Modern Latent Variable Modeling Methods

Bengt Muthén
bmuthen@ucla.edu

Tihomir Asparouhov

www.statmodel.com

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Statistical Concepts Captured By Latent Variables

Continuous Latent Variables

- Factors
- Random effects
- Frailties, liabilities
- Variance components
- Missing data
- Bayesian parameter priors

Categorical Latent Variables

- Latent classes
- Clusters
- Finite mixtures
- Missing data

Modern Latent Variable Modeling: Integration of a Multitude of Analyses

- Exploratory factor analysis
- Structural equation modeling
- Item response theory analysis
- Growth modeling
- Latent class analysis
- Latent transition analysis (Hidden Markov modeling)
- Growth mixture modeling
- Survival analysis
- Missing data modeling
- Multilevel analysis
- Complex survey data analysis
- Bayesian analysis
- Causal inference

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Latent Variable Integration: Example 1

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Latent Variable Integration: Example 1

- Exploratory factor analysis
- Structural equation modeling

Example 1: Factor Analysis of Aggressive Behavior of Males and Females in Grade 3

- 261 males and 248 females in third grade (Baltimore Cohort 3)
- Teacher-rated aggressive-disruptive behavior
- Outcomes treated as non-normal continuous variables
- Research question:
  - Does the measurement instrument function the same way for males and females?

Summary Of Separate Male/Female Exploratory Factor Analysis (Geomin Rotation)

	Loadings for Males			Loadings for Females		
Variables	Verbal	Person	Property	Verbal	Person	Property
Stubborn	**0.82***	-0.05	0.01	**0.88***	0.03	-0.22
Breaks Rules	0.47*	0.34*	0.01	**0.76***	0.06	-0.17
Harms Others and Property	-0.01	**0.63***	0.31*	0.45*	0.03	0.36
Breaks Things	-0.02	0.02	**0.66***	-0.02	0.19	**0.43***
Yells At Others	**0.66***	0.23	-0.03	**0.97***	-0.23	0.05
Takes Other's Property	0.27*	0.08	**0.52***	0.02	**0.79***	0.10
Fights	0.22*	**0.75***	-0.00	**0.81***	-0.01	0.18
Harms Property	0.03	-0.02	**0.93***	0.27	0.20	**0.57***
Lies	**0.58***	0.01	0.27*	0.42*	0.50*	-0.00
Talks Back to Adults	**0.61***	-0.02	0.30*	**0.69***	0.09	-0.02
Teases Classmates	0.46*	0.44*	-0.04	**0.71***	-0.01	0.10
Fights With Classmates	0.30*	**0.64***	0.08	**0.83***	0.03	0.21*
Loses Temper	**0.64***	0.16*	0.04	**1.05***	-0.29	-0.01

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Measurement invariance can be tested by multiple-group analysis

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Measurement invariance can be tested by multiple-group analysis

- But this involves a move from EFA to CFA
- CFA often premature
- CFA often rejected

- Why should we have to switch from EFA to CFA to test measurement invariance?

Multiple-Group Exploratory Factor Analysis (ESEM)

Asparouhov & Muthén (2009). Exploratory structural equation modeling. **Structural Equation Modeling**, 16, 397-438.

- Estimate by ML using a group-invariant unrotated factor loading matrix with a reference group having uncorrelated unit variance factors (m^2 restrictions), allowing group-varying factor covariance matrices and residual variances
- Rotate the common factor loading matrix, e.g. by oblique Geomin
- Transform the factor covariance matrices by the rotation matrix
- Factor loading invariance across groups can be tested by LR chi-square test: Not rejected for gender invariance

Male And Female Estimates From Multiple-Group EFA Using Invariant Factor Loadings (Standardized)

