Intensive Longitudinal Data: Applications to Real-Time Health Data Collection

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APHS Breakfast Club
November 11, 2018



APPLIED PUBLIC HEALTH STATISTICS SECTION

- Founded in 1908 Longest Continuously Running APHA Section!
- Webinars, Workshops, Scientific Sessions, Networking, Section Awards, . . .
- Chair: Lei Zhang (lei.zhang@msdh.state.ms.us)
- Membership: Wei Pan (wei.pan@duke.edu)

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APPLIED PUBLIC HEALTH STATISTICS SECTION

- APHA 2018 Highlights:
 - Tuesday, 10:30 AM: APHS Student Poster Competition
 - Tuesday, 12:30 PM: APHS Luncheon, Awards Ceremony, and Lowell Reed Lecture
 - Tuesday, 3:00 PM: Current and Future: Student Finalist Presentations and Spiegelman Awardee Presentation
 - Tuesday, 6:30 PM: Section Social

About the instructors

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Github site: https://github.com/lalondetl/APHSWorkshop

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Motivating Studies

Marijuana Use, Co-Use, and Motivation

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Marijuana Study

- Aims to quantify the momentary relationships among motivation, social context, marijuana craving, and marijuana use.
- Aims to describe daily co-use of alcohol and marijuana





Marijuana Study

- Use momentary behaviors such as craving, anxiety, and mood to predict upcoming marijuana use (frequency and time)
- Identify personality traits (impulsivity, volatility of mood, self-control) and contextual factors (with others, studying) associated with co-use of alcohol and MJ.
- In addition, traditional longitudinal goals of evaluating academic performance



Marijuana Study

Recruiting and Baseline Procedure:

- Convenience Sample
- Brief screening call
- Use survey and urinalysis
- Extensive baseline interview
- Training with LifeData App

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Marijuana Study

ILD Data Collection:

- Participants prompted 3 times per day for 14 consecutive days (two weekends, random start)
- Prompts scheduled randomly within windows selected so as not to interfere with work, classes, etc.
- Identical questions, some skip logic
- Momentary: "Please rate your mood in the current moment."
- Interval: "Since the last time you were prompted, how many times have you used?"
- Time Stamp: "Please provide the date(s) and time(s) of your marijuana use."

Motivating Studies

Smart-T2

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Smart-T2 Cessation Study

- Aims to compare the effects of three treatment approaches on smoking cessation outcomes.
- Aims to identify contextual factors and treatment mechanisms associated with cessation.







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Smart-T2 Cessation Study



Weighted algorithm predicts smoking lapse based on risk factors:

- Urge to smoke
- Stress
- Cigarette availability
- Low motivation to quit
- Alcohol Use
- Interacting with others smoking

Businelle et al. (2016)

Smart-T2 Cessation Study

- Study Procedure
 - Participants (n=90) followed for 5 weeks
 - 1 week before quit date
 - 4 weeks after quit date
 - All participants
 - Receive smartphone with InsightTM app and nicotine replacement therapy
 - Complete 5 EMAs per day (1 Daily Diary and 4 Random Assessments)
 - Compensated for in-person visits and percentage of EMAs completed

Smart-T2 Cessation Study

- In Smart-T intervention group only
 - Algorithm identifies level of risk using
 - EMA responses
 - Self-reported interest in quitting
 - Risk level dictates appropriate tailored message
 - Automatically pushed for just-in-time intervention

Smart-T2 Cessation Study

Condition Participant not interested • in quitting

Themes

Example Messages

General motivation Planning for quit attempt

 Benefits of quitting On average, non-smokers live 12 years longer than smokers AND ex-smokers live up to 10 years longer than smokers who don't quit.

Low Risk of Imminent Lapse

abstinence

 General cessation advice Maintaining

Remember: Every day without cigarettes is a success. The first few hours and days are the hardest. It gets easier as time goes by. HANG IN THERE! You're doing it!

