

**Latent Trait Pattern-Mixture Mixed-Models  
for Ecological Momentary Assessment Data**

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THESIS

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## LIST OF ABBREVIATIONS

AIC	Akaike Information Criteria
BIC	Bayesian Information Criteria
BS	Between-Subject
CI	Confidence Interval
EMA	Ecological Momentary Assessment
GPA	Grade Point Average
ILD	Intensive Longitudinal Data
IRT	Item Response Theory
LC	Latent Class
LTPMMM	Latent Trait Pattern-Mixture Mixed-Model
MAR	Missing at Random
MCAR	Missing Completely at Random
MI	Multiple Imputation
MLE	Maximum Likelihood Estimation
MMLE	Marginal Maximum Likelihood Estimation
MNAR	Missing Not at Random
NA	Negative Affect
NMR	Negative Mood Regulation
PA	Positive Affect

## LIST OF ABBREVIATIONS (Continued)

RMSE	Root Mean Squared Error
WS	Within-Subject

## SUMMARY

In this dissertation, a latent trait pattern-mixture mixed-model (LTPMMM) for Ecological Momentary Assessment (EMA) data is developed in which subject-level observations are collected in an intermittent fashion. Initial work with intermittent missing data has used latent class pattern-mixture models. Based on Item Response Theory (IRT) models, a latent trait is used to model the missingness mechanism and estimated jointly with a mixed-effects model for longitudinal outcomes. Both one- and two-parameter LTPMMM are presented. These pattern-mixture models offer a novel way to analyze EMA data with many unique response patterns that cannot be easily formed into latent classes. Also, the proposed model provides valuable information about the response process through item difficulty and discrimination parameters.

Data collected from an EMA study involving high-school student's positive and negative affect are presented. The EMA data used in this dissertation was collected over a varying number of days for each student and contains many unique response patterns. The two model forms will estimate a latent trait that corresponds to the students' "ability" to respond to the prompting device. The latent trait will be estimated using the respondents' unique response patterns. The proposed latent trait pattern-mixture model shows that a student's mood assessed by positive and negative affect are influenced by the latent trait. Also, the proposed model caused some model regression coefficients to change and increased statistical significance as compared to the standard model approaches.

One thousand simulations were performed to test two forms of the proposed model across different modelling scenarios. The LTPMMMs were compared to a missing at random (MAR) mixed-model and a latent class pattern-mixture model. The proposed model has lower bias and increased efficiency as compared to standard approaches such as the latent class pattern-

## SUMMARY (Continued)

mixture model. This is especially true when the latent trait for responsiveness is correlated with a model covariate such as gender.

Although the proposed pattern-mixture model provides a new method to analyze EMA data, it is not without some weaknesses such as long computing times due to estimation of many model parameters. The drawbacks and future plans to assess the proposed LTPMMM will also be presented in this work.

## CHAPTER 1

### INTRODUCTION

Missing data are very common in longitudinal studies. In some cases, missing values occur in an intermittent or non-monotone fashion where a subject can have information collected after a missed visit. In many instances, intermittent missing data are assumed to be ignorable. Assuming an incorrect missing data mechanism generally causes biased parameter estimates and inefficient variances. In cases where the missingness mechanism for intermittent missing data is assumed to be *missing not at random* (MNAR), pattern-mixture models are often used. This is because pattern-mixture models are usually less computationally intensive than selection models and do not require a correct distributional form of the missingness or drop-out mechanism. Pattern-mixture models are a useful tool if missingness patterns found from the data form natural groups of interest. For instance, pattern-mixture models are sometimes used in longitudinal clinical studies that compare dropouts and completers across treatment groups. If a longitudinal study contains more than a few time-intervals, the number of unique missingness patterns increases rapidly. Also, if many unique intermittent data patterns exist, it is usually problematic to choose an appropriate number of patterns needed in a pattern-mixture model that have a useful and clinical interpretation.

Ecological Momentary Assessment (EMA) is a modern data collection method that is often implemented to collect many repeated observations over a study period. For example, subjects may receive thirty or more prompts over the course of a week from a small hand-held computer. With some EMA studies, the collection prompts are generated at random times for each study subject and those subjects may miss or not answer a prompt. Therefore, with EMA data collection methods the number of response patterns can be large and inevitably contain

intermittent missingness. More research is needed to study the missingness properties of EMA data since very few works have thoroughly analyzed this problem.

Latent class theory provides a statistical method that can be applied to form the patterns needed in a pattern-mixture model for use with intermittent missing data. For these methods to be successful, however, a small number of unique patterns is generally needed. As was explained previously, EMA data usually contains a large number of response patterns, and many of these might be unique. With intermittent missing data, the computational techniques required to fit these models are quite complex due to the nature of the log-likelihood. Also, if a small number of meaningful groups cannot be found due to many unique intermittent missing data patterns, a different modelling approach may be needed. For instance, data collected using EMA methodology may not easily be fit using latent class pattern-mixture models, which may not determine latent classes that are meaningful, and may require a more appropriate model.

In this thesis I will extend the latent class pattern-mixture model approach of Lin et al. (2004) for intermittent missing data by developing a latent trait pattern-mixture mixed-model. The latent trait will be formed using theoretical concepts from Item Response Theory (IRT). The latent trait approach will allow each subject's "ability" to play a role in the estimation process instead of groups of subjects that are used in the latent class approach. This proposed model also bypasses the difficulty of determining a suitable number of classes needed with latent class pattern-mixture models that are descriptive and meaningful. Both one-parameter and two-parameter IRT models measuring individual "ability" to respond to random survey prompts will be explored. These two proposed models will be estimated jointly where a model fitting the latent trait is estimated concurrently with a mixed-model for longitudinal outcomes. The proposed model will be applied with EMA data where mood levels in high-school students measured by positive affect and negative affect are collected over many times in a weekly period.

In terms of organization, Chapters 2 to 5 will include a literature review. Chapter 2 will describe a brief overview of EMA collection methods and standard statistical models used for EMA data. Longitudinal mixed-effects model application and estimation are presented in Chapter 3. Chapter 4 will provide background material on missing data mechanisms and modelling approaches including multiple imputation methods, selection models, and pattern-mixture models. This chapter will also include a review of modelling techniques used with intermittent missing data. Chapter 5 will provide a summary of two latent variable methods that are used to summarize discrete categorical data: latent class and latent trait models. Estimation methods used with these two model types is also provided in this chapter. The proposed latent trait pattern-mixture mixed-model will be described in Chapter 6. Chapter 7 will fully outline the research plan for the proposed model. The next chapter provides a data analysis example of the model using EMA data. Chapter 9 describes the simulation plan applied to the proposed model using both one- and two-parameter formulations. Chapter 10 will present the simulation results from the latent trait pattern-mixture mixed-models. Chapter 11, will draw some conclusions about the proposed models. Lastly, Chapter 12 will briefly mention some directions for future research topics for the proposed LTPMMMs.



## CHAPTER 2

### ECOLOGICAL MOMENTARY ASSESSMENT DATA

In many psychological studies, accurate recordings of measures in natural settings can be done using EMA, which involves repeated sampling of subjects' current behaviors and experiences in real time, in subjects' natural environments (Shiffman et al., 2008). These methods have a long history in psychological research starting with a thirty-day study of mood by Flügel (1925). Initial methods to collect data using EMA began with paper-and-pencil daily diaries and questionnaires. Over time, EMA data has been collected using more advanced technical means including hand-held computers and cell-phones. The advantage of these electronic devices is that they allow for an accurate time-stamp of when the data were collected. Also, these devices can prompt a respondent through a method known as time-based assessment scheduling (Shiffman et al., 2008) in which random prompts are sent to study participants at different times throughout the day. This allows for more accurate measurement of the outcomes of interest as they occur. A brief overview of other timing methods used with EMA data can be found in Barrett and Barrett (2001) and Shiffman et al. (2008).

Many EMA collection methods have been applied in various settings such as clinical psychopharmacology (Moskovitz and Young, 2006), smoking studies (Shiffman et al., 2002; Hedeker et al., 2009), and behavioral medicine (Smyth and Stone, 2003). With EMA data collection, subjects go about their daily lives and respond to questions over a period of time. This allows for psychological outcomes to be measured when they happen in normal settings and lessens recall-bias that may occur with other collection methods such as paper-and-pencil diaries completed at a clinician's office. For instance, a respondent may alter their description of a mood-state after it occurs, may have trouble remembering what happened, or may under-

estimate the intensity of the event after it has taken place. The recall-bias is usually much less with EMA collection methods versus paper questionnaires because outcomes are recorded within a short time delay lasting a few minutes or less.

Sections 2.1 and 2.2 will describe statistical techniques that are used to analyze EMA data including longitudinal mixed-effects models and IRT models.

## **2.1 Ecological Momentary Assessment Data Models**

A concise overview of self-reported data in health research via EMA methods can be found in Stone et al. (2007). This work reviews the science, theory, application, and future developments of real-time data capture or EMA. Also, the collection presents analysis methods for data obtained by EMA methods, which are reviewed by Schwartz and Stone (2007) and Walls et al. (2007). The chapter by Schwartz and Stone (2007) applies the multi-level linear model of Bryk and Raudenbush (1992) for analysis of real-time momentary data. The chapter also describes how multi-level (or linear mixed-effects) models are an improvement over analysis of variance methods that were historically used for repeated measures data. The chapter by Walls et al. (2007) surveys different analytical approaches that can be used for EMA data including multi-level models, time series analysis, locally weighted polynomial regression methods, survival analysis, and point process models.

Schwartz and Stone (2007) outline various statistical issues with EMA data that need to be addressed by a potential model. One such issue is that EMA data are not equally spaced in time for all subjects, due to random collection times. Also, some covariates may vary throughout the course of a study, so a statistical method is needed that can handle time-varying covariates. Another issue is that EMA data usually has missing values due to the random nature of the prompts. Also, the assumption that the variance is constant both within-subjects and between-subjects is usually not true with EMA data. The authors stress that a

repeated measures analysis of variance model is insufficient because it cannot correctly account for these complexities seen in EMA data.

Schwartz and Stone (2007) also emphasize how mixed-effects models can handle these issues with EMA data. In particular, the longitudinal mixed-effects model developed by Laird and Ware (1982) is very suitable for data collected with an EMA mechanism for the following reasons. Longitudinal mixed-effects models can be used on outcomes containing different collection times for each subject, although these models are more complex than mixed-models with fixed collection times. The longitudinal mixed-effects models can also handle time-varying covariates and missing data. Also, longitudinal mixed-effects models are highly adaptable to different covariance structures used to model within-subjects and between-subjects variances. Also, the authors present an example using respondents' momentary assessment of their frustration levels that has a nested structure. The data contains variables at three levels: the person-level, the week-level, and the occasions-level. Schwartz and Stone (2007) conclude the chapter by describing how self-reported EMA data can be easily fit using standard statistical software including PROC MIXED in SAS. They also provide a thorough discussion of how different autocorrelation structures of the variance-covariance matrix can be tested and modeled for fitting EMA data.

The nested model structure contained in EMA data where lower level units (or data collected at random times) are nested into a higher level groups (or individuals) is appropriate with linear mixed-effects models. Also, linear mixed-effects models can handle intra-subject variability found in EMA data through the addition of random intercept and slope terms. This variability occurs due to correlated repeated measures from the same individuals collected through the course of the study. The typical way to assess this intra-subject variance is the intraclass correlation coefficient which is the ratio of the individual variance to the total variance

(Hedeker and Gibbons, 2006). In EMA studies, the intra-subject correlation can be quite high due to the large number of observations per subject and the close times in which observations are measured. For instance, in one example presented by Schwartz and Stone (2007), the estimated intraclass correlation between-persons is estimated to be 50%, which is definitely quite high. As expected, each subject's responses have a high degree of correlation over time because the EMA data were collected several times per day over a period of two weeks.

Another collection by Walls et al. (2006) describes analysis methods for Intensive Longitudinal Data (ILD) which are longitudinal data that typically have a high number of observations per subject, usually more than ten. Walls et al. (2006) present various methods to handle ILD including mixed-models, generalized estimating equations models, time series models, and item response theory (IRT) models, which are models usually used in education and testing applications. The next section will discuss some lesser-known and novel applications of IRT models in the context of EMA data.

## **2.2 Item Response Theory Models**

Item Response Theory is a method initially developed in psychological testing to score items or questions on a test. Bock (1997) provides a brief history of IRT and includes background material on estimation of these models. In IRT, the items (or questions) on a test have different difficulty and discrimination parameters that are used to determine the student's "ability" or latent trait. This latent trait is related to what the test is trying to measure. As an example, Bock (1997) explains how original work in IRT was based on measuring children's mental development through a series of word problem questions. The next paragraphs will show how IRT can be applied with EMA data by letting time-intervals (in which data are collected) represent items in an IRT model.

In the collection by Walls and Schafer (2006), Hedeker et al. (2006) present mixed-model approaches using EMA data from smoking research that was collected to study smoking behavior patterns in adolescents. Their models use IRT to assess the tendency of adolescents to smoke cigarettes early during their smoking experiences, where time-intervals are used as items and the dichotomous responses correspond to whether or not a subject smokes within the interval. Their approach is used to determine if different days and times of the week in which a subject smokes are important early markers of nicotine dependence. The longitudinal data are collected through an EMA mechanism and formed into different day and time indicators which are used in an IRT model. The models chosen in this work are basically longitudinal mixed-effects models with binary outcomes indicating if students smoked or not. With these IRT models, the authors concluded that mid-week smoking experiences have a more pronounced effect on adolescent smoking behavior and they also increase the possibility of smoking more than weekend smoking events. The method shows that these different days and times are important, and they also answer some other important issues related to smoking behavior. More recent applications combining longitudinal data and IRT models can be found in Liu and Hedeker (2006) and Liu (2008).