	Males			Females		
Variables	Verbal	Person	Property	Verbal	Person	Property
Stubborn	**0.80***	-0.01	-0.02	**0.86***	-0.00	-0.01
Breaks Rules	0.53*	0.27*	0.01	**0.59***	0.20*	0.01
Harms Others & Property	0.00	0.57*	0.35*	0.00	0.56*	0.24*
Breaks Things	-0.01	-0.02	**0.67***	-0.03	-0.03	**0.63***
Yells At Others	**0.66***	0.25	-0.03	**0.69***	0.18	-0.01
Takes Others' Property	0.32*	0.04	0.53*	0.39*	0.03	0.31*
Fights	0.28*	**0.74***	-0.03	0.35*	0.61*	-0.02
Harms Property	0.11	0.03	**0.83***	0.19	0.04	**0.68***
Lies	0.58*	0.01	0.30*	**0.67***	0.00	0.16*
Talks Back To Adults	**0.64***	-0.03	0.29*	**0.71***	-0.02	0.15*
Teases Classmates	0.44*	0.40*	0.02	0.49*	0.30*	0.01
Fights With Classmates	0.33*	0.65*	0.05	0.41*	0.53*	0.03
Loses Temper	**0.64***	0.19	0.00	**0.74***	0.14	0.00

- Measurement intercept invariance testing and group differences in factor means
- Single-group invariance testing such as invariance across time with longitudinal factor analysis
- Exploratory SEM

Asparouhov & Muthén (2009). Exploratory structural equation modeling. **Structural Equation Modeling**, 16, 397-438.

Latent Variable Integration: Example 2

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Latent Variable Integration: Example 2

- Structural equation modeling

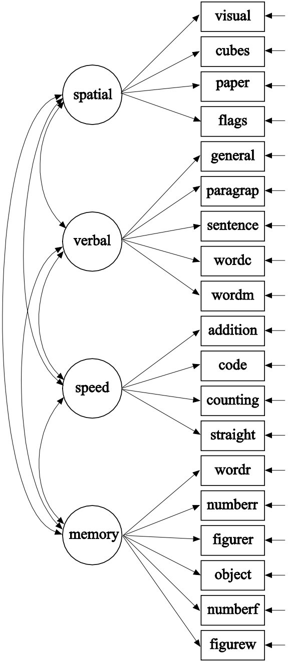
- Bayesian analysis

Example 2: Bayesian Multiple-Group CFA (BSEM)

Holzinger-Swineford (1939)

- 19 tests hypothesized to measure four mental abilities: Spatial, verbal, speed, and memory
- n=145 7th and 8th grade students from Grant-White elementary school
- n=156 7th and 8th grade students from the Pasteur elementary school

Muthén & Asparouhov (2010). Bayesian SEM: A more flexible representation of substantive theory. Under review in **Psychological Methods**. - The BSEM paper



CFA Factor Loading Pattern

	Spatial	Verbal	Speed	Memory
visual	x	0	0	0
cubes	x	0	0	0
paper	x	0	0	0
flags	x	0	0	0
general	0	x	0	0
paragrap	0	x	0	0
sentence	0	x	0	0
wordc	0	x	0	0
wordm	0	x	0	0
addition	0	0	x	0
code	0	0	x	0
counting	0	0	x	0
straight	0	0	x	0
wordr	0	0	0	x
numberr	0	0	0	x
figurer	0	0	0	x
object	0	0	0	x
numberf	0	0	0	x
figurew	0	0	0	x

ML Testing of Multiple-Group CFA Measurement Invariance for Grant-White (n=145) and Pasteur (n=156)

- ML, simple structure CFA:
    - Loading and intercept invariance: Chi-square (322) = 613 (p=0), RMSEA = 0.077, CFI = 0.852

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  - Loading invariance: Chi-square (307) = 494 (p=0), RMSEA = 0.064, CFI = 0.905
  - Conclusion: Model fits poorly, particularly for intercept invariance

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  - Conclusion: Model fits poorly, particularly for intercept invariance
- ML ESEM (EFA factor loadings, allowing cross-loadings):
  - Loading and intercept invariance: Chi-square (277)= 423 (p=0), RMSEA = 0.059, CFI = 0.926