Imminent Lapse

High Risk of

Tailored to highest risk factor (e.g., urge, stress)

Don't let negative emotions keep you from a healthier life! When you feel stressed or angry, distract yourself, go for a walk, get out of the situation for a few minutes, try deep breathing exercises.

Goals for this workshop	
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About this workshop	
■ Today's Workshop Goals - Provide an overview of ILD using contemporary	
examples - Provide foundations of ILD • Ongoing Workshop Goals	
Provide materials to facilitate the analysis of ILD Not proficiency in data analysis	
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Today's Workshop Goals	
 Identify goals, hypotheses and research questions for studies using intensive 	· · · · · · · · · · · · · · · · · · ·
longitudinal data (ILD)	

- Explain strengths and limitations of ILD methods
- Distinguish between basic designs for ILD
- Discuss basic models for ILD
- Briefly describe advanced models for ILD
- Summarize real-world examples of research projects using ILD

	Ongoing	Workshop	Goals
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- Utilize workshop materials as a guide to
 - Manipulate the format/structure of ILD
 - Visualize and summarize/describe ILD
 - Apply multilevel models to ILD with continuous and binary outcomes
 - Apply variance modeling of ILD
 - Interpret results from ILD models
 - Determine when a more advanced modeling approach is appropriate

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Define ILD

- Data from repeated measurements on same individual
 - ~30 or more measurements
 - In real-time
 - In natural environment
- Collection aided by modern technology
 - Historically pen and paper daily diaries used
- Common terms for method of collecting ILD
 - Experience Sampling
 - <u>E</u>cological <u>M</u>omentary <u>A</u>ssessments (EMA)

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Types of ILD

Researcher Initiated

- Time-based assessment prompts based on a defined schedule
 - Once per day or week
 - Participant asked to aggregate data by summarizing their experience over a day
 - Provide average measure (intensity of craving)
 - Summarize event measures (number of cigarettes smoked)
 - Asked to do both (number and intensity of headaches)
 - Less salient (or more ordinary) events may be remembered less accurately resulting in bias

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Researcher Initiated

- Time-based assessment prompts based on a defined schedule
 - Multiple times per day
 - Fixed-intervals
 - Evenly spaced
 - Helpful for modeling correlation among outcomes
 - Potential bias from participant anticipating assessment

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Researcher Initiated

- Time-based assessment prompts based on a defined schedule
 - Multiple times per day
 - Randomly within time interval
 - Unevenly spaced
 - "Random sample from an individual's experience" similar to "Random sample from population"
 - Sampling randomly inside blocks of time
 - Helpful for capturing dynamic behaviors that change over time
 - Element of "surprise" may reduce potential for bias

Researcher Initiated

- Event-based assessment prompts occur when an event detected by study device
 - Location detected
 - Device detects participant has entered a tobacco retail building
 - Characteristic detected
 - Device detects participant has high heart rate

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Participant Initiated



- Event-based participant chooses to interact with study staff/device without being prompted
 - Record completed action or event

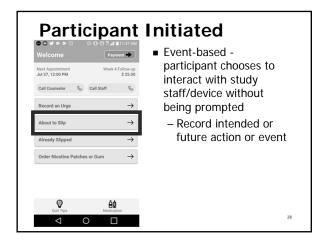
Quit Tips ÉÓ

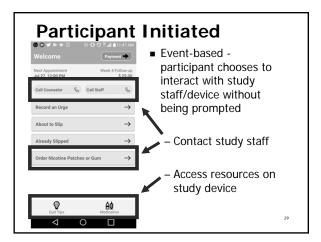
Participant Initiated



- Event-based participant chooses to interact with study staff/device without being prompted
 - Record current emotional state or behavior







Event-based EMAs

- For both researcher and participant initiated
 - Must have clear definition of event
- For participant initiated
 - Train individuals to identify event
 - Participants will still fail to report events
 - \blacksquare Cannot know when "missing event" occurred
 - Cannot assess compliance