### **2.3 Location and Scale Effect Models**

As was discussed above, EMA data collection methods allow for many time-intervals to be collected over the study period. Therefore, EMA data allow for between-subject and within-subject changes to be studied using longitudinal mixed-models of Laird and Ware (1982). More recently, the article by Hedeker et al. (2008) develops location and scale models for data collected by EMA. These are models which allow the assumptions for constant error variance (or within-subjects variance) and variance of random effects (or between-subjects variance) to be relaxed. In particular, these two variance terms are modeled under a log-linear structure. Also, these

variances can easily be modeled in a mixed-model framework, and they can depend on model covariates as well. The location (mean) and scale (variance) of these distributions reveal more information about the changes in moods across time and in particular, the variation in these mood changes.

## 2.4 Missing Data

The two collections Stone et al. (2007) and Walls et al. (2006) present valuable tools for EMA data analysis and stress the importance of missing data techniques. Missing data can occur for various reasons in EMA studies. These reasons can be separated into two types: respondent missingness and device missingness. In device missingness, some flaw genuinely occurs with the prompting device causing a prompt to be generated, but not heard by the respondent. In respondent missingness, prompts are not answered by the respondent because they do not want to answer it. Although both types are important, the focus in this dissertation will be on the respondent missingness, where a prompt was heard and not answered, a prompt was not heard and therefore, not answered, or the prompting device was turned off. A thorough discussion of other types of missingness from EMA data can be found in Stone and Shiffman (2002).

Ecological momentary assessment methods using time-based assessment schedules use phones, beepers, or hand-held computers to prompt study subjects over the course of the study. Many of these times may be very inconvenient for a subject to respond. For example, in EMA data collected from high-school students, a subject may be in class or with a group of friends and may not want to answer a prompt. Also, subjects may turn the prompting device off at certain times so that the prompts are less bothersome. Therefore, EMA data may contain many patterns of intermittent missing values among study subjects. A mixed-model used to analyze

EMA data will then need to account for the intermittent missing data, especially if these data are missing due to a non-random process.

Usual approaches to handling missing data from EMA collection make mention of the missing values found in the data, but typically do not present formal modelling methods for the missingness structure. An example of this is found in Thomas et al. (2011), who state that missing values were not imputed in any generalized mixed models fit to EMA data collected to study normal eating or overeating behavior. A similar study by Munsch et al. (2009) uses mean substitution of missing outcome values, where the number of weekly eating binges is of interest. A paper by Granholm et al. (2008) mentioned that the extent of EMA missing data were unrelated to study covariates such as age, gender, and symptom severity of schizophrenia. These techniques may be appropriate in the works cited here, but it is not usually true that missing data do not influence study outcomes. As stated by Shiffman et al. (2008) missing assessments have the potential to bias the obtained sample of behavior and experience, especially if the missing data mechanism is non-random.

Other research has documented the extent or reasons for missing data from EMA. Collins et al. (2003) compares paper-and-pencil reporting to EMA data collection from cellular phones and concluded that compliance rates are comparable in two arms of ten subjects. Another study by Aaron et al. (2004) documents reasons interviews were missed in EMA assessment of pain, mood, and stress. The most common reason was that respondents did not hear the alarm, but other factors such as emotional, pain, and inconvenience were noted as well. These two papers show that researchers are aware that missingness is an issue with EMA data, but may be not aware of statistical techniques that can be used with missing data.

A doctoral dissertation by Gloster (2006) used linear interpolation to account for missing data within individuals who missed one or more EMA observations. Although this method has

advantages by ensuring that no information is deleted due to missingness, the drawbacks of this simple method have been described by Verbeke and Molenberghs (2000) and Little and Rubin (2002). Interpolation or mean substitution methods tend to artificially reduce variability, especially in situations where data are collected in a longitudinal fashion.

One excellent example using more sophisticated statistical methodology is found in a recent article by Bunouf et al. (2012), who describe a technique to analyze intensive longitudinal data of pain evaluations from a clinical trial. A total of 126 daily evaluations of pain were collected by electronic diary and multiple imputation methods based on a multivariate normal distribution were used for missing outcomes. In this article, the authors assume that the effect of intermittent missing data on the outcome is weak, and therefore use a dropout mechanism modeled with a generalized estimating equations (GEE).

The examples shown above highlight the need to have more missing data techniques that can be used with EMA data, especially if the missingness process is non-random. The proposed LTPMMM is a start in the right direction. Development of the model will be provided in subsequent chapters in this work. A discussion of the theoretical background for missing-data will be presented in Chapter 4 and the application and estimation of the proposed model is in Chapter 6 and Chapter 7. Also, because the longitudinal mixed-effects model plays such an important role in the analysis of EMA and ILD, details concerning the application and estimation of these models are developed in the next chapter.



## CHAPTER 3

### THE LONGITUDINAL MIXED-EFFECTS MODEL

As was explained in the previous chapter, some characteristics of data collected with EMA are worth noting. One example is that multiple subject responses are collected resulting in high intra-subject correlation among these observations. Usually EMA data have a different number of total responses for each study participant and these responses are usually collected at non-fixed times. Also, EMA data collection methods typically contain missing observations, where in many cases the missingness occurs intermittently. When data are collected through EMA methods both time-invariant and time-varying subject characteristics can be measured. Therefore, a modelling procedure is needed for EMA that can suitably handle these data characteristics. Otherwise, results can be biased and lead to incorrect conclusions.

The longitudinal mixed-effects model of Laird and Ware (1982) can handle these issues particularly well. In their presentation, the authors state that data containing variation among individuals in the number and timing of observations are typically unbalanced and that general multivariate models with unrestricted variance structures are usually not appropriate for longitudinal data. The following sections in this chapter will outline the use of longitudinal mixed-effects models in which multiple observations are collected for each subject. Both EMA and ILD data are examples of longitudinal data that have this nested structure. Section 3.1 will outline how a longitudinal mixed-effects model can be represented as a multi-level model containing lower level observations nested within subjects, with the next level containing random parameters such as intercepts and slopes that are allowed to vary among these subjects. Section 3.2 will describe how different covariance structures are tested and fitted in the longitudinal mixed-effects model. Section 3.3 will discuss the flexibility of the longitudinal

mixed-effects model in fitting various type of data, including continuous, binary, and ordinal outcomes. Section 3.4 in the chapter will explain estimation procedures for linear mixed-effects models including computational aspects to fitting the model using both maximum likelihood and expectation-maximization approaches. Section 3.4.5 and Section 3.4.6 will describe quadrature methods used to estimate mixed-effects models.

### 3.1 Level-1 and Level-2 Models

A two-level model is presented in which repeated observations for each subject are collected over a period of time. Level-1 of the model contains longitudinal outcomes ( $y_{ij}$ ) measured for each subject  $i$  at occasion  $j$ . The level-1 model is flexible so that repeated observations can be collected at both fixed or random times. The total number of subjects is represented by  $N$ , and it is simply the sum of individual subjects  $i$ . The number of occasions  $j$  are allowed to differ among subjects. Therefore, the index  $j$  varies from 1 to  $n_i$ . The total number of covariates in the level-1 model is denoted as  $C_{ws}$ . Following similar notation contained in Walls et al. (2006) and Hedeker and Gibbons (2006), the level-1 within-subjects model is written as:

$$\begin{aligned} y_{ij} &= \pi_{i0} + \pi_{i1}X_{ij1} + \dots + \pi_{iC_{ws}}X_{ijC_{ws}} + e_{ij} \\ &= \sum_{c=0}^{C_{ws}} \pi_{ic}X_{ijc} + e_{ij} \text{ with } X_{ij0} = 1. \end{aligned}$$

This equation represents a within-subjects model because it contains multiple outcomes  $y_{ij}$ , and  $C_{ws}$  covariates collected for each subject. The level-1 error terms  $e_{ij}$  are assumed to be from a normal distribution with mean 0 and constant variance  $\sigma_e^2 I_{n_i}$ . This assumption of constant within-subjects variance can be modified to suit other situations. The  $\pi_{i0} \dots \pi_{iC_{ws}}$  terms are coefficients which will be formulated in the level-2 model.

The second level of the longitudinal mixed-effects model allows the coefficients in the level-1 equation to vary for each subject, therefore it is known as a between-subjects model. This between-subjects model is sometimes referred to a “slopes as outcomes” or “coefficients as outcomes model.” Let  $B_{bs}$  be the number of covariates in the level-1 model that are collected at the subject level.

$$\begin{aligned}\pi_{ic} &= \beta_{c0} + \beta_{c1}x_{i1} + \dots \beta_{cB_{bs}}x_{iB_{bs}} + v_{ci} \\ &= \sum_{b=0}^{B_{bs}} \beta_{cb}x_{ib} + v_{ci} \text{ with } x_{i0} = 1.\end{aligned}$$

This model shows that each coefficient shown in the level-1 model can vary across subjects and can estimated as a function of covariates  $x_{ib}$  and person level deviations  $v_{ci}$  or random effects. The number of coefficients that vary between subjects will be denoted as  $r$ . In a linear mixed model fit to longitudinal data, random intercept and random slope terms are typically included in the level-2 models, therefore  $r$  is equal to 2. Combining the level-1 and level-2 models results in the full longitudinal mixed-effects model. This full model can be written as:

$$y_{ij} = \sum_{c=0}^{C_{ws}} \pi_{ic} X_{ijc} + e_{ij} \quad (3.1)$$

$$= \sum_{c=0}^{C_{ws}} \left[ \sum_{b=0}^{B_{bs}} \beta_{cb} x_{ib} + v_{ci} \right] X_{ijc} + e_{ij} \quad (3.2)$$

$$= \beta_{00} + \sum_{b=1}^{B_{bs}} \beta_{0b} x_{ib} + \sum_{p=1}^{C_{ws}} \beta_{c0} X_{ijc} + \sum_{c=1}^{C_{ws}} \sum_{b=1}^{B_{bs}} \beta_{cb} x_{ib} X_{ijc} + v_{0i} + \sum_{c=1}^{C_{ws}} v_{ci} X_{ijc} + e_{ij} \quad (3.3)$$

$$= \sum_{c=0}^{C_{ws}} \sum_{b=0}^{B_{bs}} \beta_{cb} x_{ib} X_{ijc} + \sum_{c=0}^{C_{ws}} v_{ci} X_{ijc} + e_{ij} \quad (3.4)$$

The term  $\sum_{b=1}^{B_{bs}} \beta_{0b} x_{ib}$  represents the main effects of person-level predictors,  $\sum_{c=1}^{C_{ws}} \beta_{c0} X_{ijc}$  represents the main effects of measurement occasion-level predictors, and  $\sum_{c=0}^{C_{ws}} v_{ci} X_{ijc}$  represents

the effect of random-effects multiplied by level-1 covariates. The quantity  $\sum_{c=1}^{C_{ws}} \sum_{b=1}^{B_{bs}} \beta_{cb} x_{ib} X_{ijc}$  represents an interaction effect of cross-level predictors. For example, in a longitudinal clinical trial measuring outcomes at three time points, an interaction term between treatment group and time is a cross-level predictor. Time is a covariate in the within-subjects (level-1) model and the treatment group is a covariate contained in the between-subjects (level-2) model. Let the number of cross-level interaction terms be equal to  $C_c$ . By definition, the total number of fixed covariates in the full model will equal the sum of the number of level-1 covariates, level-2 covariates, and cross-level covariates. To simplify notation, the sum of these covariates plus 1 will be denoted by the quantity  $p$ :

$$p = C_{ws} + B_{bs} + C_c + 1 \quad (3.5)$$

The one is added to account for the overall intercept term ( $\beta_0$ ) in the fully combined model. The final mixed-model equation shown above can be reduced by using design matrices for fixed effects and random effects and vectors containing unknown fixed parameters and random parameters. Therefore, the longitudinal mixed-effects model in full matrix form is written as:

$$\mathbf{y}_i = \mathbf{X}_i \boldsymbol{\beta} + \mathbf{Z}_i \mathbf{v}_i + e_i. \quad (3.6)$$

In this equation,  $i$  references the number of individuals and  $i = 1, \dots, N$  where  $N$  is equal to the total number of subjects. The number of time points ( $j$ ) measured for each subject is allowed to differ, therefore,  $j = 1, \dots, n_i$ . Also, the vector  $\mathbf{y}_i$  refers to the collected longitudinal responses for a given subject. The design matrix for the model covariates  $\mathbf{X}_i$  includes all fixed and time-varying covariates including a column of ones for the intercept term and has dimension  $n_i \times p$ . The vector  $\boldsymbol{\beta}$  includes all fixed coefficients for the model and has dimension  $p \times 1$ . The term  $\mathbf{Z}_i$

represents the  $n_i \times r$  design matrix for the random effects terms  $\mathbf{v}_i$ . This design matrix includes a column of ones for the random intercept terms  $v_{0i}$  and additional columns for covariates that are allowed to vary among subjects. In most cases, the columns in  $\mathbf{Z}_i$  are a subset of columns included in  $\mathbf{X}_i$ .

