1.82 (.13)	0.23 (.08)
13. Hopeless about future	2.16 (.21)	-1.99 (.15)
14. Acts to harm self	1.75 (.36)	-4.30 (.43)
15. Thinks about killing self	1.83 (.24)	-3.76 (.27)
16. Blue	2.54 (.23)	-0.46 (.11)
17. No interest in things	1.62 (.15)	-0.99 (.10)

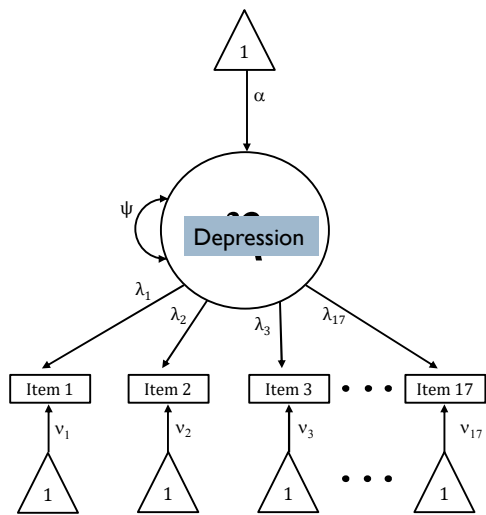
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Nonlinear Confirmatory Factor Analysis



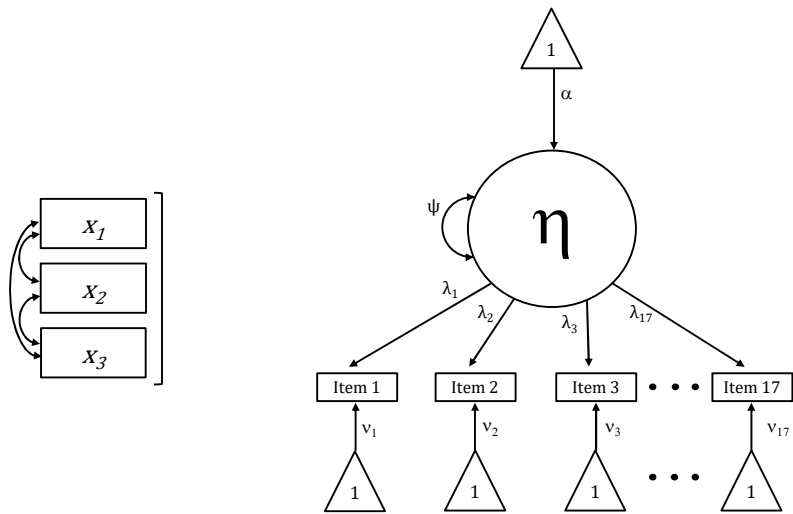
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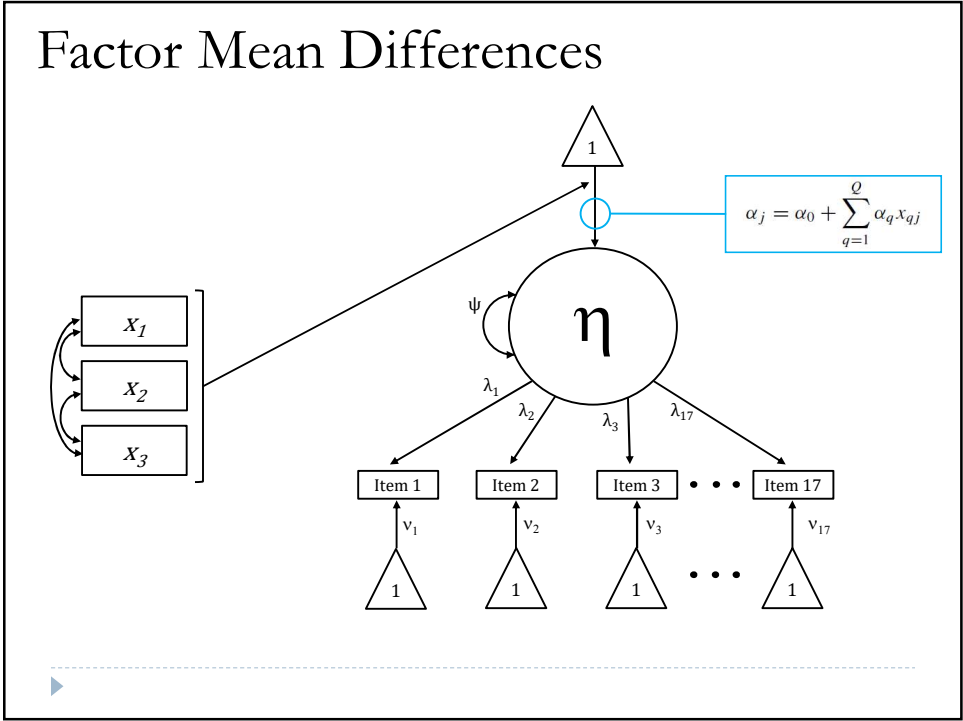