Passive/Incidental

- Data that is automatically collected on a study device without a specific prompt by researcher or initiation by participants
 - Smart devices that collect GPS coordinates
 - Accelerometers that track physical activity or sedentary behavior
 - Technology-enhanced pill bottles that track when bottle opened (medication compliance)

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Strengths and Limitations of ILD

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Strengths of ILD

- Behaviors/measures observed in natural environment
- Measurement in "near real-time" reduces recall bias
- Identify relationships between variables within a subject/participant
- Directly observe processes of change in relationship among variables
 - Within subject changes across time
 - Between subject differences

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- Participant burden
 - 4 random assessments per day for 5 weeks
 - 4 X 7 X 5 = 140 observations per person
 - 1 daily diary per day for 5 weeks
 - 1 X 7 X 5 = 35 observations per person
 - All 5 daily assessments
 - 5 X 7 X 5 = 175 observations per person
 - Over course of study
 - 2 minute EMA -> more than 5 hours
 - 3 minute EMA -> more than 8 hours

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Limitations of ILD

- Large amount of data produced
 - All 5 daily assessments (n=150)
 - 175 X 150 = 26,250 total observations
 - Only daily diary (n=150)
 - Daily diaries = 35 X 500 = 5,250
 - Passive data i.e. accelerometer
 - 13 million total observations for one school
- Storing capacity, server space
- Data processing and manipulation slower

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Limitations of ILD

- Requires complex models which are more difficult to interpret
- Not appropriate for rare events
- Requires alternative method of assessing measurement reliability
- Reactivity

Goals of ILD	
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Goals of ILD Studies Estimation of relationships that change over time both among individuals and	
within them - Distinguish between-subject and within-subject effects - Allow for variability in within-subject process	
(random effects)Identify differences based on person-level baseline predictors	
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Goals of ILD Studies

- Estimate associations with cyclic or periodic patterns
- Estimate impact of predictor on outcome
 - Actual value or change in value
 - Synchronous or sequential
- Estimate variability or volatility
 - Identify differences based on person-level baseline predictors
 - Identify difference before versus after an event

Format and Structure of ILD

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Format and Structure of ILD

- "Wide" format
 - Each column includes one measurement time of a variable
 - Each row contain only one participant
- "Long" format
 - Each column contains a variable
 - Each row includes one measurement time for a participant

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Format and Structure of ILD

- "Wide" format
 - Each column includes one measurement time of a variable
 - Each row contain only one participant

Wide format

				Y at Time 2		Z at Time 2
1	5	3	1	0	2	2
2	4	4	1	1	1	1

Format and Structure of ILD

- "Long" format
 - Each column contains a variable
 - Each row includes one measurement time for a participant

Long format

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
2	1	4	1	1
2	2	4	1	1

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Format and Structure of ILD

Long format

ID	Time	X	Y	
1	1	5	1	2
1	2	3	0	2
2	1	4	1	1
2	2	4	1	1

Wide format

				Y at Time 2		Z at Time 2
1	5	3	1	0	2	2
2	4	4	1	1	1	1

Format and Structure of ILD

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

Simplified example data

- ID study ID
- Time time point
- X stress level
 - Likert scale
 - 1= very low to 7= very high

Format and Structure of ILD

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

Simplified example data

- Y smoked since last contact
 - Binary/dichotomous
 - 1= Yes or 0= No
- Z Treatment group
 - Binary/dichotomous
 - 1= Intervention or 2= Control

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Format and Structure of ILD

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

Simplified example data

- Long format
 - Multiple rows per subject
- Static variables
 - Z (Treatment Group)
- Time varying variables
 - X (Stress)
 - Y (Smoke)

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Format and Structure of ILD

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

Simplified example data

- Time varying variables
 - Can vary within subject
 - Within subject variability can differ across subjects
- Each row represents a specific time or time frame

Temporality in ILD

ID	Time			
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

How can we assess the relationship between X and Y?