The response vector  $\mathbf{y}_i$  for each subject  $i$  is of dimension  $n_i \times 1$ , where  $n_i$  are the total number of observations for that subject. As shown above, longitudinal mixed-effects model for unit  $i$  is the sum of two quantities (one representing fixed effects and the other representing the random effects) and a vector of error terms. The quantity representing the fixed effects is also of dimension  $n_i \times 1$  due to the fact that the design matrix  $\mathbf{X}_i\boldsymbol{\beta}$  is of dimension  $n_i \times p$  and the vector of known fixed parameters is of dimension  $p \times 1$ . The vector representing random effects is also of length  $n_i \times 1$  because the design matrix for the random effects  $\mathbf{Z}_i$  is of dimension  $n_i \times r$  and the vector of unknown random effects is of dimension  $r \times 1$ .

The  $n_i \times 1$  vector of error terms, are assumed to be distributed normally where  $e_i \sim N(0, \sigma_e^2 \mathbf{I}_{n_i})$ . The random effects  $\mathbf{v}$  are distributed  $\sim N(0, \boldsymbol{\Sigma}_v)$ . Due to properties of the multivariate normal model, the outcomes  $y_i$  are distributed marginally as a normal distribution with mean  $\mathbf{X}_i\boldsymbol{\beta}$  and variance  $\mathbf{Z}_i\boldsymbol{\Sigma}_v\mathbf{Z}_i' + \sigma_e^2\mathbf{I}_{n_i}$ .

The system of equations shown above can be written as follows: let  $\mathbf{y}_i$  represent the outcomes vector for subject  $i$  and the matrix  $\mathbf{X}_i$  represent the fixed-effects covariates (which include level-1 covariates, level-2 covariates, and cross-level interactions). Also, the vector of fixed-effects coefficients as  $\boldsymbol{\beta}$ . The covariates that can vary between-subjects are represented

by  $\mathbf{Z}_i$  and the coefficients for these random effects are written by  $\mathbf{v}_i$ . The error terms are represented by  $\mathbf{e}_i$ . Combining these terms results in the matrix form shown above.

$$\begin{bmatrix} y_{i1} \\ \vdots \\ y_{in_i} \end{bmatrix} = \begin{bmatrix} 1 & X_{i1}^1 & \dots & X_{i1}^{p-1} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & X_{in_i}^1 & \dots & X_{in_i}^{(p-1)} \end{bmatrix} \begin{bmatrix} \beta_0 \\ \vdots \\ \beta_{p-1} \end{bmatrix} + \begin{bmatrix} 1 & x_{i1}^1 & \dots & x_{i1}^{r-1} \\ \vdots & \vdots & \ddots & \vdots \\ 1 & x_{in_i}^1 & \dots & x_{in_i}^{r-1} \end{bmatrix} \begin{bmatrix} v_{0i} \\ \vdots \\ v_{(r-1)i} \end{bmatrix} + \begin{bmatrix} e_{i1} \\ \vdots \\ e_{in_i} \end{bmatrix}$$

### 3.2 Covariance Structure

Hedeker and Gibbons (2006) describe how the variance-covariance matrix may have a direct impact on standard errors of model parameters. Therefore, in order to select and fit a longitudinal mixed-effects model that has the best model precision, the covariance structure must be correctly identified. As is described above, if the longitudinal outcomes  $\mathbf{y}_i$  are from a normal distribution, the marginal distribution of  $\mathbf{y}_i$  has a mean of  $\mathbf{X}_i\boldsymbol{\beta}$  and a variance matrix of  $\mathbf{Z}_i\boldsymbol{\Sigma}_v\mathbf{Z}_i' + \sigma_e^2\mathbf{I}_{n_i}$ . The first term of this matrix refers to the variance structure of the random effects and the second term refers to the error variance structure. Standard longitudinal analysis texts such as Verbeke and Molenberghs (2000), Hedeker and Gibbons (2006), and Diggle et al. (2002) describe exploratory methods to determine the best set of fixed covariates, random effects, and model variance-covariance matrix. Verbeke and Molenberghs (2000) explain how a correctly identified mean structure will have a direct impact on a model's covariance structure.

If the error terms are not independent and normally distributed, longitudinal mixed-effects models can easily be adapted to fit various structures that model serial dependence.

Verbeke and Molenberghs (2000) present methods using SAS PROC MIXED to fit error terms that have a Gaussian, exponential, autoregressive, or moving average structures. Hedeker and Gibbons (2006) describe procedures to test various models that have different covariance matrices which vary the number of random effects and or the error structure to find the best model fit. In conclusion, the linear mixed-effects model can be adapted to handle complicated longitudinal data by using methods to find a suitable covariance structure that may insure lower standard errors and valid model inferences.

### **3.3 Model Outcomes**

Longitudinal mixed-effects models can handle many types of outcome variables. In the continuous case, longitudinal mixed-effects models assume that the outcomes,  $y_{ij}$  are continuous and conditionally normally distributed with an unknown error variance  $\sigma_e^2$ . Longitudinal mixed-effects models can also be derived for dichotomous outcomes. Under the logit link function, these type of models are known as mixed-effect logistic models and can have random slopes and intercepts. These models can be fit by using a logit or probit link for the outcomes since the outcome is related to the probability of an event. Works describing the longitudinal mixed-effects logistic model can be found in Hedeker and Gibbons (2006), Gibbons and Hedeker (1994) and Rabe-Hesketh and Skrondal (2009).

Longitudinal mixed-effects models for nominal and ordinal outcomes can also be derived. Presentations outlining methods to fit these models can be found in Hedeker and Gibbons (2006), Hedeker and Gibbons (1994), and Liu (2008). The hierarchical structure inherent in the longitudinal mixed-effects model can easily be used with these different outcomes. Selected books exploring the application of the longitudinal mixed-effects model to various types of non-continuous outcomes from health, science, and psychology are Hedeker and Gibbons (2006), Pinheiro and Bates (2000), and Diggle et al. (2002). A recent collection highlighting

advanced applications of the longitudinal mixed-effects model including missing data, parametric and semi-parametric longitudinal models, and estimation of joint outcomes can be found in Fitzmaurice et al. (2009). The longitudinal models and estimation methods discussed in this chapter will be applicable to continuous and binary outcomes. Further details of how the proposed LTPMMs will jointly estimate these two types of outcomes will be provided in Chapter 6 and Chapter 7.

### 3.4 Estimation of the Longitudinal Mixed-Effects Model

The next section will outline estimation of the posterior mean of the random effects  $\tilde{\mathbf{v}}$  and the corresponding posterior variance terms  $\Sigma_{\mathbf{v}|y_i}$  in the longitudinal mixed-effects model through an empirical Bayes approach. Hedeker and Gibbons (2006) and Laird and Ware (1982) describe how an Expectation-Maximization (EM) algorithm can be used to derive these quantities. The estimated posterior mean and variance of the random effects will then be used as parameters in likelihood-based equations for the vector of unknown fixed effects coefficients  $\beta$ , the error variance  $\sigma_e^2$ , and the covariance matrix of the random effects  $\Sigma_v$ . The maximum likelihood estimates of  $\beta$ ,  $\sigma_e^2$ , and  $\Sigma_v$  are calculated using the original estimates of  $\tilde{\mathbf{v}}$  and  $\Sigma_{\mathbf{v}|y_i}$ . This iterative process is continued until the difference between subsequent estimates is very small. The following sections will describe estimation methods for the longitudinal mixed-effects model for both continuous and binary outcomes because these two types of outcomes play an important and necessary role in the proposed LTPMMM.

#### 3.4.1 Random Effects

Random effects estimation using Bayes theorem is done in the following manner. We define the posterior density of the random effects ( $v_i$ ) as  $p_i$ , the likelihood function or probability density of  $y_i$  as  $f_i$ , the prior density for the random effects as  $g$  and the marginal log-likelihood of a given observation  $y_i$  as  $h_i$ . A Bayesian method can be used since the random effects are



random and not fixed. Bayes theorem states that the probability density of the random effects given the data is equal to:

$$p(\mathbf{v}|y_i) = \frac{f(y_i|\mathbf{v}_i; \boldsymbol{\zeta})g(\mathbf{v}; \boldsymbol{\eta})}{\int_{\mathbf{v}} f(y_i|\mathbf{v}_i; \boldsymbol{\zeta})g(\mathbf{v}; \boldsymbol{\eta})d\mathbf{v}}$$

Two processes are needed to apply this formula. One process describes the data given random effects  $\mathbf{v}_i$ , fixed effects parameters  $\boldsymbol{\beta}$ , and error structure  $\sigma_e^2$  as a probability density  $f(y_i|\mathbf{v}_i; \boldsymbol{\zeta})$ . Another process for the random effects uses  $g$ , which is a prior probability density defined by  $g(\mathbf{v}; \boldsymbol{\Sigma}_v)$ . Hedeker (2011) shows that the mean of the posterior distribution of the random effects is given by:

$$\tilde{\mathbf{v}}_i = (\mathbf{Z}_i' \mathbf{Z}_i + \sigma_e^2 \boldsymbol{\Sigma}_v^{-1})^{-1} \mathbf{Z}_i' (\mathbf{y}_i - \mathbf{X}_i \boldsymbol{\beta}) \quad (3.7)$$

and the variance-covariance matrix is given by:

$$\boldsymbol{\Sigma}_{v|y_i} = (\mathbf{Z}_i' (\sigma_e^2 \mathbf{I}_{n_i})^{-1} \mathbf{Z}_i + \boldsymbol{\Sigma}_v^{-1})^{-1} \quad (3.8)$$

Using standard software such as SAS PROC MIXED, the estimates of the random effects and their standard errors from a longitudinal mixed-effects model can be studied for model fit, normality, and possible irregularities. Verbeke and Molenberghs (2000) provide a detailed review and many examples. The next section will describe how the estimated random-effects  $\tilde{\mathbf{v}}$  and covariance matrix  $\boldsymbol{\Sigma}_{v|y_i}$  will be used with the Expectation-Maximization algorithm to fit the longitudinal mixed-effects model.

### **3.4.2 Expectation-Maximization Algorithm**

In the Expectation-Maximization (EM) algorithm developed by Dempster et al. (1977), two steps are involved to obtain the maximum likelihood estimates for the linear mixed-effects

model. For illustrative purposes, the EM algorithm will be applied using a linear mixed-effects model with random intercept terms as it is similar to the proposed LTPMMM. The first step, which is called the expectation step (or E-step), solves for the expected values (or empirical Bayes estimates) of the random effects  $\mathbf{v}_i$  and the variance of the random effects given the observed outcomes  $\mathbf{y}_i$ :

$$\begin{aligned}\tilde{\mathbf{v}}_i &= \rho_{n_i n_i} \left[ \frac{1}{n_i} \sum_{j=1}^{n_i} y_{ij} - \mathbf{x}'_{ij} \boldsymbol{\beta} \right] \\ \sigma_{v|y_i}^2 &= \sigma_v^2 (1 - \rho_{n_i n_i})\end{aligned}$$

The solutions depend on the Spearman-Brown reliability defined as:

$$\rho_{n_i n_i} = \frac{n_i r}{1 + (n_i - 1)r}$$

and the intraclass correlation coefficient defined as:

$$r = \frac{\sigma_v^2}{\sigma_v^2 + \sigma_e^2}.$$

The next step called the maximization step (or M-step) solves for the maximum likelihood estimates of  $\boldsymbol{\beta}$ ,  $\sigma_e^2$ , and  $\sigma_v^2$ :

$$\begin{aligned}\hat{\boldsymbol{\beta}} &= \left( \sum_i^N \mathbf{X}_i' \mathbf{X}_i \right)^{-1} \sum_i^N \mathbf{X}_i (\mathbf{y}_i - \mathbf{1}_i \tilde{\mathbf{v}}_i) \\ \hat{\sigma}_v^2 &= \frac{1}{N} \sum_i^N \tilde{\mathbf{v}}_i^2 + \sigma_{v|y_i}^2 \\ \hat{\sigma}_e^2 &= \left( \sum_i^N n_i \right)^{-1} \sum_i^N (\mathbf{y}_i - \mathbf{X}_i - \mathbf{1}_i \tilde{\mathbf{v}}_i)' (\mathbf{y}_i - \mathbf{X}_i - \mathbf{1}_i \tilde{\mathbf{v}}_i) + n_i \sigma_{v|y_i}^2.\end{aligned}$$

The EM algorithm repeats these two steps until convergence, which usually occurs when the difference in the maximum likelihood estimates of  $\beta$ ,  $\sigma_e^2$ , and  $\sigma_v^2$  are very small. This approach will always find a solution but convergence may be quite slow. Another drawback is that the EM algorithm does not typically provide standard errors for the estimates of  $\beta$ ,  $\sigma_e^2$ , and  $\sigma_v^2$ . Other iterative approaches such as Fisher scoring or Newton-Raphson techniques can be used to obtain the standard errors. Further details and methods to compute standard errors are provided by Lindstrom and Bates (1988) and Louis (1982).

### 3.4.3 Continuous Outcomes

Two approaches can be used to fit the longitudinal mixed-effects model with continuous outcomes: Maximum Likelihood Estimation (MLE) and Restricted Maximum Likelihood Estimation (REML). These are two common likelihood-based methods for the longitudinal mixed-effects model. Reviews of these methods can be found in Pinheiro and Bates (2000) and Verbeke and Molenberghs (2000). With REML, likelihood equations are maximized with respect to the random effects parameters. REML has an adjustment for the number of parameters, and the REML estimate is an unbiased estimator for small sample sizes. The derivations that will be presented in this work apply to ordinary MLE, since the sample data set for analysis is not small.