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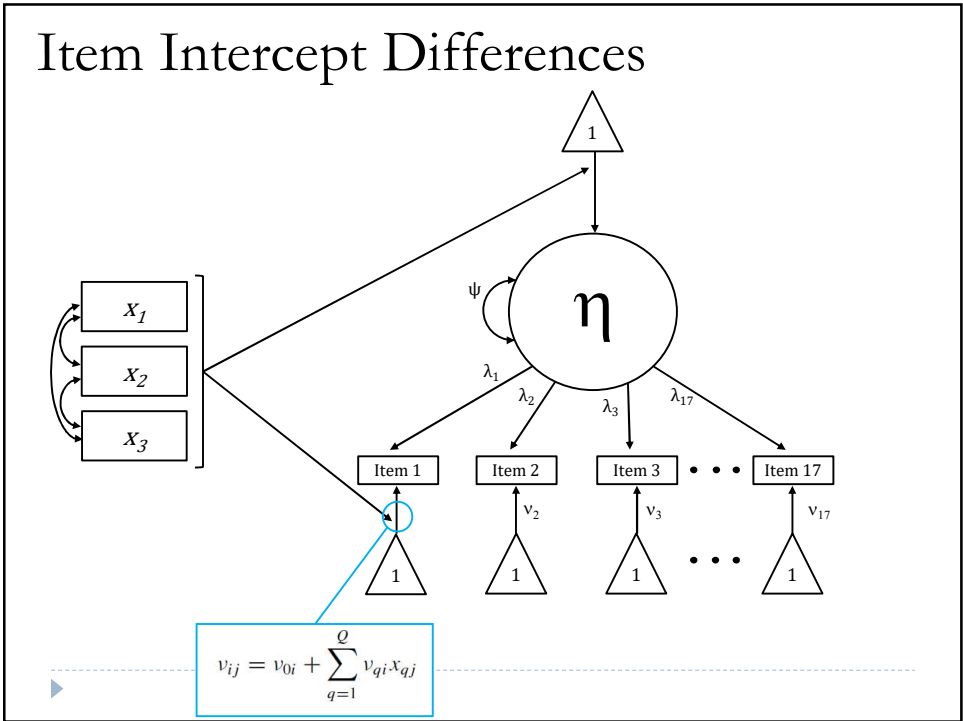
CFA with Exogenous Covariates



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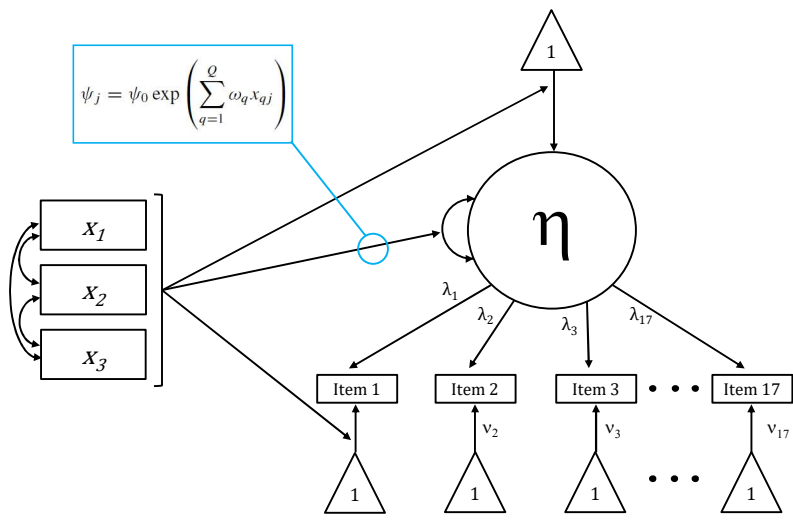