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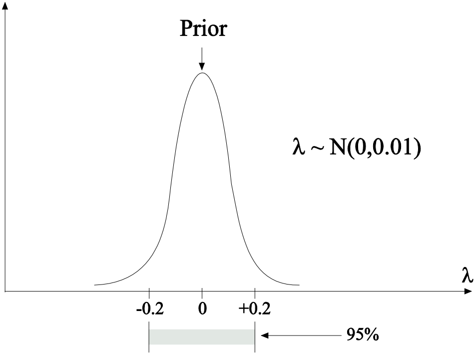
- ML ESEM (EFA factor loadings, allowing cross-loadings):
  - Loading and intercept invariance: Chi-square (277)= 423 (p=0), RMSEA = 0.059, CFI = 0.926
  - Loading invariance: Chi-square (262) = 311 (p=0.02), RMSEA = 0.035, CFI = 0.975
  - Conclusion: Cross-loadings needed, intercepts not invariant

Bayes Testing of Multiple-Group CFA Measurement Invariance for Grant-White (n=145) and Pasteur (n=156)

- BSEM using zero-mean, small-variance priors for:
  - Cross-loadings in each group
  - Group differences in intercepts and major loadings



Bayes Testing of Multiple-Group CFA Measurement Invariance for Grant-White (n=145) and Pasteur (n=156)

Model testing via Posterior Predictive Checking (Gelman et al., 1996) using the LR chi-square fit statistic ($[95\% \ CI]$ and p-value).

- Bayes simple structure CFA
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- Bayes simple structure CFA
  - Loading and intercept invariance: PPC = [212, 344], p=0
  - Loading invariance: PPC = [106, 244], p = 0
  - Conclusion: Model fits poorly, particularly for intercept invariance
- Bayes with small-variance priors for cross-loadings and group differences in loadings and intercepts: PPP = [-49, 94], p=0.268

Bayes Multiple-Group Solution using Small-Variance Priors

	Grant-White Factor loading pattern for Bayes				Pasteur Factor loading pattern for Bayes				Intercept
Variables	Spatial	Verbal	Speed	Memory	Spatial	Verbal	Speed	Memory	Difference
visual	**1.000**	-0.001	0.063	0.057	**1.000**	0.247	0.004	0.053	-0.013
cubes	**0.769***	0.003	-0.035	-0.018	**0.782**	-0.021	-0.071	-0.056	0.153
paper	**0.676***	0.061	0.055	0.081	**0.710***	0.055	-0.002	-0.219	0.012
flags	**1.010**	0.032	-0.020	0.004	**1.048**	-0.115	0.053	0.176	-0.429*
general	0.063	**1.000**	0.077	-0.069	-0.047	**1.000**	0.078	-0.136	0.141
paragrap	0.013	**1.020**	-0.086	0.099	0.052	**0.996***	-0.026	0.081	-0.146
sentence	-0.082	**1.157**	0.038	-0.110	-0.061	**1.234**	-0.052	-0.058	-0.023
wordc	0.088	**0.800***	0.146	0.018	0.113	**0.818***	-0.001	0.118	0.284*
wordm	0.024	**1.030**	-0.113	0.079	0.155	**0.862***	0.005	0.010	-0.120
addition	-0.294	0.079	**1.000**	0.025	-0.263	0.027	**1.000**	0.083	-0.278
code	-0.002	0.090	**0.689***	0.257	0.002	0.200	**0.727***	0.148	0.002
counting	0.070	-0.095	**1.014**	-0.084	0.063	-0.093	**0.966***	-0.090	0.180
straight	0.371*	0.085	**0.754***	-0.091	0.271*	-0.088	**0.777***	0.022	0.022
wordr	-0.108	0.059	-0.074	**1.000**	-0.069	0.019	-0.158	**1.000**	0.086
numberr	0.020	-0.048	-0.049	**0.900***	0.033	-0.152	-0.194	**0.904***	-0.154
figurer	0.283*	-0.051	-0.090	**0.863***	0.314*	0.054	0.106	**0.852***	0.172
object	-0.205	0.003	0.150	**0.979***	-0.205	0.018	0.212	**0.913***	-0.372*
numberf	0.226	-0.119	0.213	**0.714***	-0.062	0.077	-0.021	**0.694***	0.071
figurew	0.033	0.126	0.005	**0.624***	0.096	0.035	0.163	**0.626***	0.428*