In order to estimate the vector of unknown fixed parameters  $\beta_i$ , and the error variance  $\sigma_e^2$ , and covariance matrix  $\Sigma_v$  of the random effects  $v_i$  the log-likelihood equations for the mixed-model are shown below. The equations are modified versions of the approach presented in Hedeker (2011). In that approach, a likelihood function  $f$  or probability density for outcomes is multiplied by a prior density  $g$  for the random effects. A maximum likelihood solution is obtained by integration of the likelihood function over the distribution of random effects ( $v_i$ ). This likelihood method is also known as marginal maximum likelihood estimation since

integration is performed over a marginal distribution. The equation to be maximized is denoted  $h(\mathbf{y}_i)$  and is written as:

$$h(\mathbf{y}_i) = \int_{\mathbf{v}} f(\mathbf{y}_i|\mathbf{v}; \boldsymbol{\beta}, \sigma_e^2) g(\mathbf{v}; \boldsymbol{\Sigma}_v) d\mathbf{v}$$

The equation for  $(g)$  has the form shown below because we are assuming a multivariate normal distribution for the random effects  $v$ .

$$g(\mathbf{v}; \boldsymbol{\Sigma}_v) = (2\pi)^{-r/2} |\boldsymbol{\Sigma}_v|^{-1/2} \exp \left[ -\frac{1}{2} \mathbf{v}' \boldsymbol{\Sigma}_v^{-1} \mathbf{v} \right]$$

We also assume that the outcomes  $\mathbf{y}_i$  are from a multivariate normal distribution of the form:

$$\mathbf{y}_i \sim N(\mathbf{X}\boldsymbol{\beta}, \sigma_e^2 \mathbf{I}_{n_i} + \mathbf{Z}_i \boldsymbol{\Sigma}_v \mathbf{Z}_i'). \quad (3.9)$$

Therefore, the distribution of  $\mathbf{y}_i$ , conditional on  $\mathbf{v}$ ,  $\boldsymbol{\beta}$ , and  $\sigma_e^2$  is written as:

$$\begin{aligned} f(\mathbf{y}_i|\mathbf{v}; \boldsymbol{\beta}, \sigma_e^2) &= \\ &= (2\pi)^{-n_i/2} |\sigma_e^2 \mathbf{I}_{n_i}|^{-1/2} \\ &\times \exp \left[ -1/2 (\mathbf{y}_i - \mathbf{X}_i \boldsymbol{\beta} - \mathbf{Z}_i \mathbf{v})' (\sigma_e^2 \mathbf{I}_{n_i})^{-1/2} (\mathbf{y}_i - \mathbf{X}_i \boldsymbol{\beta} - \mathbf{Z}_i \mathbf{v}) \right]. \end{aligned}$$

All of the marginal log-likelihoods will be summed over the sample of subjects  $N$  and maximized with respect to the parameters  $\boldsymbol{\beta}$ ,  $\sigma_e^2$ , and the variance-covariance matrix of random effects  $\boldsymbol{\Sigma}_v$ .

$$\log L = \sum_{i=1}^N \log h(\mathbf{y}_i). \quad (3.10)$$

The solution for the vector of coefficients  $\beta$  for the fixed effects is found by taking the partial derivative of  $\log L$  with respect to  $\beta$ , setting equal to zero and solving for  $\beta$ :

$$\begin{aligned}
\frac{\partial \log L}{\partial \beta} &= \sum_{i=1}^N \frac{\partial \log h_i}{\partial \beta} \\
&= \sum_{i=1}^N \frac{1}{h_i} \frac{\partial [\int_{\mathbf{v}} f_i \times g \, d\mathbf{v}]}{\partial \beta} \\
&= \sum_{i=1}^N \frac{1}{h_i} \int_{\mathbf{v}} \frac{\partial f_i}{\partial \beta} g \, d\mathbf{v} \\
&= \sum_{i=1}^N \frac{f_i \times g}{h_i} \frac{\partial \log f_i}{\partial \beta} \, d\mathbf{v} \\
&= \sum_{i=1}^N \int_{\mathbf{v}} p_i \mathbf{X}_i' (\sigma_e^2 \mathbf{I}_{n_i})^{-1} (\mathbf{y}_i - \mathbf{X}_i \beta - \mathbf{Z}_i \mathbf{v}) \, d\mathbf{v}.
\end{aligned}$$

The expression  $\int_{\mathbf{v}} \mathbf{v} p_i d\mathbf{v}$  is the posterior mean of the random effects vector  $\mathbf{v}$ . We can denote this quantity by  $\tilde{\mathbf{v}}$ . Simplifying the above expression yields:

$$\begin{aligned}
\frac{\partial \log L}{\partial \beta} &= \sigma_e^{-2} \sum_{i=1}^N \mathbf{X}_i' (\mathbf{y}_i - \mathbf{X}_i \beta - \mathbf{Z}_i \tilde{\mathbf{v}}_i) \\
&= \sigma_e^{-2} \sum_{i=1}^N \mathbf{X}_i' \mathbf{y}_i - \mathbf{X}_i' \mathbf{X}_i \beta - \mathbf{X}_i' \mathbf{Z}_i \tilde{\mathbf{v}}_i.
\end{aligned}$$

Equating  $\frac{d \log L}{d \beta}$  to 0 provides the solution to  $\beta$ :

$$\begin{aligned}
&\sum_{i=1}^N \mathbf{X}_i' \mathbf{y}_i - \mathbf{X}_i' \mathbf{X}_i \beta - \mathbf{X}_i' \mathbf{Z}_i \tilde{\mathbf{v}}_i = 0 \\
\hat{\beta} &= \left[ \sum_{i=1}^N \mathbf{X}_i' \mathbf{X}_i \right]^{-1} \left[ \sum_{i=1}^N \mathbf{X}_i' (\mathbf{y}_i - \mathbf{Z}_i \tilde{\mathbf{v}}_i) \right]. \tag{3.11}
\end{aligned}$$

The same approach will be used to maximize the marginal log-likelihood with respect to the error variance  $\sigma_e^2$  where  $\mathbf{e}_i = \mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i$ . The derivative of the log-likelihood with respect to  $\sigma_e^2$  is:

$$\frac{\partial \log L}{\partial \sigma_e^2} = \sum_{i=1}^N \frac{1}{h_i} \int_{\mathbf{v}} \frac{\partial f_i}{\partial \sigma_e^2} g \, d\mathbf{v}.$$

Applying Bayes theorem where the posterior probability  $p_i$  equals the likelihood function  $f_i$  times the prior  $g_i$  divided by the marginal log-likelihood  $h_i$ :

$$\begin{aligned} \frac{\partial \log L}{\partial \sigma_e^2} &= \sum_{i=1}^N \int_{\mathbf{v}} \frac{f_i \times g}{h_i} \frac{\partial \log f_i}{\partial \sigma_e^2} d\mathbf{v} \\ &= \sum_{i=1}^N \int_{\mathbf{v}} p_i \left[ -\frac{n_i}{2} \sigma_e^{-2} + \frac{1}{2} \sigma_e^{-4} (\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\mathbf{v})' (\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\mathbf{v}) \right] d\mathbf{v} \\ &= \frac{1}{2} \sigma_e^{-4} \left( -n_i \sigma_e^2 + \mathbf{e}_i' \mathbf{e}_i + \text{tr}[\mathbf{Z}_i \boldsymbol{\Sigma} \mathbf{v} | \mathbf{y}_i \mathbf{Z}_i'] \right). \end{aligned}$$

where the trace ( $\text{tr}$ ) of a square matrix  $\mathbf{A}$  of dimension  $n \times n$  is defined as the sum of diagonal elements  $a_{ii}$ :

$$\text{tr} \mathbf{A} = a_{11} + a_{22} + \dots + a_{nn} = \sum_{i=1}^n a_{ii} \quad (3.12)$$

The solution shown above for the derivative of the log-likelihood with respect to  $\sigma_e^2$  is true since the quantity  $(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\mathbf{v})$  can be rewritten as  $\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i - \mathbf{Z}_i(\mathbf{v} - \tilde{\mathbf{v}}_i)$ .

$$\begin{aligned}
& \int_{\mathbf{v}} p_i(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\mathbf{v}_i)'(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\mathbf{v}_i) d\mathbf{v}_i \\
&= \int_{\mathbf{v}} p_i [(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i) - \mathbf{Z}_i(\mathbf{v} - \tilde{\mathbf{v}}_i)]' \\
&\quad \times [(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i) - \mathbf{Z}_i(\mathbf{v} - \tilde{\mathbf{v}}_i)] d\mathbf{v} \\
&= (\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i)'(\mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i) + \text{tr} \mathbf{Z}_i \boldsymbol{\Sigma}_{\mathbf{v}|\mathbf{y}_i} \mathbf{Z}_i'
\end{aligned}$$

The last expression shown above applies because  $\boldsymbol{\Sigma}_{\mathbf{v}|\mathbf{y}_i}$  is defined as:

$$\boldsymbol{\Sigma}_{\mathbf{v}|\mathbf{y}_i} = \int_{\mathbf{v}} (\mathbf{v} - \tilde{\mathbf{v}}_i)(\mathbf{v} - \tilde{\mathbf{v}}_i)' p_i d\mathbf{v}_i$$

Setting the equation  $\frac{\partial \log L}{\partial \sigma_e^2}$  equal to zero and the fact that  $\hat{\mathbf{e}}_i = \mathbf{y}_i - \mathbf{X}_i\boldsymbol{\beta} - \mathbf{Z}_i\tilde{\mathbf{v}}_i$

$$\hat{\sigma}_e^2 = \left( \sum_i^N n_i \right)^{-1} \sum_i^N \hat{\mathbf{e}}_i' \hat{\mathbf{e}}_i + \text{tr} [\mathbf{Z}_i \boldsymbol{\Sigma}_{\mathbf{v}|\mathbf{y}_i} \mathbf{Z}_i']. \quad (3.13)$$

To derive log-likelihood equations with respect to  $\boldsymbol{\Sigma}_{\mathbf{v}}$ , the vector operations of *vec* and *vech* will be needed. Henderson and Searle (1979) define the *vec* of a square matrix  $\mathbf{A}$  of size  $n \times n$ , as the column vector created by stacking each column vector in  $\mathbf{A}$  one on top of each other. In mathematical notation,

$$\text{vec } \mathbf{A} = [\mathbf{a}'_1, \mathbf{a}'_2, \dots, \mathbf{a}'_n]' \quad (3.14)$$

resulting in one column vector. The *vech* operator is similar, except it stacks entries from matrix  $\mathbf{A}$  that are on or above the main diagonal to form one column vector:

$$vech \mathbf{A} = [a_{11}, a_{21}, a_{22}, a_{31}, a_{32}, a_{33}, \dots, a_{nn}]' \quad (3.15)$$

where  $a_{ij}$  represents the element in matrix  $\mathbf{A}$  from the  $i^{th}$  row and  $j^{th}$  column. The following two quantities will be needed for the solution of  $\Sigma_v$  and are found in Henderson and Searle (1979):

$$\begin{aligned} \frac{\partial \log |\Sigma_v|}{\partial vec \Sigma_v} &= vec \Sigma_v^{-1} \\ \frac{\partial \mathbf{v}' \Sigma_v^{-1} \mathbf{v}}{\partial vec \Sigma_v} &= \frac{\partial tr \Sigma_v^{-1} \mathbf{v} \mathbf{v}'}{\partial vec \Sigma_v} \\ &= -vec \Sigma_v^{-1} \mathbf{v} \mathbf{v}' \Sigma_v^{-1} \end{aligned}$$

An additional equation needed is:

$$\begin{aligned} \int_v p_i \mathbf{v} \mathbf{v}' d\mathbf{v} &= \int_v p_i [(\mathbf{v} - \tilde{\mathbf{v}}_i) + \tilde{\mathbf{v}}_i] [(\mathbf{v} - \tilde{\mathbf{v}}_i) + \tilde{\mathbf{v}}_i]' d\mathbf{v} \\ &= \Sigma_{v|y_i} + \tilde{\mathbf{v}}_i \tilde{\mathbf{v}}_i' \end{aligned}$$

Derivatives are taken with respect to the  $r(r+1)/2$  unique elements of  $\Sigma_v$ :

$$\begin{aligned} \frac{\partial \log L}{\partial vec \Sigma_v} &= \sum_{i=1}^N \frac{1}{h_i} \int_v \frac{\partial g}{\partial vec \Sigma_v} f_i d\mathbf{v} \\ &= \sum_{i=1}^N \int_v \frac{f_i \cdot g}{h_i} \frac{\partial \log g}{\partial vec \Sigma_v} d\mathbf{v} \\ &= \mathbf{G}' vec \sum_i \int_v p_i \left[ -\frac{1}{2} \Sigma_v^{-1} + \frac{1}{2} \Sigma_v^{-1} \mathbf{v} \mathbf{v}' \Sigma_v^{-1} \right] \\ &= \frac{1}{2} \mathbf{G}' \sum_i vec \Sigma_v^{-1} \left( -\Sigma_v + \Sigma_{v|y_i} + \tilde{\mathbf{v}}_i \tilde{\mathbf{v}}_i' \right) \Sigma_v^{-1} \end{aligned}$$



The matrix  $\mathbf{G}$  transforms the *vech* of a square matrix into the *vec* of that matrix (McCulloch, 1982):

$$\text{vec}\mathbf{A} = \mathbf{G} \text{vech } \mathbf{A}. \quad (3.16)$$

Setting the whole quantity equal to zero results in:

$$\hat{\Sigma}_v = \frac{1}{N} \sum_i^N (\tilde{\mathbf{v}}_i \tilde{\mathbf{v}}_i' + \Sigma_{v|y_i}) \quad (3.17)$$

This solution can be described as the sample estimate of the variance of the empirical Bayes estimate plus the empirical Bayes estimate about uncertainty of the effect (Hedeker, 2011).