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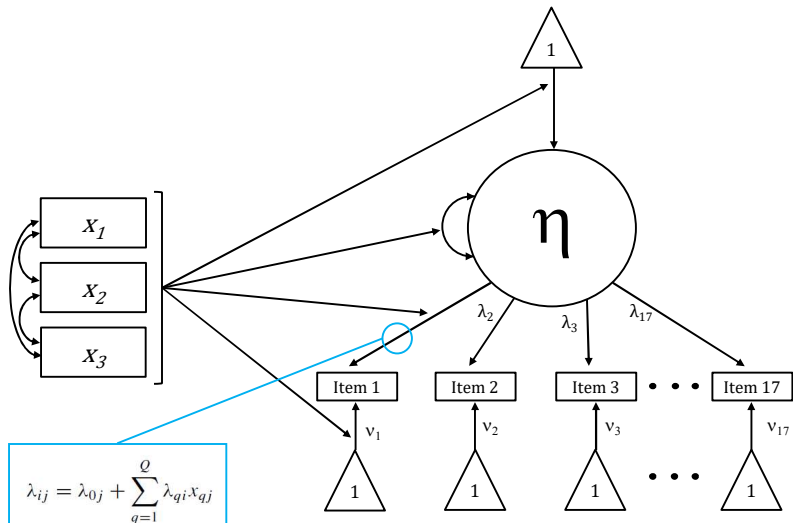
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Factor Variance Differences