- Data can be used "as is" when current contextual or environmental cues are of interest
- Example: interest in immediate effect of cigarette ad on intention to quit smoking

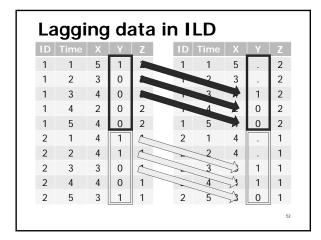
Temporality in ILD

ID	Time	Х	Υ	Z
1	1	5	1	2
1	2	3	0	2
1	3	4	0	2
1	4	2	0	2
1	5	4	0	2
2	1	4	1	1
2	2	4	1	1
2	3	3	0	1
2	4	4	0	1
2	5	3	1	1

How can we assess the relationship between X and Y?

- Data must be manipulated when exposure must precede outcome
- Example, interest in effect of stress on subsequent smoking behavior

Lagging data in ILD



Lagging data in ILD

- Depends on research question and variables of interest
 - Determine how far before the event of interest an exposure must occur
 - Determine types of ILD to include
 - Researcher or participant initiated
 - Fixed or random interval
- May require further manipulation of data
 - Limiting dataset to relevant observations

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Basic Description of ILD

Dasic Description of the	Basic	Descriptio	n of ILD
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- Individual variable and pairwise relationships
 - Central tendency for continuous data
 - Distribution for categorical data
- Aggregated within person
 - Total or mean number of events
 - Throughout study
 - In certain time periods
- Important to minimize aggregating across individuals -> ignores repeated observations on individuals

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Basic Description of ILD

- Exploring your data:
 - NOT intended to inform hypotheses tested
 - Intended to **provide context** for conclusions
 - Intended to describe sample
 - Can identify potential issues with proposed models

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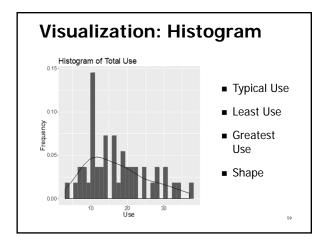
Visualization of ILD

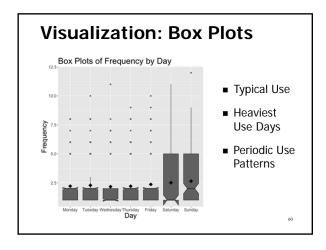
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Visualization of ILD

While not often published, visualization is a crucial component of exploring ILD

- Summary Statistics and Raw Data: Distributions by Participant
 - Histogram
 - Box Plot





Visualization of ILD

While not often published, visualization is a crucial component of exploring ILD

- Raw Data: Relationships and Time Trends
 - Interaction Plots
 - Time Plots
 - Spaghetti Plots

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Visualization: Spaghetti Plots Spaghetti plot 12.5 10.0 10.0 20.5 TimeInStudy 50.0

Visualization: Spaghetti Plots

Important Information from Spaghetti Plots:

- <u>Time Trends:</u> Do participants appear to show a discernible increase, decrease, periodic trend?
- <u>Interactions:</u> Do the time trends appear to change for different sub-populations?
- <u>Variation:</u>
 - Do participants show similar fluctuations over time?
 - Is the volatility consistent across the study?
 - How does variation between subjects compare to variation within subjects?