Bayes Multiple-Group Solution using Small-Variance Priors (Continued)

	Grant-White factor covariance for Bayes				Pasteur factor covariance for Bayes			
Variables	Spatial	Verbal	Speed	Memory	Spatial	Verbal	Speed	Memory
Spatial	0.514*				0.516*			
Verbal	0.291*	0.666*			0.162	0.724*		
Speed	0.246*	0.251*	0.651*		0.115	0.225*	0.465*	
Memory	0.226*	0.267*	0.258*	0.445*	0.157	0.095	0.168	0.546*
Factor Means								
	0.012	0.554*	-0.219	0.054	0.000	0.000	0.000	0.000

Latent Variable Integration: Example 3

- Exploratory factor analysis
- Structural equation modeling
- Item response theory analysis
- Growth modeling
- Latent class analysis
- Latent transition analysis (Hidden Markov modeling)
- Growth mixture modeling
- Survival analysis
- Missing data modeling
- Multilevel analysis
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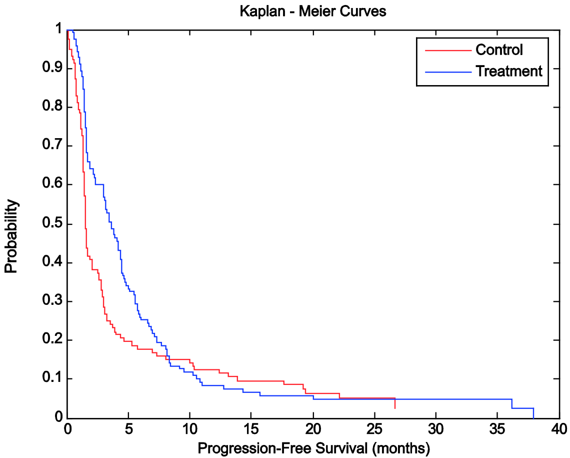
- Bayesian analysis
- Causal inference

Latent Variable Integration: Example 3

- Survival analysis

- Latent class analysis

Example 3: Cancer Survival Trial of Second-Line Treatment of Mesothelioma



- Larsen (2004). Joint analysis of time-to-event and multiple binary indicators of latent classes. **Biometrics**
- Larsen (2005). The Cox proportional hazards model with a continuous latent variable measured by multiple binary indicators. **Biometrics**
- Asparouhov, Masyn, & Muthén (2006). Continuous time survival in latent variable models. Proceedings of the Joint Statistical Meeting in Seattle, August 2006. ASA section on Biometrics, 180-187
- Muthén, Asparouhov, Boye, Hackshaw & Naegeli (2009). Applications of continuous-time survival in latent variable models for the analysis of oncology randomized clinical trial data using Mplus. Technical Report

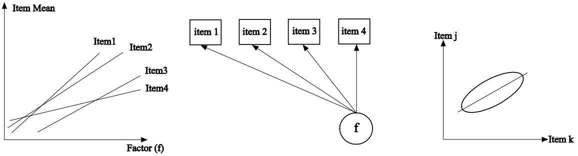
Patient-Reported Lung Cancer Symptom Scale (LCSS)

Directions: Please place a mark along each line where it would best describe the symptoms of your lung illness DURING THE PAST DAY (during the past 24 hours)

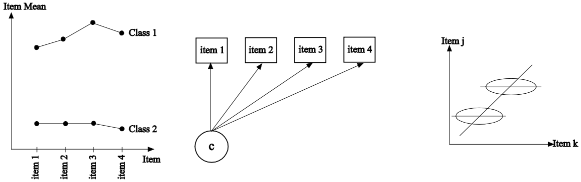
1. How is your appetite?	
As good as it could be	As bad as it could be
2. How much fatigue do you have?	
None	As much as it could be
3. How much coughing do you have?	
None	As much as it could be
4. How much shortness of breath do you have?	
None	As much as it could be
5. How much blood do you see in your sputum?	
None	As much as it could be
6. How much pain do you have?	
None	As much as it could be
7. How bad are your symptoms from your lung illness?	
I have none	As much as it could be
8. How much has your illness affected your ability to carry out normal activities?	
Not at all	So much that I can do nothing for myself
9. How would you rate the quality of your life today?	
Very high	Very low