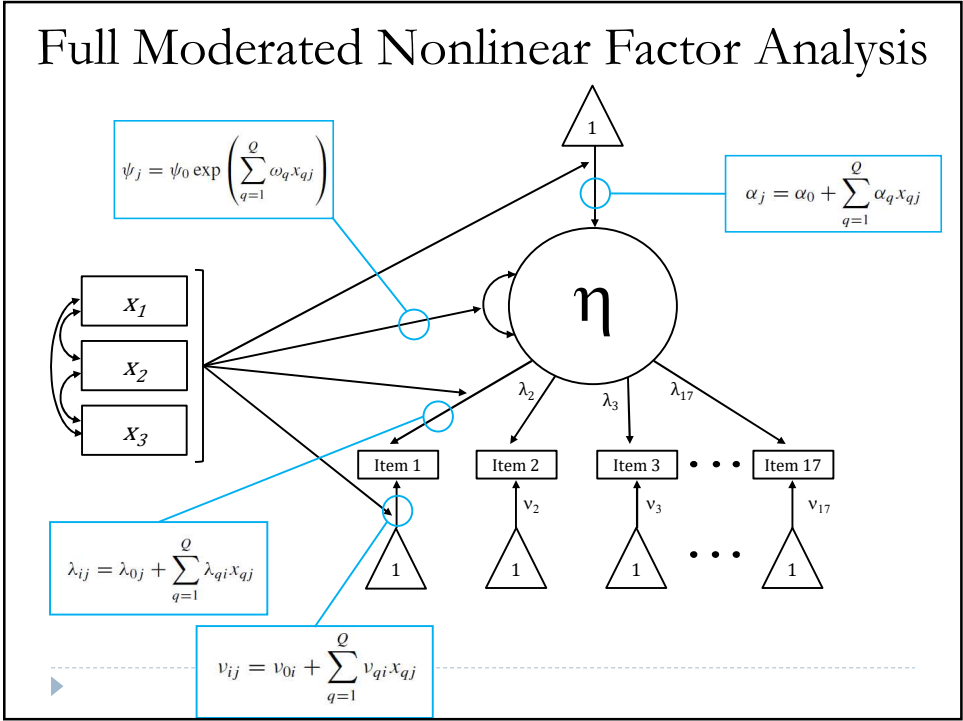


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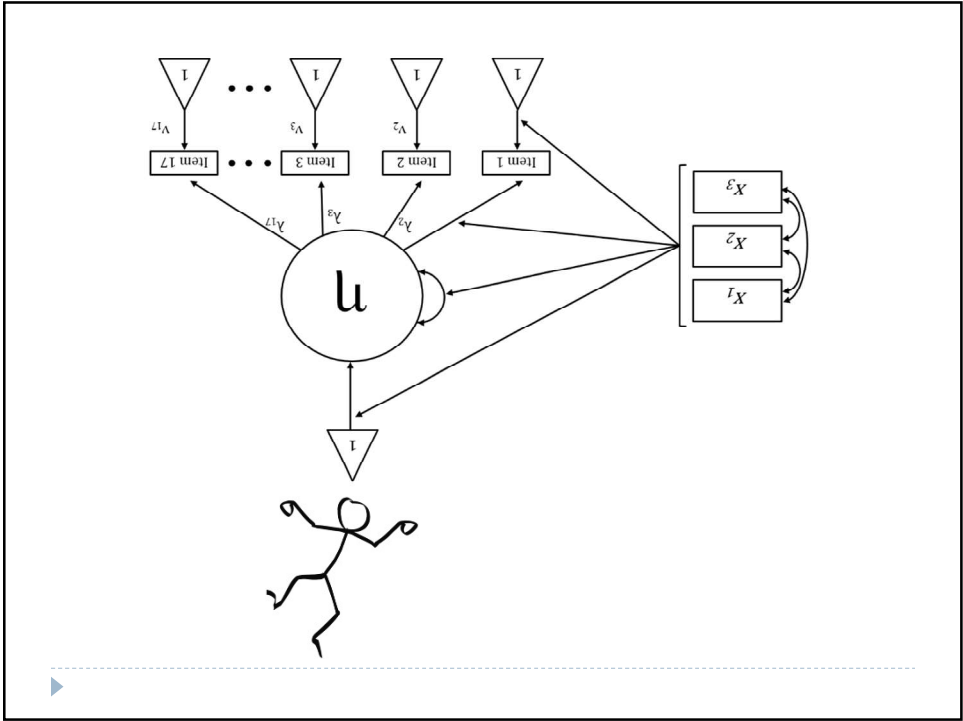
Factor Loading Differences



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MNLFA allows testing of harmonization assumptions about:

IMPACT

- ▶ Mean differences in underlying factors across studies (and other covariates) – do the studies differ in levels of depression?
- ▶ Variance differences in factors across studies – are depression scores more widely spread in some studies than in others?

DIFFERENTIAL ITEM FUNCTIONING OR DIF

- ▶ Differences in item factor loadings – is the item ‘cries a lot’ a better indicator of depression in one study versus another?
- ▶ Differences in item intercepts – at the same level of depression, is one item more likely to be endorsed in one study versus another?

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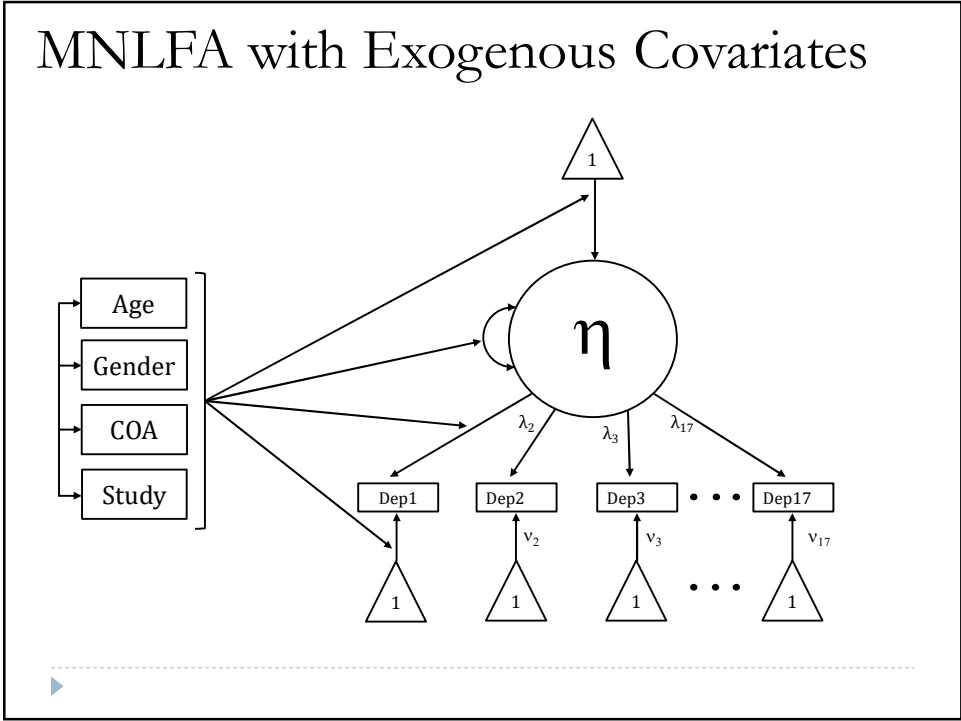
Where do differences come from?