#### 3.4.4 Binary Outcomes

Using the same technique as shown for continuous outcomes, Hedeker and Gibbons (2006) also present the necessary steps to estimate longitudinal mixed-effects models with binary outcomes. With binary outcomes, the log-odds ratio (logit) that an event occurs ( $p_{ij}=1$ ) for subject  $i$  at time  $j$  is related to model covariates  $\beta$  in a linear fashion. Here, for simplicity, only one random effect  $v_i$  is assumed:

$$\log \left[ \frac{p_{ij}}{1 - p_{ij}} \right] = \mathbf{x}_{ij}' \boldsymbol{\beta} + v_i. \quad (3.18)$$

In this notation,  $\mathbf{x}_{ij}$  is a  $(p+1) \times 1$  covariate vector that includes a column of ones for the intercept,  $\boldsymbol{\beta}$  is a  $(p+1) \times 1$  vector of unknown regression parameters, and  $v_i$  is a random intercept term for each subject that is assumed to be distributed normally as a  $\sim N(0, \sigma_v^2)$  variable. Also

for computational purposes, the random effects can be represented in standardized form, where  $v_i/\sigma_v = \theta_i$ . This results in a reformulation of Equation 3.18 to:

$$\log \left[ \frac{p_{ij}}{1 - p_{ij}} \right] = \mathbf{x}'_{ij} \boldsymbol{\beta} + \sigma_v \theta_i. \quad (3.19)$$

Also, the left hand side of this equation can be rewritten as

$$z_{ij} = \mathbf{x}'_{ij} \boldsymbol{\beta} + \sigma_v \theta_i. \quad (3.20)$$

The conditional probability of this outcome given the standardized random effect  $\theta_i$  can be written as:

$$p_{ij} = P(Y_{ij} = 1 | \theta_i) = \Psi(z_{ij}). \quad (3.21)$$

where  $\Psi_i$  is the cumulative density function for the logistic distribution and  $\Psi(z_{ij}) = \frac{1}{1 + \exp(-z_{ij})}$ . Since the observations for each subject are independent given the standardized random effect  $\theta_i$  (i.e., the conditional independence assumption), the probabilities that an event occurs ( $p_{ij} = \Psi(z_{ij})$ ) or does not occur ( $1 - p_{ij} = 1 - \Psi(z_{ij})$ ) can be multiplied across all time-intervals and equals a conditional probability of response  $p(\mathbf{Y}_i | \theta_i)$ . Here  $\mathbf{Y}_i$  is a  $n_i \times 1$  vector of indicators for subject  $i$ :

$$\ell(\mathbf{Y}_i | \theta_i) = \prod_{j=1}^{n_i} \Psi(z_{ij})^{Y_{ij}} [1 - \Psi(z_{ij})]^{1-Y_{ij}}. \quad (3.22)$$

In order to solve this likelihood equation for subject  $i$ , the marginal distribution of  $\mathbf{Y}_i$  is derived by integrating over the random effects  $\theta_i$

$$h(\mathbf{Y}_i) = \int_{\theta} \ell(\mathbf{Y}_i | \theta) g(\theta) d\theta. \quad (3.23)$$

In this equation,  $g(\theta)$  represents the probability density function of the standardized random effect  $\theta$ , which is distributed as a  $\sim N(0, 1)$  variable. If the marginal likelihoods for all subjects are then multiplied, the marginal likelihood of  $\mathbf{Y}_i$  for subjects is:

$$L = \prod_{i=1}^N h(\mathbf{Y}_i) \quad (3.24)$$

which can be solved by taking the logarithm of both sides,

$$\log L = \sum_{i=1}^N \log h(\mathbf{Y}_i). \quad (3.25)$$

If the quantity  $\eta$  equals  $\beta$  or  $\sigma_v$ , the maximum likelihood solutions can be found by taking the derivatives of Equation 3.25 with respect to  $\eta$  and setting them equal to 0:

$$\frac{\partial \log L}{\partial \eta} = \sum_{i=1}^N h^{-1}(\mathbf{Y}_i) \frac{\partial h(\mathbf{Y}_i)}{\partial \eta}. \quad (3.26)$$

The marginal likelihood can be re-expressed as:

$$\begin{aligned} \int_{\theta} l(\mathbf{Y}_i|\theta) g(\theta) d\theta &= \int_{\theta} \left( \prod_{j=1}^{n_i} (\Psi(z_{ij}))^{Y_{ij}} [1 - \Psi(z_{ij})]^{1-Y_{ij}} \right) g(\theta) d\theta \\ &= \int_{\theta} \left[ \exp \left( \log \sum_{i=1}^{n_i} \Psi(z_{ij})^{Y_{ij}} [1 - \Psi(z_{ij})]^{1-Y_{ij}} \right) \right] g(\theta) d\theta \\ &= \int_{\theta} \exp \left[ \sum_{i=1}^{n_i} Y_{ij} \log[\Psi(z_{ij})] + (1 - Y_{ij}) \log[1 - \Psi(z_{ij})] \right] g(\theta) d\theta. \end{aligned}$$

Letting  $\ell(\mathbf{Y}_{ij}|\theta) = \ell_i$  and taking derivatives with respect to  $\boldsymbol{\eta}$  yields

$$\begin{aligned}\frac{\partial h(\mathbf{Y}_{ij})}{\partial \boldsymbol{\eta}} &= \int_{\theta} \sum_{i=1}^{n_i} \left[ \frac{Y_{ij}}{\Psi(z_{ij})} \partial \Psi(z_{ij}) + \frac{1 - Y_{ij}}{1 - \Psi(z_{ij})} (-\partial \Psi(z_{ij})) \right] \frac{\partial z_{ij}}{\partial \boldsymbol{\eta}} \ell_i g(\theta) d\theta \\ &= \int_{\theta} \sum_{i=1}^{n_i} \frac{Y_{ij} - \Psi(z_{ij})}{\Psi(z_{ij})(1 - \Psi(z_{ij}))} \partial \Psi(z_{ij}) \frac{\partial z_{ij}}{\partial \boldsymbol{\eta}} \ell_i g(\theta) d\theta.\end{aligned}$$

Since  $\partial z_{ij}$  is the probability density function of the logistic distribution which is equal to  $\Psi(z_{ij}) \times (1 - \Psi(z_{ij}))$ , Equation 3.25 can be simplified to

$$\frac{\partial \log L}{\partial \boldsymbol{\eta}} = \sum_{i=1}^N h^{-1}(\mathbf{Y}_i) \int_{\theta} \sum_{i=1}^{n_i} \frac{Y_{ij} - \Psi(z_{ij})}{\Psi(z_{ij})(1 - \Psi(z_{ij}))} \partial \Psi(z_{ij}) \frac{\partial z_{ij}}{\partial \boldsymbol{\eta}} \ell_i g(\theta) d\theta$$

where  $\frac{\partial z_{ij}}{\partial \boldsymbol{\beta}} = \mathbf{x}'_{ij}$  and  $\frac{\partial z_{ij}}{\partial \sigma_v} = \theta$ . Therefore, the maximum likelihood solutions for  $\boldsymbol{\beta}$  and  $\sigma_v$  can be solved by the following equations:

$$\frac{\partial \log L}{\partial \boldsymbol{\beta}} = \sum_{i=1}^N h^{-1}(\mathbf{Y}_i) \int_{\theta} \sum_{i=1}^{n_i} Y_{ij} - \Psi(z_{ij}) \mathbf{x}'_{ij} \ell_i g(\theta) d\theta \quad (3.27)$$

$$\frac{\partial \log L}{\partial \sigma_v} = \sum_{i=1}^N h^{-1}(\mathbf{Y}_i) \int_{\theta} \sum_{i=1}^N Y_{ij} - \Psi(z_{ij}) \theta \ell_i g(\theta) d\theta. \quad (3.28)$$

Estimation of the linear mixed-effects model using MLE can be enhanced by using a computational technique such as the EM algorithm, Fisher scoring, or Gaussian quadrature. Since the proposed models will be estimated using quadrature methods from SAS statistical software, an introduction to this method is explained next.

#### 3.4.5 Gauss-Hermite Quadrature

The solutions shown above for random intercepts logistic model can be solved using Gauss-Hermite quadrature. In order to derive a solution, integration over the random effects distribution is needed. Gauss-Hermite quadrature approximates the full integral by evaluation

of the function at a series of points in the integral, multiplying them by a weight, and sums these products. Quadrature points and weights for the standard normal univariate distribution are found in Stroud and Secrest (1966). With the univariate case (the mixed-effects logistic model shown above) where a random intercept is estimated, the quantity  $B_q$  represents the  $q^{th}$  point and  $A(\cdot)$  a series of weights. In this notation,  $B_q$  replaces the unknown random effect  $\theta_i$  in the model and the total number of quadrature points is equal to  $Q$ . Also, if the quantity  $z_{ij}$  is reformulated as  $z_{ijq}$  where

$$z_{ijq} = \mathbf{x}'_{ij}\beta + \sigma_v B_q$$

then the log-likelihood of  $\mathbf{Y}_i$  can be rewritten as:

$$\ell(\mathbf{Y}_i|B_q) = \sum_{j=1}^{n_i} \Psi(z_{ijq})^{Y_{ij}} [1 - \Psi(z_{ijq})]^{1-Y_{ij}}.$$

Hedeker and Gibbons (2006) expand these equations and show that the solution to the marginal likelihood is approximately equal to

$$h(\mathbf{Y}_i) \approx \sum_{q=1}^Q \ell(\mathbf{Y}_i|B_q) A(B_q)$$

$$\frac{\partial \log L}{\partial \boldsymbol{\eta}} \approx \sum_{i=1}^N h^{-1}(Y_{ij}) \sum_{q=1}^Q \sum_{j=1}^{n_i} Y_{ij} - \Psi(z_{ijq}) \frac{\partial z_{ijq}}{\partial \boldsymbol{\eta}} \ell(\mathbf{Y}_i|B_q) A(B_q) \quad (3.29)$$

where

$$\frac{\partial z_{ijq}}{\partial \boldsymbol{\beta}} = \mathbf{x}'_{ij} \quad (3.30)$$

and

$$\frac{\partial z_{ijq}}{\partial \sigma_v} = B_q. \quad (3.31)$$

### 3.4.6 Adaptive Quadrature

Gauss-Hermite quadrature usually becomes computationally intensive as the number of random effects increases or if the intraclass correlation coefficient is high (Rabe-Hesketh et al., 2002). Adaptive Gaussian quadrature (Rabe-Hesketh et al., 2002; Pinheiro and Bates, 1995) allows accurate estimation of longitudinal mixed-effects models with fewer points than Gauss-Hermite quadrature methods. Adaptive Gaussian quadrature is used SAS PROC NLMIXED. In adaptive Gaussian quadrature, an algorithm updates the weights and nodes at each step of the iterative process. Hedeker and Gibbons (2006) and Rabe-Hesketh et al. (2002) show that estimation of the posterior mean and variance of the random subject effect is used at each iteration with adaptive Gaussian quadrature. If the posterior mean of the random effect is  $\hat{\theta}_i$  (estimated through empirical Bayes) and the variance of the random effect is denoted as  $s_i^2$ , then the adapted quadrature points ( $B_{iq}$ ) are:

$$B_{iq} = \hat{\theta}_i + s_i B_q.$$

The adapted quadrature weights are:

$$A_{iq} = \sqrt{2\pi s_i} \exp(B_q^2/2) \phi(B_{iq}) A_q$$

where  $\phi$  is the normal probability density function. An iterative procedure using these adaptive quadrature points and weights is substituted in Equation 3.29 in order to find a solution. Pinheiro and Bates (2000) and Davidian and Gallant (1993) provide reviews of techniques to use adaptive Gaussian quadrature in cases where nonlinear mixed-effects models are used.

Since the proposed LTPMMs will be applied to EMA data containing intermittent missing data, background information relating to missing data mechanisms and estimation approaches are presented in the next chapter.

## CHAPTER 4

### MISSING DATA

Due to the longitudinal nature of EMA data collected over many time periods, missing observations inevitably occur. In almost all cases where data are collected by EMA methods, the missingness occurs in an intermittent fashion. In order to correctly analyze and form longitudinal mixed-models using EMA data, a complete understanding of missingness mechanisms is needed.

#### 4.1 Missingness Mechanisms

Rubin (1976) formally introduced the mathematical representation of missing data mechanisms. These missingness mechanisms are further elaborated in comprehensive books on missing data analysis by Little and Rubin (2002) and Verbeke and Molenberghs (2000). For notational purposes, let  $\mathbf{Y}_i = (y_{i1}, y_{i2}, \dots, y_{ij})'$  be a vector of longitudinal outcomes for the  $i^{th}$  subject ( $i = 1, 2, \dots, N$ )' observed on  $j$  occasions ( $t_1, t_2, \dots, t_j$ ). Also, let  $\mathbf{R}_i = (R_{i1}, R_{i2}, \dots, R_{ij})'$  be a vector of random variables indicating missing data status where  $R_{ij} = 1$  denotes an observed visit and  $R_{ij} = 0$  denotes a missed visit for subject  $i$  at time  $j$ . The vector of outcomes  $\mathbf{Y}_i$  contain both observed outcomes  $\mathbf{Y}_i^o$  and missing outcomes  $\mathbf{Y}_i^m$ . Lastly, any model covariates will be denoted by  $X_i$ .