Brief Overview Of Latent Variable Models

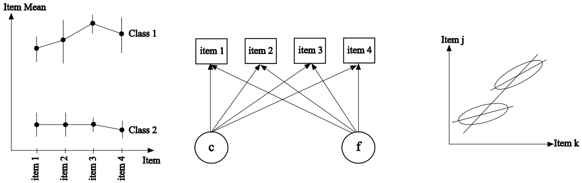
Factor Analysis (IRT)



Latent Class Analysis



Factor Mixture Analysis



Latent Variable Models For 7 LCSS Items (Not Including Hemoptysis Or Cough) At Visit 0, n=216

Model	Loglikelihood	# par.'s	BIC	Comments
Factor analysis				
M1: EFA 1f	-6857	21	13827	$\chi^2(14) = 63$, CFI = 0.92
M2: EFA 2f	-6836	27	13818	$\chi^2(8) = 22$, Heywood
M3: EFA 3f	-6827	32	13827	$\chi^2(3) = 31$, Heywood
M4: CFA 1gf 1sf	-6840	25	13814	$\chi^2(10) = 31$, CFI = 0.97, Heywood
M5: MIMIC 4x 3y	-6839	27	13824	$\chi^2(8) = 20$, CFI = 0.95

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Latent class analysis				
M6: LCA 2c	-6915	22	13947	52% in high class
M7: LCA 3c	-6843	30	13848	
M8: LCA 4a	-6815	38	13835	
M9: LCA 5c	-6798	46	13843	

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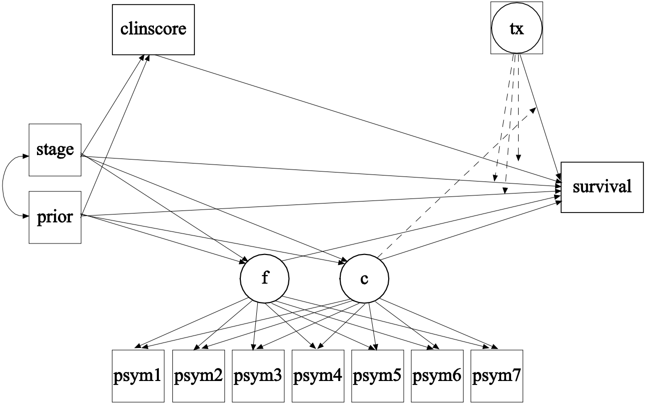
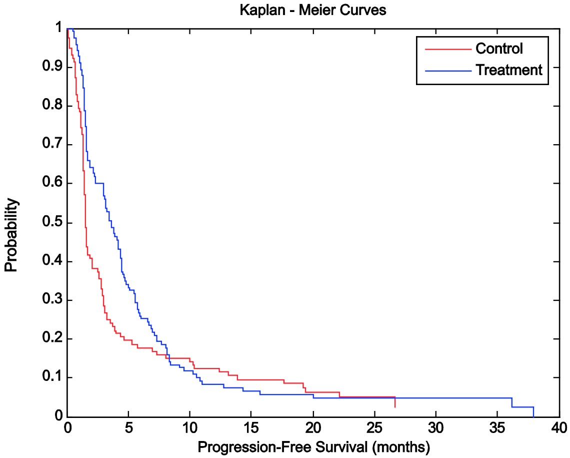
Factor mixture analysis				
M10: FMA 2c 1f	**-6823**	**29**	**13802**	**39% in high class, entropy = 0.840**
M11: FMA 3c 1f	-6796	37	13791	only 3% in one class