Multilevel	Modeling	of
ILD		

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Multilevel Modeling (MLM)

- MLM used when observations correlated
 - Natural grouping
 - Students in a classroom
 - Clinics in a hospital
 - Members in a family
 - Repeated measures (longitudinal data)
 - Before and after intervention
 - Follow-up time points after intervention
 - Intensive longitudinal data

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Multilevel Modeling of ILD

- Two-level model
 - Single equation describes relationship between predictors and outcome
 - Conceptualized as two separate equations
 - Level 1
 - Level 2

Two-level Modeling of ILD

- Level 1
 - Describes within person relationship of predictor and outcome
 - Models momentary predictors of momentary outcomes (occasion level)
 - Regression coefficients (intercepts, slopes) estimated for each moment level predictor variable
 - Intercepts and slopes can vary randomly across persons (random effect)

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Two-Level Modeling of ILD

- Level 2
 - Regression coefficients (intercept, slope) from level 1 treated as dependent variable
 - Describes individual differences in the effect of momentary variable on the outcome
 - Person-level predictors modelled (not expected to change across time points)
 - Residual term accounts for portion of individual differences in coefficients not accounted for by person-level predictors

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Multilevel Modeling of ILD

- Fixed effects
 - Assume effect of predictor on outcome constant across people
 - Or that person-level variables account for all differences in effect of predictor on outcome
- Random effects
 - Allows effect of predictor on outcome to vary across people (Level 1)
 - In other words, allow people to differ in their within-person relationships

Multilevel Modeling (MLM)

- Why use MLM?
 - Correctly accounts for clustering in data
 - Allows variability across participants and groups
 - Group treated as random sample from population of groups
 - Thus, can generalize to the population of groups
 - Robust to missing data
 - Participants do not need same number or timing of observations

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MLM of ILD

Models the dependent variable in terms of baseline and ILD variables and time

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MLM of ILD

Models the dependent variable in terms of baseline and ILD variables and time



- For ILD Variables, can decompose effects
- Allows for direct interpretation of effects between people and effects across time
- We will focus on this method in these slides

Neuhaus and Kalbfleisch, 1998

Models the mean of an outcome, in terms of

Dependent Variable Baseline Variables Variables Time Across Within Individuals Variables

$$Y_{it}$$

$$= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it})$$

$$+ \beta_t t_{it} + \upsilon_i + \varepsilon_{it}$$

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MLM of continuous ILD

■ Models the mean of an outcome

$$Y_{it} = \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \beta_t t_{it} + \upsilon_i + \varepsilon_{it}$$

- lacksquare β_0 is intercept term
- Z_i is a baseline, time-independent predictor with effect β_1

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MLM of continuous ILD

■ Models the mean of an outcome

$$Y_{it}$$

$$= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it})$$

$$+ \beta_t t_{it} + \upsilon_i + \varepsilon_{it}$$

- lacktriangle χ_{it} is an ILD, time-dependent predictor with,
 - Between effect β_{2B} , and
 - Within effect $\beta_{2\textit{W}}$

■ Models the mean of an outcome

$$Y_{it} = \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \beta_t t_{it} + \upsilon_i + \varepsilon_{it}$$

- lacktriangle t_{it} is the time in the study with effect eta_t
- ullet v_i is the random individual effect
- \bullet ϵ_{it} is the random variation over time

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MLM of continuous ILD

- Consider the following model
 - Alcohol craving as outcome, Y_{it}
 - Age as time-independent baseline predictor, $Z_{\it i}$
 - Mood as time-dependent ILD predictor, χ_{it}

$$\begin{aligned} Y_{it} &= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \beta_t t_{it} + \upsilon_i + \varepsilon_{it} \end{aligned}$$

 $lack eta_1$ represents the expected difference in the mean alcohol craving across populations that differ, on average, by one year in age

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MLM of continuous ILD

- Consider the following model
 - Alcohol craving as outcome, Yit
 - Age as time-independent baseline predictor, $\boldsymbol{Z_i}$
 - Mood as time-dependent ILD predictor, χ_{it}

$$\begin{aligned} Y_{it} \\ &= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \ \beta_t t_{it} + \upsilon_i + \varepsilon_{it} \end{aligned}$$

 β_{2B} represents the expected difference in the mean alcohol craving across populations that differ by one unit of average mood reported