If missingness  $\mathbf{R}_i$  of the outcome variable  $\mathbf{Y}_i$  does not depend on model covariates  $X_i$ , observed outcomes  $\mathbf{Y}_i^o$ , or missing outcomes  $\mathbf{Y}_i^m$ , the missingness mechanism is considered *missing completely at random* (MCAR). Also, if the missingness mechanism is considered MCAR, the subset of observations can be assumed to be a random sample of the population. In this case, modelling of the missingness mechanism is usually not needed and using a complete case analysis will result in unbiased estimates of model coefficients. If the missingness process



indicated by  $\mathbf{R}_i$  only depends on covariates  $X_i$ , then the missingness mechanism is considered *covariate dependent missingness*, a special case of MCAR noted by Little and Rubin (2002). As an example, suppose that missing values of blood pressure readings occur when a person's weight in the study is above a certain level and that weight is a fully measured covariate.

A *missing at random* (MAR) process occurs if the missingness  $\mathbf{R}_i$  of the outcomes  $\mathbf{Y}_i$  depends additionally on observed previous values of  $\mathbf{Y}_i^o$  and possibly measured covariates  $X_i$ . For instance, in a longitudinal study, if the missingness in outcomes at a given time point is related to outcomes measured at a previous time point then MAR holds. This can occur if patients dropout before the last study time-point due to a previous measured value crossing a certain level. Lastly, when the missingness process  $\mathbf{R}_i$  is dependent on the missing values  $\mathbf{Y}_i^m$  conditionally on observed outcomes  $\mathbf{Y}_i^o$  and observed covariates  $X_i$ , then the missingness mechanism is considered *missing not at random* (MNAR).

## 4.2 Ignorable and Non-Ignorable Missingness

Little and Rubin (2002) also developed a formal definition of ignorable missingness mechanisms. If the missingness process for the missing data is independent of the outcome process, then the mechanism is ignorable. This is presented more rigorously by examining the full-data likelihood in a mixed-model context. Following the notation used by Rubin (1976), Little and Rubin (2002), and Verbeke and Molenberghs (2000), the full-data density for a mixed-model with longitudinal outcomes can be written as:

$$f(\mathbf{Y}_i, \mathbf{R}_i | X_i, Z_i, \gamma, \phi). \quad (4.1)$$

The term  $\mathbf{Y}_i$  refers to the longitudinal outcomes for  $i = 1, \dots, N$  individuals,  $\mathbf{R}_i$  is the missingness indicator for each of the outcomes,  $X_i$  represents the fixed components of the mixed-model,

and  $Z_i$  refers to the random components of the mixed-model. The parameters for the outcomes are represented by  $\gamma$  and the parameters contained in  $\phi$  index the missing data process. With MAR or MCAR the full-data likelihood for the  $i^{th}$  subject is:

$$\begin{aligned} f(\mathbf{Y}_i^o, \mathbf{R}_i | X_i, Z_i, \gamma, \phi) &= f(\mathbf{R}_i | \mathbf{Y}_i^o, X_i, Z_i, \phi) \\ &\times \int f(\mathbf{Y}_i^o, \mathbf{Y}_i^m | X_i, Z_i, \gamma) d\mathbf{Y}_i^m \\ &= f(\mathbf{R}_i | \mathbf{Y}_i^o, X_i, Z_i, \phi) f(\mathbf{Y}_i^o | X_i, Z_i, \gamma). \end{aligned}$$

The solution holds if the missing values  $\mathbf{Y}_i^m$  can be integrated out of the above integral. Therefore, the missingness process  $f(\mathbf{R}_i | \mathbf{Y}_i^o, X_i, Z_i, \phi)$  does not depend on the missing outcomes  $\mathbf{Y}_i^m$ . If MNAR holds, the likelihood usually cannot be factored this way and a different approach is needed to handle the missing data process. One technique which can be applied to missing data in both ignorable and non-ignorable settings is multiple imputation (MI).

### 4.3 Multiple Imputation

As discussed by Rubin (1987), MI handles issues with non-response in sample surveys. In multiple imputation, an assumed model for the missing data  $\mathbf{Y}_i^m$  is formed based on the observed data  $\mathbf{Y}_i^o$ . Multiple copies of the missing values are then generated based on the assumed model. Rubin (1987) shows that a small number of imputations is needed (usually less than 10) and that desired parameter estimates and standard errors can easily be combined using a set of rules. Major statistical software such as SAS (2008), SPLUS (2009), and R (2009) contain code to run multiple imputation in various settings.

Schafer (1997) explores many facets of MI in his informative text which describes how to impute continuous, categorical, and multinomial missing data values. Demirtas (2005) uses MI on a longitudinal data set containing non-ignorable dropout. The paper suggests that dropout

in a longitudinal trial to treat schizophrenia is non-ignorable for two reasons. First of all, patients treated with a schizophrenia drug dropped out of the study because they were getting better. On the other hand, placebo patients dropped out because their health status worsened over the course of the study. The models shown here are unique in that they combine random-coefficient pattern-mixture models with multiple imputation. Although the data set has been analyzed elsewhere by Hedeker and Gibbons (1997, 2006), the author presents a valuable MI approach that complements the results presented in the initial papers.

#### 4.4 Selection Models

Selection models can be traced back to the initial work of Heckman (1976), who developed a model to determine how individuals enter and leave the labor force using a probabilistic model. Diggle and Kenward (1994) later extended this approach to model informative dropouts in a biomedical setting. Selection models are one method to factor the joint likelihood of outcomes and the missingness mechanism. The joint distribution of  $\mathbf{R}_i$  (the missingness indicator vector for each subject) and  $\mathbf{Y}_i$  (the outcomes for each subject) is written as  $f(\mathbf{R}_i, \mathbf{Y}_i | X_i, Z_i, \gamma, \phi)$ . The vector  $X_i$  includes the measured covariates for each subject and the vector  $Z_i$  includes possible random effects terms. The unknown parameters  $\gamma$  are to be estimated from the outcomes  $\mathbf{Y}_i$ , and  $\phi$  refers to parameters describing the missing data mechanism. With selection models, the joint distribution of  $\mathbf{R}_i$  and  $\mathbf{Y}_i$  is separated as a marginal distribution of  $\mathbf{Y}_i$  multiplied by a conditional distribution of  $\mathbf{R}_i$  given  $\mathbf{Y}_i$ .

$$f(\mathbf{R}_i, \mathbf{Y}_i | X_i, Z_i, \gamma, \phi) = f_Y(\mathbf{Y}_i | X_i, Z_i, \gamma) f_{R|Y}(\mathbf{R}_i | X_i, \mathbf{Y}_i, \phi). \quad (4.2)$$

More precisely with longitudinal data, selection models combine a model for the observed data with a separate model for missingness process. If the data are MNAR, then the selection model

approach requires full specification of the model for the missing-data mechanism which is often identified by untested distributional assumptions (Little, 1993).

#### 4.5 Pattern-Mixture Models

Pattern-mixture models factor the full data likelihood in a different manner than selection models. The final distribution of outcomes is considered a mixture of marginal distributions formed from each missing data pattern.

$$f(\mathbf{Y}_i, \mathbf{R}_i | X_i, Z_i, \gamma, \phi) = f_{Y|R}(\mathbf{Y}_i | \mathbf{R}_i, X_i, Z_i, \gamma) f_R(\mathbf{R}_i | X_i, \phi). \quad (4.3)$$

The quantity  $\mathbf{Y}_i$  refers to the longitudinal outcomes,  $\mathbf{R}_i$  is the missingness indicator vector,  $X_i$  refers to model covariates, and  $Z_i$  refers to subject-level random effects. Most often in pattern-mixture models, the dropout times of each subject are used to form separate patterns  $\mathbf{R}_i$ . The  $\gamma$  parameter represents the outcomes process, and the  $\phi$  parameter represents the missingness process. Pattern-mixture models form distinct patterns or groups in the data, and average over those patterns to determine the effect of covariates  $X_i$  on model outcomes  $\mathbf{Y}_i$ . Random-coefficient pattern-mixture models (Little, 1995; Hedeker and Gibbons, 1997; Demirtas and Schafer, 2003) are extensions of pattern-mixture models that allow for random effects to be included in a pattern-mixture model. These random-coefficient models are used if the drop-out or missing data are related to an underlying process which the outcome variable may not capture (Little, 1995; Demirtas and Schafer, 2003). Random-coefficient models link the dropout and outcomes processes by one or more shared parameters.

##### 4.5.1 Advantages

Pattern-mixture models are an advantage over selection models for two main reasons. One advantage is that no model form of the drop-out or missingness mechanism is needed

as is usually done with selection models. Selection models have been criticized because the distribution of the missingness model cannot be verified (Little, 1993; Laird, 1988). In many cases, an iterative solution is needed to solve selection models that may not converge (Little, 1994).

Another advantage is that pattern-mixture models allow flexibility in determining the number of patterns needed for the question of interest. For instance, in longitudinal studies with fixed study visits, any drop-outs occurring before these visits can be used to form patterns needed in a pattern-mixture model where the patterns are formed by the time of drop-out. It is also possible to form patterns if the study visits are not fixed, these type of pattern-mixture models are described in more detail by Lin et al. (2004) and Roy and Daniels (2008).

#### 4.5.2 Disadvantages

Pattern-mixture models are typically under-identified. This is described in more fully by Little (1993). Pattern-mixture models are under-identified because means and covariances across the separate missing-data patterns cannot always be identified. As an example, consider a study where outcomes  $Y_{i1}$  and  $Y_{i2}$  are collected at two time points ( $j = 1, 2$ ) on  $N$  subjects and all values of  $Y_{i1}$  are observed and some values of  $Y_{i2}$  are missing. The missing values of  $Y_{i2}$  supply no information about the parameters of the distribution of  $Y_{i2}$  given  $Y_{i1}$  where  $Y_{i2}$  is missing. Therefore, assumptions must be made about the distribution of  $Y_{i2}$  given  $Y_{i1}$  for this missingness pattern. Little (1993) describes this type of restriction as a complete-case missing-variable restriction. Other restrictions such as neighboring-case polynomial-coefficient restrictions and available-case polynomial-coefficient restrictions are described in more detail by Demirtas and Schafer (2003) and Verbeke and Molenberghs (2000).

Pattern-mixture models do not derive the marginal effects of the model parameters as is done with selection models. These marginal estimates are derived by averaging over the

separate patterns. Also, the delta method is needed to form standard errors of the model parameters, since they are not provided using the pattern-mixture model framework. These additional calculations may not be troublesome to do, but require extra computational steps that are not necessary with selection models. Little (1993) believes that there may be cases with survey data where it is natural to analyze non-response patterns of separate demographic groups, so this averaging step may not be necessary.

### 4.5.3 Examples

Pattern-mixture models are highly adaptable to different data types and settings. Some of these settings include intermittent missing data (Lin et al., 2004), multi-level pattern-mixture models (Demirtas, 2005), binary outcomes (Albert and Follman, 2007), and latent class pattern-mixture models (Lin et al., 2004; Roy, 2007).

The paper by Lin et al. (2004) explores intermittent missing continuous data by forming patterns based on latent classes. A main property noted in this work is that the missingness process is assumed to be conditionally independent of the longitudinal outcomes given the latent classes. Also, this work is unique in that irregularly spaced outcome visits are accommodated in the model. The final model developed has a total of four latent classes related to participation of homeless veterans in counselling sessions and uses these unobserved latent classes as patterns. The mean number of days homeless differed by the assigned behavioral intervention and by the distinct latent classes. Additional insight and precision was gained by analyzing outcomes with a latent class pattern-mixture model versus a linear mixed-model that did not account for the missingness process.

A three-level pattern-mixture model for non-ignorable drop-out is provided by Demirtas (2005). This work develops pattern-mixture models using a Bayesian perspective. The random level for dropout group is added to the usual two-level linear mixed-model for longitudinal

data described by Laird and Ware (1982). The work analyzed the same schizophrenic data set presented by Hedeker and Gibbons (1997). Demirtas (2005) varies model assumptions and imputation techniques to show that model uncertainty can be reduced by using the proposed three-level pattern-mixture model. The technique developed in this work provides a method to generate multiple data sets containing features of a real data set (parameter means and variances) and under MAR and MNAR scenarios. The computational methods provided in Demirtas (2005) will be adapted to simulate and assess the proposed latent trait pattern-mixture mixed models fit to EMA data. The full development of these steps will be provided in Chapter 7.

Other research using pattern-mixture models in non-ignorable missing-data settings include the following approaches. Albert and Follman (2007) investigate random effects and latent process approaches for longitudinal binary data. Roy (2003) uses latent class pattern-mixture models for non-ignorable longitudinal dropout. Also, a summary of latent class modelling in a pattern-mixture context can be found in Roy (2007). All of these approaches provide a basis to analyze longitudinal data that involve a missingness mechanism that is assumed to be MNAR.