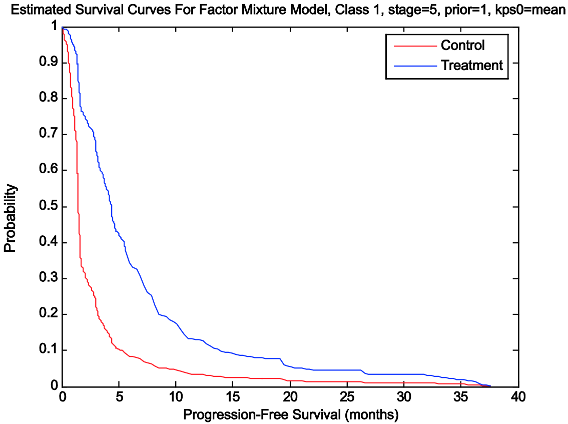
Predicting Survival From Visit 0 Using a Factor Mixture Model For LCSS Items



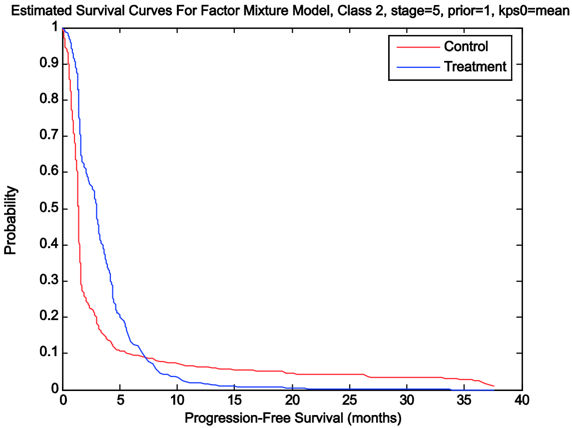
Survival Curves Showing Overall Treatment Effect



Survival Curves For Low-Symptom Class



Survival Curves For High-Symptom Class



Latent Variable Integration: Example 4

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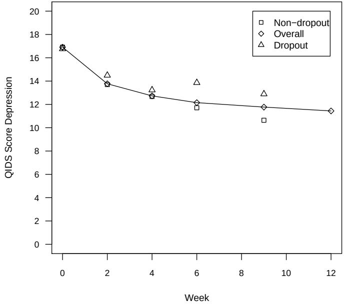
Latent Variable Integration: Example 4

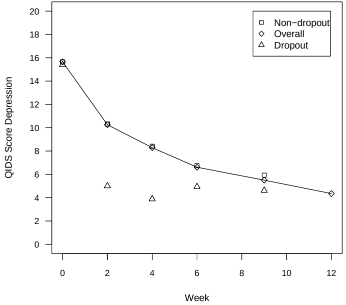
- Growth mixture modeling
- Survival analysis
- Missing data modeling

Example 4: Longitudinal Data From An Antidepressant Trial (STAR*D) $n = 4041$

Subjects treated with citalopram (Level 1). No placebo group
Sample means of the QIDS depression score at each visit:

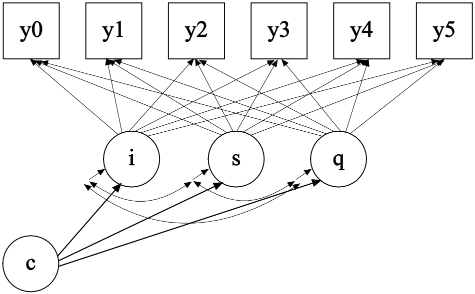


Next level

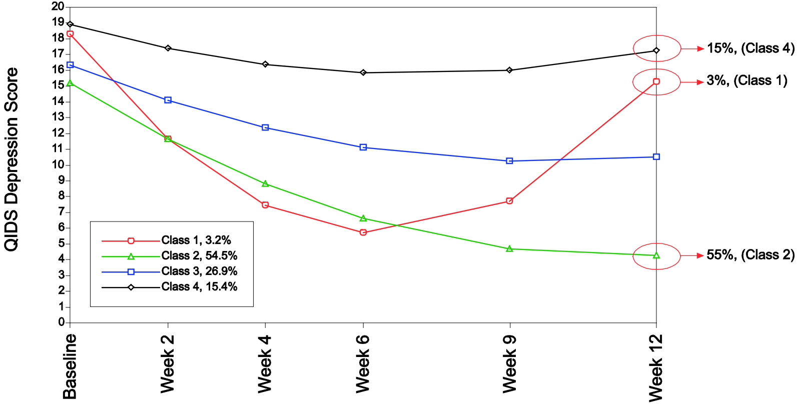


Follow-up

Growth Mixture Model Assuming MAR



4-Class Growth Mixture Model



Not Missing At Random (NMAR): Non-Ignorable Dropout Modeling

NMAR: Missingness influenced by latent variables

- Data to be modeled are not only outcomes but also missing data indicators

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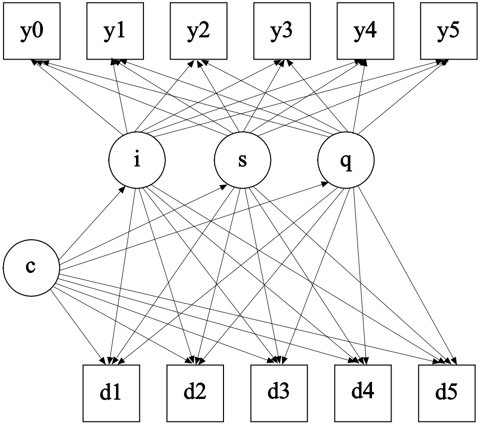
NMAR: Missingness influenced by latent variables

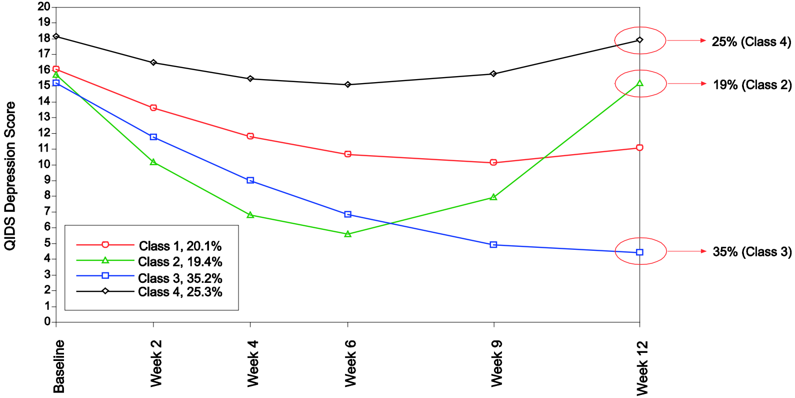
- Data to be modeled are not only outcomes but also missing data indicators
- Two general approaches:
    - Pattern-mixture modeling: Dropout occasion influences growth parameters
    - Selection modeling: Growth features influence dropout occasion

Muthén, Asparouhov, Hunter & Leuchter (2011). Growth modeling with non-ignorable dropout: Alternative analyses of the STAR*D antidepressant trial. **Psychological Methods**.

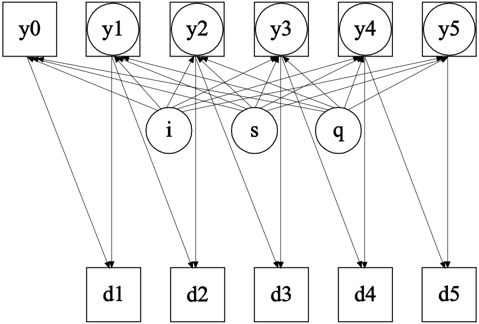
Beunckens Mixture Model (Mixture Wu-Carroll Model): Adding Dropout Information (Survival Indicators)