Study differences

- ▶ in measurement (failed harmonization)
- ▶ in design influences
- ▶ in the people in the samples

If we model differences in sources, we can control for those differences (and it matters later in our prediction models). But we won't know them all, and sometimes we just want to control for any study differences for harmonization.

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Covariate Effects on Factor

Covariate Effect	Estimate (SE)	<i>t</i>	<i>p</i>
Factor mean			
1. Age	−0.70 (.14)	−5.04	< .0001
2. Age ²	−0.63 (.25)	−2.58	.0098
3. Age ³	0.56 (.18)	3.12	.0018
4. MLS	−0.86 (.08)	−10.87	< .0001
5. AHBP	−0.28 (.12)	−2.28	.0227
6. Gender	−0.48 (.08)	−5.82	< .0001
7. COA	0.23 (.06)	4.07	< .0001
8. Age by MLS	0.85 (.15)	5.81	< .0001
9. Age by AHBP	−3.77 (.91)	−4.13	< .0001
10. Age ² by AHBP	4.84 (1.64)	2.95	.0033
11. Age ³ by AHBP	−1.73 (.76)	−2.29	.0222
12. Age by Gender	0.25 (.16)	1.58	.1140
13. Age ² by Gender	1.03 (.31)	3.29	.0010
14. Age ³ by Gender	−0.74 (.23)	−3.18	.0015
Factor variance			
15. Age	0.02 (.10)	0.21	.8372
16. AHBP	−0.13 (.19)	−0.66	.5106
17. Age by AHBP	0.80 (.27)	2.90	.0038

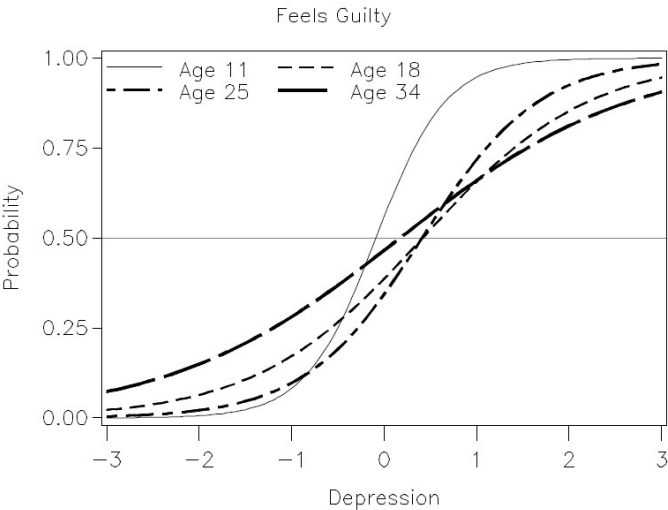
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Covariate Effects on Items