#### **4.6 Sensitivity**

Sensitivity analysis is a necessary step to assess model selection and performance under different conditions for use with missing-data models. Curran et al. (2004) explores sensitivity of pattern-mixture models to assumptions. A concise work which presents modelling of intermittent missing data in a Bayesian framework is presented in Daniels and Hogan (2008). Other works that outline sensitivity analysis approaches are Verbeke and Molenberghs (2000), Verbeke et al. (2001), and Beunckens et al. (2008). These authors warn of using one final MNAR model to obtain estimates and draw conclusions about longitudinal outcomes with missing data. They stress the importance of comparing various models by modifying missing data assumptions.

Verbeke et al. (2001) use a local influence approach for non-random dropout. In this technique, observations that cause large differences in model estimates after deletion are investigated. A likelihood displacement is computed for the full set of observations as compared to a reduced model without the influential observations. The approach is used with a selection model framework. Although this approach allows an assessment of the selection model fit, it still does certify that the dropout model chosen is the correct one.

#### 4.7 Modelling Intermittent Missing Data

Intermittent missing longitudinal data (such as data collected via EMA methods) are usually quite difficult to handle in both practical and applied settings. During the course of a clinical trial, intermittent values are problematic in terms of patient follow-up. Some models previously used for missing intermittent data points have usually assumed that the missing values are MAR (Hedeker and Gibbons, 1997; Yang and Shoptaw, 2005) when the number or proportion of intermittent values are low. Also, the intermittent values add a layer of complexity as compared to dropout models which on their own can be difficult to model. Gad and Ahmed (2007) describe an example which involves an EM algorithm with intermittent missing data which is assumed to follow a non-normal distribution.

Various ways of modelling intermittent missing longitudinal data have experienced rapid growth in the last few years. The types of approaches fall into five main types: Markov chain models (Deltour et al., 1999; Albert, 2000), pseudo-likelihood models (Troxel et al., 1998?), inverse intensity-of-visit process weighted estimators (Robins et al., 1994, 1995; Lin et al., 2004), shared parameter models (Albert et al., 2002; Roy, 2007), and latent class pattern-mixture models (Lin et al., 2004; Roy, 2007; Birmingham and Fitzmaurice, 2002).

The Markov chain model of Deltour et al. (1999) uses three health states to model disease severity. Deltour's method is based on Bayesian statistical methods as it uses a Gibbs



sampler and a stochastic EM algorithm to model the intermittent missing data that has a non-ignorable missingness process. This method can be perceived as a variant form of maximum likelihood. An extra step of using the Markov chain is needed before the EM algorithm or Gibbs sampler is used. The model may not be applicable to use with the EMA data set due to the fact that study individuals do not move between different disease states.

The pseudo-likelihood model approach in Troxel et al. (1998) is similar to the method in Deltour et al. (1999) and uses a Markov dependence structure for the responses. The estimation method develops a Nelder-Mead algorithm to estimate the final likelihood. The authors use a logistic model to estimate the missingness probabilities. The approach cannot be easily run with more than three or four time points. It may not be an applicable method with EMA data due to the large number of observations for each participant.

Inverse probability weighted estimators were initially presented by Robins et al. (1994, 1995). These techniques can be considered a new class of semi-parametric estimators. In these papers, methods are presented for analysis of data that are missing at random. Lin et al. (2004) modify the initial techniques to include arbitrary missing data patterns. This is done by developing marginal regression models for longitudinal responses that are observed in continuous time. Their technique requires the correct specification of a visit process intensity model. In this study, the overall model performs better in terms of biases and standard errors than a standard GEE model that assumes that missingness follows a MAR process.

Within the shared parameter approach, the article by Albert et al. (2002) presents a latent autoregressive model for longitudinal data subject to informative missingness. With this autoregressive model, the latent process is shared between binary outcomes and the missing data process. His model uses a Monte Carlo EM algorithm to estimate model parameters and is quite difficult to program. The data analyzed contain two types of missingness: intermittent

missing observations and missingness due to dropout. The model presented allows for intra-subject autocorrelation by linking the binary response and missing data process through a Gaussian auto-regressive process.

Lin et al. (2004) introduce a latent class approach to determine patterns needed for a pattern-mixture model. In this work, the data analyzed contain intermittent missingness and is assumed to be missing not at random (MNAR). The study examined veterans visits to receive counselling and job training help. The subjects observed here do not have a fixed set of visit times. The model uses four latent classes to link the response patterns to outcomes. The latent classes were formed using a joint model that estimated longitudinal outcomes, covariates, and the latent classes. The latent classes related to intensity of visit trajectories for the veterans in the study. In this work, the outcomes are assumed to be missing at random given the random effects and the latent classes. Further discussion of latent classes and methods used to estimate these models is presented in the next chapter. Also, an introduction to latent trait models will be presented as well.

## CHAPTER 5

### LATENT CLASS AND LATENT TRAIT THEORY

Latent variables are unobserved random variables whose realized values are hidden (Skrondal and Rabe-Hesketh, 2007). Latent class and latent trait analysis are data reduction techniques that transform observed categorical variables into meaningful summary variables. Latent class analysis reduces observed categorical outcomes into categorical groups. For instance, latent classes can be formed to group individuals based on their history of voting patterns into “conservative,” “liberal,” or “independent” voters (McCutcheon, 1987). In this case, the categorical variables are nominal values of the selected candidates collected over a period of time. These voting groups form natural clusters of interest for political research. Estimation and applications of the latent class model will be presented in Section 5.1 and Section 5.2.

Conversely, latent trait methods reduce the observed categorical variables to continuous outcomes. These continuous outcomes or latent traits link the unobserved ability of subjects to observed responses that are categorical. As an example, latent traits can be used to form a continuous distribution of mathematical “ability” for grade-school students who take a math exam. The observed categorical responses correspond to the incorrect and correct answers for each student and are used to estimate mathematical ability represented by the latent trait. In latent trait methods, the latent variable or “ability” of a subject is typically assumed to follow a standard normal distribution. Background information and estimation of latent trait models will be discussed in Section 5.3.

#### **5.1 Latent Class Theory**

In latent class theory, individuals with similar characteristics are grouped together into classes which represent unmeasurable traits or behaviors. In political science applications,

latent classes are used to analyze characteristics such as voting interest and apathy towards politics where these characteristics are measured through a sequence of items. McCutcheon (1987) provides a concise introductory presentation with many applied examples. A more mathematical and theoretical presentation of latent class analysis is contained in Clogg (1995).

### 5.1.1 Modelling Latent Classes

Agresti (2002) and Lanza et al. (2007) both provide a description of how latent class models can be fit using maximum likelihood methods. Let  $C$  represent a latent class variable with  $c$  categories or classes. Due to the properties of latent class model, the  $T$  responses to the categorical variables  $R$  are independent given latent class membership in class  $c$ :

$$P(R_1 = r_1, \dots, R_T = r_T | C = c) = P(R_1 = r_1 | C = c) \dots P(R_T = r_T | C = c). \quad (5.1)$$

Two important probabilities are needed to estimate the latent class model. The first is  $P(C = c)$ , the probability of being in an individual latent class  $c$ . The second is the conditional probability of a specific outcome  $r_t$  within latent class  $c$  and is represented as  $P(R_T = r_T | C = c)$ . A  $T$ -dimensional contingency table classifying all of the observed responses in  $R_t$  can be formed. The latent class approach forms a  $(T + 1)$ -dimensional table that adds one more dimension to the  $T$ -dimensional table for the unobserved latent classes. If we denote the number of categories in each  $R_t$  by  $I$ , the number of latent classes by  $q$ , and the observed probabilities as  $\pi_{r_1, \dots, r_T} = P(R_1 = r_1, \dots, R_T = r_T)$ , a multinomial distribution can be assumed for the  $I^T$  cells.

$$\pi_{r_1, \dots, r_T} = \sum_{c=1}^q P(R_1 = r_1, \dots, R_T = r_T | C = c) P(C = c). \quad (5.2)$$

Equation 5.2 represents the probability that given item-responses  $r_1, \dots, r_T$  occur within a given cell. The conditional independence assumption will factor Equation 5.2 to

$$\pi_{r_1, \dots, r_T} = \sum_{c=1}^q \left[ \prod_{t=1}^T P(R_t = r_t | C = c) \right] P(C = c) \quad (5.3)$$

since the probabilities  $P(R_t = r_t)$  are independent given membership in latent class  $c$ . If the observed table counts are  $[n_{r_1, \dots, r_T}]$  and the  $I^T$  cells are summed in the observed table, the multinomial log-likelihood that will need to be maximized is written as

$$\sum n_{r_1, \dots, r_T} \log \pi_{r_1, \dots, r_T}. \quad (5.4)$$

As shown by Lin et al. (2004) the probability that subject  $i$  belongs to latent class  $c$  given a covariate vector  $\mathbf{v}_i$  and class-specific coefficient vector  $\eta_c$  is:

$$P(C = c) = \frac{\exp(\mathbf{v}_i' \eta_c)}{\sum_{c=1}^C \exp(\mathbf{v}_i' \eta_c)} \quad (5.5)$$

and can be modeled with a baseline category logit model as described by Agresti (2002). This type of model will determine posterior probabilities of membership for each subject in all of the latent classes  $p_1, \dots, p_c$ . Final assignment of individual  $i$  to latent class  $c$  is done by choosing the highest posterior probability of class membership from this set. For instance, if a three latent classes are modeled and the posterior probabilities for subject  $i$  are  $[p_{c1}^\wedge = 0.65, p_{c2}^\wedge = 0.23, p_{c3}^\wedge = 0.12]$  then this subject will be classified into the first latent class  $c1$ .

## 5.2 Estimation of Latent Class Models

An iterative process maximizing Equation 5.4 using the parameters from Equation 5.2 can be done using Newton-Raphson or EM algorithms (Agresti, 2002). The EM algorithm is

useful but it does not provide estimated standard errors for the parameters, therefore Newton-Raphson may be preferred. The first step of the process starts with initial trial values of the latent class probabilities  $P(C = c)$  and the conditional probabilities  $P(R_t = r_t|C = c)$  shown in Equation 5.4. The next step will calculate counts  $n_{r_1, \dots, r_T}$  and the new proportions  $\mu_{r_1, \dots, r_T, c}^{(s)}$  shown in the following equation:

$$n_{r_1, \dots, r_T, c}^{(s+1)} = n_{r_1, \dots, r_T} \frac{\mu_{r_1, \dots, r_T, c}^{(s)}}{\sum_{k=1}^c \mu_{r_1, \dots, r_T, k}^{(s)}}. \quad (5.6)$$

This iterative process is continued until the differences between estimates of  $P(C = c)$  and  $P(R_t = r_t|C = c)$  at each step are small. One may set the desired number of iterations or a tolerance criteria and then evaluate the fit of the model by comparing the observed values for each response pattern to the predicted counts from the latent class. The usual approach is to form two latent classes and increase the number of classes until an appropriate model is fit using selection criteria such as log-likelihood statistics, Bayesian information criteria, or Akaike information criteria. Further discussion outlining methods to select number of classes needed is found in Garrett and Zeger (2000). These authors argue that  $\chi^2$  and deviance statistics may not be adequate diagnosis tools and Markov chain Monte Carlo methods may be more suitable because they can be used to determine parameters that are well identified. It is also important that the number of classes not be too high, so that models can be easier to interpret. Additional presentation of maximum likelihood approaches for latent class analysis can be found in Fienberg et al. (2010).

The maximum likelihood method shown here will be used to classify students in the EMA data set based on the response indicators  $R_{ij}$ . The response indicators are simply a series of binary indicators representing whether an EMA prompt was answered or not. The ability

to group respondents into latent classes is available with different computer packages such as SAS PROC LCA (Lanza et al., 2006), R package LCA (Waller, 2004), and R package poLCA (Linzer and Lewis, 2007). A more detailed discussion outlining the latent class pattern-mixture model will be provided in Chapter 6.

### 5.2.1 Examples

As mentioned previously, Lin et al. (2004) introduces a latent class approach to determine patterns needed for a pattern-mixture model. In this work, the data analyzed contain intermittent missingness and are assumed to be MNAR. Each latent class is determined by the time of dropout. The observed subjects do not have a fixed set of visit times. The model uses four latent classes to link patient visit intensities to outcomes. The approach of these intermittent data techniques used by Lin et al. (2004) will be extended to develop the proposed LTPMMs for use with an EMA data set.

## 5.3 Latent Trait Theory

Two introductions to latent trait or IRT models can be found in Baker (2001) and Embretson and Reise (2000). Latent trait theory (also known as item response theory), is a psychometric technique in which trait level estimates depend on a person's response to individual items and the properties of those items (Embretson and Reise, 2000). As an example, IRT models can be used with the Scholastic Aptitude Test (SAT) college entrance exam to derive a latent trait for each individual that measures their intelligence. Suppose that the SAT test contains 100 questions. A series of responses can be formed for a student taking this exam containing indicators that equal 1's for correct answers and 0's for incorrect answers. This categorical data pattern representing all correct or incorrect items for each subject is reduced to a continuous latent trait variable. Students that answer more questions correctly would receive a higher total score and have a higher latent trait that represents intelligence.