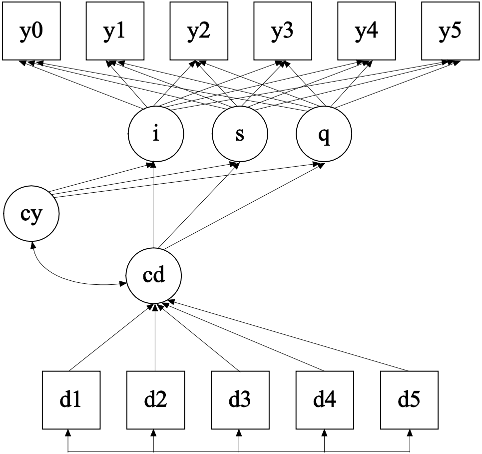
4-class Beunckens Selection Mixture Model



Diggle-Kenward NMAR Selection Model



Muthén-Roy Pattern-Mixture Model (d's are dropout dummies)



Comparing Trajectory Class Percentages Across Models

The NMAR approach of adding dropout information gives a less favorable conclusion regarding drug response than assuming MAR

Model	Response class	Temporary response class	Non-response class
MAR	55 %	3 %	15 %
NMAR models:			
Beuncken	35 %	19 %	25%
Muthén-Roy	32 %	15 %	14 %

Latent Variable Integration: Example 5

- Exploratory factor analysis
- Structural equation modeling
- Item response theory analysis
- Growth modeling
- Latent class analysis
- Latent transition analysis (Hidden Markov modeling)
- Growth mixture modeling
- Survival analysis
- Missing data modeling
- Multilevel analysis
- Complex survey data analysis
- Bayesian analysis
- Causal inference

Latent Variable Integration: Example 5

- Latent class analysis

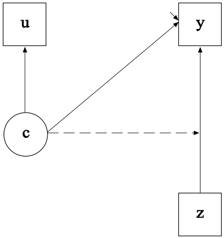
- Causal inference

Example 5: Estimating Treatment Effects in Randomized Trials with Non-Compliance

- Angrist, Imbens, Rubin (1996). Identification of causal effects using instrumental variables. **Journal of the American Statistical Association**
- Little & Yau (1998). Statistical techniques for analyzing data from prevention trials: treatment of no-shows using Rubins causal model. **Psychological Methods**
- Jo (2002). Estimation of intervention effects with noncompliance: Alternative model specifications. **Journal of Educational and Behavioral Statistics**

Potential outcomes, principal stratification, latent classes (mixtures)

Causal Effect For Compliers (CACE) Via Mixture Modeling



- z is a 0/1 dummy variable indicating treatment assignment
- c is a latent class variable (Complier and Non-Complier)
- u is a categorical variable with categories Show and No-Show.
  - u is missing for the control group
  - u is identical to c for the treatment group (c observed for Tx)

CACE Mixture Modeling

CACE modeling is popular:

- Overall treatment effect often insignificant while the effect in the complier class is significant (e.g. JOBS data)

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New developments, Part 1:

- Model weakness 1: Participation dichotomized and assumed to be the same as compliance class ($u = c$)

CACE Mixture Modeling

CACE modeling is popular:

- Overall treatment effect often insignificant while the effect in the complier class is significant (e.g. JOBS data)
  - - but the modeling has weaknesses:

New developments, Part 1:

- Model weakness 1: Participation dichotomized and assumed to be the same as compliance class ($u = c$)
- New solution: Estimate the relationship between c and u ($u \neq c$), where u need not be binary but can be counts or continuous
  - Fits JOBS data better and indicates a weaker relationship between c and u, giving a different treatment effect

CACE Mixture Modeling

New developments, Part 2:

- Model weakness 2: All compliers are assumed to benefit equally from the treatment

New developments, Part 2:

- Model weakness 2: All compliers are assumed to benefit equally from the treatment
- New solution: Add a complier class with no treatment effect
- Fits JOBS data better and shows a sizeable group who don't benefit, giving a different treatment effect

Sobel & Muthén (2011). Compliance mixture modelling with a zero effect complier class and missing data. Paper submitted for publication.

Further Latent Variable Integration

- Tihomir Asparouhov talk on multilevel modeling
- Katherine Masyn talk on growth and survival modeling

- Talk handout at www.statmodel.com