- Consider the following model
 - Alcohol craving as outcome, Y_{it}
 - Age as time-independent baseline predictor, Z_i
 - Mood as time-dependent ILD predictor, χ_{it}

$$\begin{aligned} Y_{it} &= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \beta_t t_{it} + \upsilon_i + \varepsilon_{it} \end{aligned}$$

 β_{2W} represents the expected change over time for an individual in their mean alcohol craving as their mood changes

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MLM of continuous ILD

- Consider the following model
 - Alcohol craving as outcome, Y_{it}
 - Age as time-independent baseline predictor, $Z_{\it i}$
 - Mood as time-dependent ILD predictor, χ_{it}

$$Y_{it} = \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) + \beta_t t_{it} + \upsilon_i + \varepsilon_{it}$$

 $lack v_i$ represents the variation in individual alcohol craving among the population of individuals

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MLM of continuous ILD

Consider an example:

- Model the outcome of desire to use marijuana in terms of
 - Momentary indicator of whether individual is with others, time-dependent variable
 - Energy level, decomposed into
 - Average energy level, a person-level, timeindependent variable
 - Momentary energy level, a lagged, timedependent variable

Example: Model "Desire" in terms of "With Others" and "Energy Level"

- With Others: $\beta = -3.43$, p=0.038
 - Expect populations with others to show lower Desire (by about 3.43), all other factors equivalent
- Energy (Between): $\beta = -0.09$, p=0.502
 - Expect populations with greater energy to show lower Desire (by about 0.09)
- Energy (Within): $\beta = 0.02$, p=0.371
 - Expect individuals to show an increase in Desire over time with increased energy (by about 0.02)

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MLM of Binary ILD

Models the **probability** of an outcome, in terms of

$$\begin{aligned} & \operatorname{logit}(\pi_{it}) \\ &= \beta_0 + \beta_1 Z_i + \beta_{2B} \overline{\chi}_{i.} + \beta_{2W} (\overline{\chi}_{i.} - \chi_{it}) \\ &+ \beta_t t_{it} + v_i \end{aligned}$$

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MLM of Binary ILD

Consider an example:

- Model the outcome of use of marijuana in terms of
 - Momentary indicator of whether individual is with others, time-dependent variable
 - Energy level, decomposed into
 - Average energy level, a person-level, timeindependent variable
 - Momentary energy level, a lagged, timedependent variable

MLM of Binary ILD

Example: Model Likelihood of "Use" in terms of "With Others" and "Energy Level"

- With Others: $\theta > 7.9e10$, p=0.865
 - Expect odds of use for populations with others to increase by a multiple of 7.9e10, all other factors remaining constant
- Energy (Between): $\theta = 0.98$, p=0.279
 - Expect odds of use for populations with greater energy to decrease by a multiple of 0.98
- Energy (Within): $\theta = 1.004$, p=0.156
 - Expect odds of use to show an increase over time by a multiple of 1.004 with increased energy

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Additional ILD Considerations

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Some Recent Methods in ILD

- Hurdle models for zero-inflated data
- Recurrent survival models for recurrent time-to event outcomes
- Time-varying effect models to estimate if and how effect changes over time
- Just-in-time adaptive interventions (JITAI)

JITAI

- Intervention based on decision rules
- Aim to provide the right amount of intervention or support at the right time
 - No intervention when not needed
- Uses dynamically changing information
- Identifies opportunities to provide intervention in the natural environment
- Four key components to consider

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JITAI

- Examples
 - Alert participant after 30 continuous minutes of sedentary behavior
 - Alert participant when technology-enhanced pill bottle not opened 30 minutes past scheduled medication time
 - Provide message or video intervention after assessment indicates participant who has quit smoking is at risk of smoking a cigarette

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Missingness in ILD

- Can be due to the usual suspects
 - Loss to follow up
 - Sporadic missing
 - MCAR, MAR, or NMAR
- Can be due to technology specific issues
 - Phone
 - Cell tower Server

Communication across technologies

 Develop a plan for dealing with both in staff procedures and in analyses

Acknowledgements

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