Item Covariate Effect	Intercept (SE)	Loading (SE)	Item Covariate Effect	Intercept (SE)	Loading (SE)
1. Lonely	0.79 (.20)	2.36 (.16)	11. Unhappy/Sad/Depressed	0.98 (.19)	1.93 (.19)
AHBP	1.05 (.22)	—	MLS	—	0.95 (.29)
2. Cries a lot	0.45 (.15)	1.45 (.12)	12. Worried	1.51 (.18)	1.66 (.13)
Age	−0.34 (.12)	—	Age	0.59 (.15)	—
Gender	−2.09 (.17)	—	MLS	−0.70 (.18)	—
3. Fears will behave badly	−0.68 (.17)	1.22 (.16)	Age by MLS	−0.91 (.31)	—
4. Has to be perfect	0.70 (.11)	1.06 (.08)	13. Hopeless about future	−0.49 (.24)	2.07 (.21)
5. No one loves me	−2.00 (.25)	2.55 (.23)	Age	1.04 (.36)	—
Age	−0.64 (.20)	—	Age ²	−1.41 (.37)	—
MLS	0.88 (.27)	—	Gender	0.89 (.24)	—
6. Worthless/Inferior	−1.23 (.20)	2.49 (.19)	14. Acts to harm self	−3.06 (.31)	1.66 (.35)
MLS	0.55 (.21)	—	15. Thinks about killing self	−2.38 (.20)	1.67 (.23)
7. Prefers to be alone	0.18 (.15)	0.91 (.12)	16. Blue	2.02 (.38)	2.83 (.36)
8. Feel guilty	−0.46 (.13)	1.11 (.15)	Age	3.33 (.78)	2.96 (.77)
Age	−0.63 (.21)	−0.12 (.32)	17. No interest in things	−0.37 (.25)	1.69 (.21)
Age ²	0.52 (.18)	2.05 (.69)	Gender	0.56 (.21)	—
Age ³	—	−1.31 (.42)	COA	0.68 (.21)	—
MLS	−0.83 (.19)	—	Age	—	2.97 (.88)
9. Is secretive	1.34 (.21)	1.38 (.15)	Age ²	—	3.02 (.99)
10. Is underactive	0.14 (.16)	1.02 (.13)	Age ³	—	−2.96 (.93)
Age	0.71 (.24)	—			

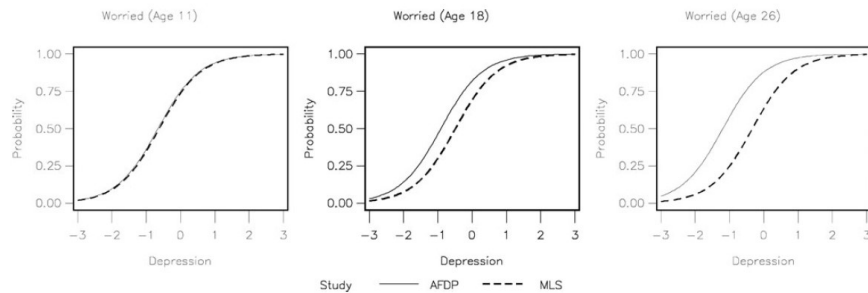
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DIF Item: *Feels Guilty* by Age



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DIF Item: *Worried* by Study & Age

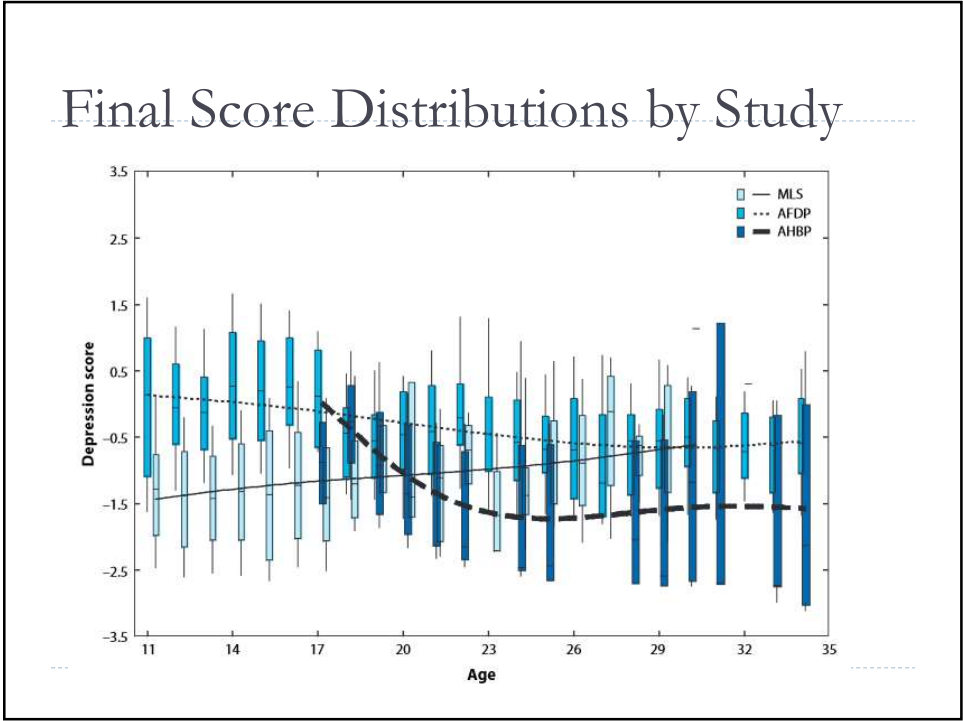


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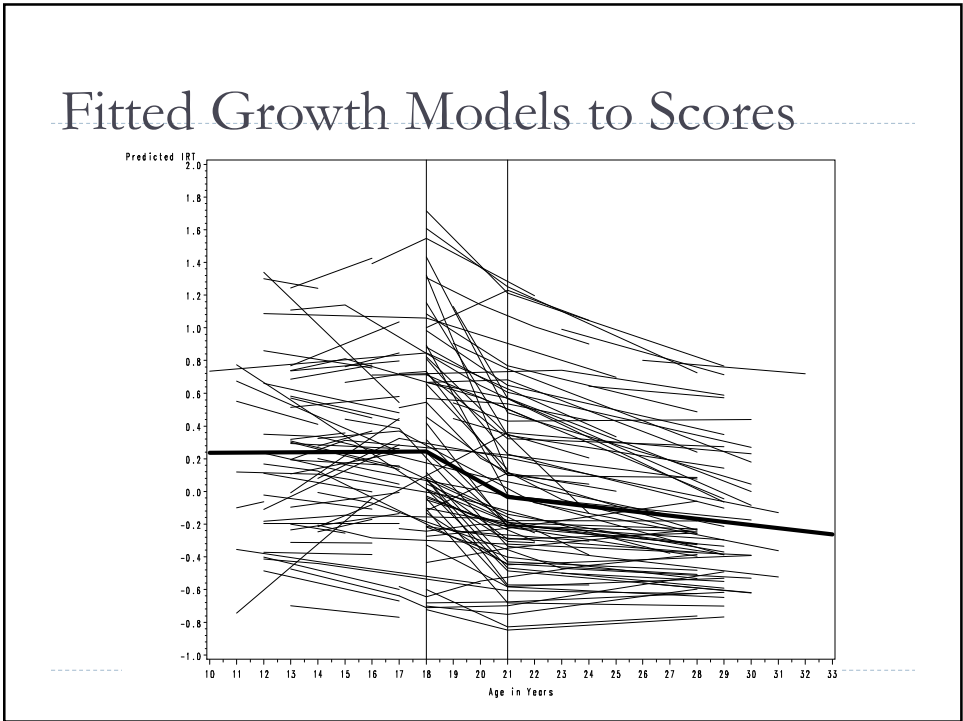
Scoring Phase

- ▶ Establish final MNLFA model
 - ▶ some items are invariant over covariates
 - ▶ some items differentially relate to latent factor as function of covariates
 - ▶ latent factor itself differentially relates to covariates
- ▶ Take all parameters from final MNLFA and use to obtain optimal scores on depression
 - ▶ called Empirical Bayes Estimates of underlying latent factor
- ▶ Each subject gets person- and time-specific score of depression that reflects item responses and covariates
 - ▶ literally using MNLFA as an incredibly complex calculator

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Modeling Study Differences

- ▶ With a limited number of studies, we recommend including Study as a predictor within the model (and Study x Covariate interactions)
 - ▶ general approach known as the *fixed-effects approach*
- ▶ With a large number of studies, can consider participants to be nested within studies and apply a multilevel model
 - ▶ general approach known as the *random-effects approach*
 - ▶ much more powerful when seeking to generalize effects to broader population

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Unpacking Study Differences

- ▶ In some cases, it's possible to remove certain sources of study differences by controlling for confounding covariates
- ▶ For instance, in MLS, a majority of participants recruited into the sample were children of alcoholics
- ▶ In AFDP and AHBP, roughly equal numbers of children of alcoholics and matched controls were recruited
- ▶ Study differences may be mitigated somewhat by jointly including COA in IDA models

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Practical Recommendations

- ▶ Always include a main effect of Study in IDA models
 - ▶ Control for factors known to differ over studies to minimize study effects
- ▶ Also check for interactions of Study with other predictors
 - ▶ But trim non-significant interactions from the model
- ▶ Testing study effects is a blessing and a curse
 - ▶ Can empirically test generality versus specificity of effects
 - ▶ Yet increases complexity of models and it is often hard to pinpoint source of study differences

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Data Coverage Considerations

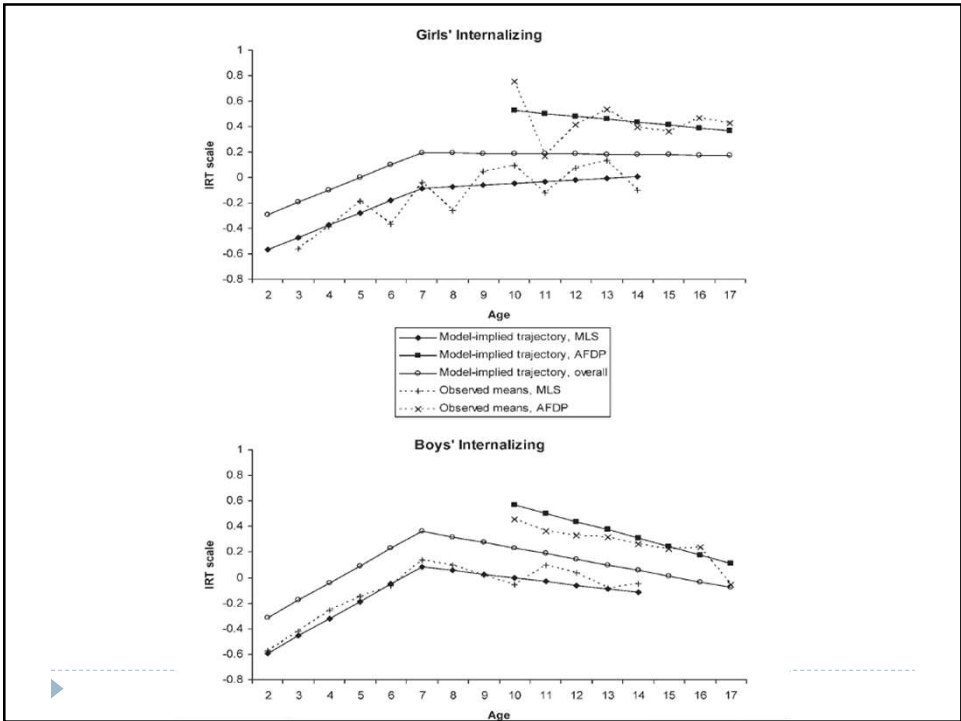
- ▶ An effect can't be estimated when there is no data coverage for the effect
- ▶ Simple Example:
 - ▶ only one study includes Latino participants
 - ▶ no way to dissociate effect of being Latino from Study effect
 - ▶ must exclude Latino effect from model, knowing absorbed in study differences

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Data Coverage Considerations

- ▶ An effect can't be estimated when there is no data coverage for the effect
- ▶ Complex Example:
 - ▶ Fit piecewise linear model to capture longitudinal change over time
 - ▶ Piece 1 covers only ages in Study 1
 - ▶ Piece 2 covers only ages in Study 2
 - ▶ Can't estimate a covariance between piece 1 slope and piece 2 slope
 - ▶ Must remove covariance from model

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Table 5. Latent growth modeling results testing the effect of parent alcoholism subtypes on mother report of internalizing trajectories

Covariate	Growth Factor					
	Intercept (Age 13)		Slope Age 2–7		Slope Age 7–17	
	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>	<i>b</i>	<i>SE</i>
Model 3a						
Control vs. COA contrast	0.06****	0.02	0.00	0.01	0.01	0.00
Alcohol-only vs. comorbid contrast	0.11****	0.03	0.00	0.01	0.01	0.01
Depressed vs. ASP subtype contrast	0.16**	0.08	0.03	0.04	0.01	0.02
Model 3b						
Control vs. alcohol only	−0.04	0.06	−0.01	0.03	0.00	0.01
Depressed subtype vs. alcohol only	0.49****	0.15	0.03	0.05	0.02	0.02
ASP subtype vs. alcohol only	0.17*	0.09	−0.03	0.05	0.04	0.02

Note: COA, children of alcoholic parents; ASP, antisocial personality disorder; *N* = 811. The effects of study, gender, ethnicity, and parent education are not in the table, although they were covariates in each model.
p* < .10. *p* < .05. *****p* < .001.