Also, IRT is used to estimate difficulties for each item. For example, the SAT exam as proposed above would have 100 item difficulties, one for each question. These difficulty parameters or thresholds represent the minimum ability or latent trait where the likelihood that the question is answered correctly is increased. Questions that are easiest would have a low level of item difficulty and harder questions would have a higher level of difficulty. In addition, IRT models allow a discrimination or slope parameter to be estimated for each item. In the one-parameter Rasch model all item discrimination parameters are assumed to be equal. Two-parameter IRT models allow these discrimination parameters to vary among the individual items. Items with higher slopes are able to easily distinguish or discriminate different levels of the trait. Items with a very low slope poorly distinguish different values of the latent trait amongst individuals taking the test or exam.

### 5.3.1 One-Parameter Item Response Theory Model

In the context of EMA data that will be used in this dissertation, the outcome variable in the IRT model will be defined as  $R_{ij}$ . The one-parameter IRT model or Rasch model has the following logistic form modelling the probability of response:

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-a(\theta_i - b_j)]} \quad (5.7)$$

where  $R_{ij}$  represents the response to item  $j$  from subject  $i$ .  $P(R_{ij})$  is the probability that person  $i$  responds to item  $j$ , the latent trait is represented by  $\theta_i$ ,  $a$  is the common slope for each item, and  $b_j$  is the difficulty parameter for each item. With this notation, the number of subjects ranges from 1 to  $N$ , and the number of items  $j$  ranges from 1 to  $m_i$ , allowing for a different number of items for each subject. In looking at the denominator, if an individual has a higher latent trait  $\theta_i$  compared to the item difficulty  $b_j$ , the probability that the person



responds correctly to the item is increased. The one-parameter model can be written in a slightly different form

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-(c_j + a\theta_i)]} \quad (5.8)$$

where the item-intercept parameter is expressed as  $c_j = ab_j$ . As noted by Bock and Aitkin (1981) and Hedeker et al. (2006) this change is convenient because it simplifies the estimation of the item parameters.

### 5.3.2 Two-Parameter Item Response Theory Model

The two-parameter IRT model is similar to the one-parameter model

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-a_j(\theta_i - b_j)]} \quad (5.9)$$

but allows for different slopes  $a_j$ , instead of a fixed slope  $a$  used in the one-parameter model shown in Equation 5.8. The two-parameter IRT model can be written in the form

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-(c_j + a_j\theta_i)]} \quad (5.10)$$

where  $c_j = -a_jb_j$  represents the item-intercept parameter.

Further inspection of these reformulated models show that they are versions of mixed-effects logistic models for binary outcomes that include random intercept terms (Hedeker et al., 2006). This can be seen by rewriting the one-parameter model in Equation 5.8 in terms of the log-odds of response

$$\log \left[ \frac{P(R_{ij} = 1|\theta_i)}{1 - P(R_{ij} = 1|\theta_i)} \right] = c_j + a\theta_i. \quad (5.11)$$

Let  $\boldsymbol{\lambda}_i$  represent the  $m_i \times 1$  vector of logits for subject  $i$ . Since each subject can answer a different number ( $m_i$ ) of prompts, their design matrix  $\mathbf{X}_i$  will be of dimension  $m_i \times m$  where

$m$  represents the total number of items. Let  $\mathbf{V}_j$  be a  $m \times 1$  vector of zeros or ones. If item  $j$  is answered, then the  $j^{th}$  row of  $\mathbf{V}_j$  is set to 1, otherwise it remains the value 0. The design matrix  $\mathbf{X}_i$  is formed by concatenation of the  $j$  column vectors  $\mathbf{V}_j$ . If we also let the vector  $\boldsymbol{\beta}$  represent the difficulties for item  $j$  and  $\sigma_v$  represent the item discrimination parameter  $a$ , the Rasch model can be written as

$$\lambda_i = X_i\boldsymbol{\beta} + \mathbf{1}_i\sigma_v\theta_i. \quad (5.12)$$

In this model representation,  $\mathbf{1}_i$  is a  $m_i$  vector of ones, and  $\theta_i$  is the latent trait value of subject  $i$ , which is distributed  $\sim N(0,1)$ . In this case, the value of  $\theta_i$  behaves as a random effect and also influences the log-odds of response. Equation 5.12 is a random-intercept logistic regression model where the intercepts are defined by the latent trait  $\theta_i$ . The latent traits are assumed to be normally distributed with a mean of 0 and a variance of 1 because the random effects are standardized by letting  $\theta_i = v_i/\sigma_v$ .

The two-parameter model can also be written in mixed-model form as:

$$\log \left[ \frac{P(R_{ij} = 1|\theta_i)}{1 - P(R_{ij} = 1|\theta_i)} \right] = c_j + a_j\theta_i. \quad (5.13)$$

where the discrimination parameters  $c_j$  vary by item  $j$ . Accordingly, the matrix form of the two-parameter IRT model is written

$$\boldsymbol{\lambda}_i = \mathbf{X}_i'\boldsymbol{\beta} + \mathbf{X}_i'\mathbf{T}\theta_i \quad (5.14)$$

where  $\mathbf{T}$  represents a vector of discriminations or slope parameters that are allowed to vary across items.

$$\mathbf{T}' = \begin{bmatrix} \sigma_{v_1} & \sigma_{v_2} & \dots & \sigma_{v_n} \end{bmatrix}. \quad (5.15)$$

## 5.4 Estimation of Latent Trait Models

Various approaches can be used to fit latent trait models and estimate the item parameters (difficulties and discriminations) and the latent traits. An EM algorithm is presented in an early article by Bock and Aitkin (1981). A comprehensive survey of different estimation techniques is outlined in Johnson (2007). The article reviews many estimation procedures including joint maximum-likelihood, conditional maximum-likelihood, and marginal maximum-likelihood. It also describes how Bayesian estimation methods using Markov chain Monte Carlo techniques can be used as well. Other techniques found in the literature include presentations by Feddag and Mesbah (2006) who describe a generalized linear mixed model approach to estimation of latent trait models and Zwinderman (1995) who presents a pseudo-likelihood approach to fitting the Rasch model.

## 5.5 Identifiability

Stable and valid estimation of model parameters is important in any statistical model. Identifiability is defined as a condition where all model parameters can be identified and estimated by the data. If too many parameters (both item difficulties and item discriminations) are specified, a latent trait model may not converge to a meaningful solution. Various sources outlining the identifiability issues inherent in IRT models can be found in the psychometric, educational testing, and statistical literatures.

Moran (1986) outlines how in the two-parameter IRT model, all parameters are identifiable under wide conditions, provided that the number of items is more than two and all appropriate discrimination parameters are positive. Independence and likelihood conditions necessary for identifiability of latent trait models are discussed by Junker (1991). These conditions are required if the latent trait model is fit under a parametric form such as a logistic or probit model. In contrast, identifiability can be assessed with non-parametric IRT estimation

(Douglas and Cohen, 2001). Other works describing identifiability conditions of the one- and two-parameter latent trait models are Stout (2007) and Holland (1990).

A full description of the estimation process needed for the latent trait components of the proposed LTPMMMs will be provided in Chapter 7. Also, that chapter will describe some of the identifiability assumptions that were used in order to fit the IRT components of the proposed models.

## CHAPTER 6

### PROPOSED MODELS

As explained in earlier chapters in this dissertation, very little work has focused on missing data techniques with EMA data. Also, previous statistical techniques that have focused on intermittent missing data may not be applicable with the data presented here. For instance, for latent class pattern-mixture models to work successfully, distinct and meaningful classes must be formed. The LTPMMM is a novel technique that will use the uniqueness of the response patterns from EMA collection to have an effect on model outcomes. Also, the proposed LTPMMMs are unique in that a latent trait will be used as a model covariate. This latent trait of "responsiveness" will determine a possible relationship between missingness and mood outcomes.

#### 6.1 Formulation

This chapter outlines the development of the four proposed mixed-models that will be fit with EMA data. The first model is a MAR longitudinal mixed-effects model with random intercept terms. The remaining models will use latent variable approaches to model the missingness mechanism. A latent class pattern-mixture model will use three classes to represent similar missingness patterns. A one-parameter LTPMMM, and a two-parameter LTPMMM are the remaining models. With these two IRT-based models each subject's propensity to respond will be modeled by the latent trait. In all of the proposed models, the outcome variable is conditionally normal  $\mathbf{y}_i$ , given the error terms  $\mathbf{e}_i$ , and random effect terms which are both assumed to be normally distributed.

A longitudinal mixed-effects model with only a random intercept term ( $v_{0i}$ ) will be used to account for the high intra-subject correlation due to the multiple responses from each subject.

This first model does not model the missingness mechanism in any way. More details about the EMA data set with model covariates will be presented in the next chapter. The four models will use the baseline covariates: smoker (yes or no), gender (male), negative mood regulation, and student grade point average (GPA) to model negative or positive affect outcomes ( $y_{ij}$ ). All models will separate the time-varying variable  $Alone_{ij}$  into its between ( $\overline{Alone_i}$ ) and within-subjects ( $Alone_{ij} - \overline{Alone_i}$ ) effects. A description of this technique to handle time-varying covariates is found in Hedeker and Gibbons (2006).

### 6.1.1 Missing at Random Mixed-Model

The level-1 and level-2 MAR models are:

Level 1: Occasions-level:

$$y_{ij} = b_{0i} + b_{1i}(Alone_{ij} - \overline{Alone_i}) + e_{ij}.$$

Level 2: Between-subjects:

$$\begin{aligned} b_{0i} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i + \beta_4 GPA_i \\ &\quad + \beta_5 \overline{Alone_i} + v_{0i} \\ b_{1i} &= \beta_6. \end{aligned}$$

The full MAR mixed-model is written as:

$$\begin{aligned} y_{ij} = & \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i \\ & + \beta_4 GPA_i + \beta_5 \overline{Alone_i} + \beta_6 (Alone_{ij} - \overline{Alone_i}) + v_{0i} + e_{ij}. \end{aligned} \tag{6.1}$$

## 6.2 Response Vector

The latent class pattern-mixture, and the two LTPMMs will use a response vector of thirty-five time bins to estimate latent classes or latent traits that will be added to a longitudinal mixed-effect model. A full description of how these bins are defined will be presented in Section 8.2. In this case, the outcomes  $R_{ij}$  correspond to a response made to the EMA prompting device for subject  $i$  in time-bin  $j$ . Let the categorical variables  $(R_1, R_2, \dots, R_T)$  represent responses to prompts in time intervals formed from an EMA data set where the number of time intervals ranges from 1 to  $T$ .  $R_t$  at any given time-interval can have three possible values. If a prompt was answered at time interval  $t$  then  $R_t = 1$  and if it was unanswered then  $R_t = 0$ . In addition, if no prompt was generated in the given time-interval,  $R_t$  is set to a missing value ”.”. The estimated latent trait will therefore be an estimate of each subjects “responsiveness” to the prompts from the EMA device.

### 6.2.1 Latent Class Pattern-Mixture Model

The second model is based on techniques presented by Lin et al. (2004) who fit a latent class mixture model to intermittent missing data. The second proposed model includes indicators for latent class membership in class 2 and class 3. Therefore, the coefficients represent differences in the intercept relative to the first latent class. The latent classes will be formed by using each subjects response pattern  $R_{ij}$ . This model differs from the MAR mixed model by modelling the missingness mechanism by latent class membership. A latent class pattern-mixture model with three classes was chosen because it had the best fit (over models with 2, 4, 5, and 6 classes) in terms of its Bayesian Information Criteria (BIC) statistic. The level-1 and level-2 latent class pattern-mixture models are shown using the following equations. Note that the level-1 model used here is identical to the one used in the MAR mixed-model shown above.

The level-2 model differs from the MAR mixed-model by adding latent class indicators.

Level-1: Occasions-level:

$$y_{ij} = b_{0i} + b_{1i}(Alone_{ij} - \overline{Alone_i}) + e_{ij}.$$

Level-2: Between-subjects:

$$\begin{aligned} b_{0i} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i + \beta_4 GPA_i \\ &+ \beta_5 \overline{Alone_i} + \beta_7 LatentClass2_i + \beta_8 LatentClass3_i + v_{0i} \\ b_{1i} &= \beta_6. \end{aligned}$$

The full latent class pattern-mixture model is written as:

$$\begin{aligned} y_{ij} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i + \beta_4 GPA_i \\ &+ \beta_5 \overline{Alone_i} + \beta_6 (Alone_{ij} - \overline{Alone_i}) + \beta_7 LatentClass2_i + \beta_8 LatentClass3_i + v_{0i} + e_{ij}. \end{aligned} \tag{6.2}$$

### 6.2.2 One-Parameter Latent Trait Pattern-Mixture Mixed-Model

The third proposed formulation uses a one-parameter latent trait model to represent the missingness mechanism combined with a longitudinal mixed-effects model. The latent trait  $\theta_i$  is entered into the model as a between-subjects covariate. The level-1 and level-2 one-parameter LTPMMs are:

Level-1: Occasions-level:

$$y_{ij} = b_{0i} + b_{1i}(Alone_{ij} - \overline{Alone_i}) + e_{ij}.$$



Level-2: Between-subjects:

$$\begin{aligned}
 b_{0i} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i + \beta_4 GPA_i \\
 &\quad + \beta_5 \overline{Alone_i} + \gamma\theta_i + v_{0i} \\
 b_{1i} &= \beta_6.
 \end{aligned}$$

The full one-parameter LTPMMM is written as:

$$\begin{aligned}
 y_{ij} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i \\
 &\quad + \beta_4 GPA_i + \beta_5 \overline{Alone_i} + \beta_6 (Alone_{ij} - \overline{Alone_i}) + \gamma\theta_i + v_{0i} + e_{ij}.
 \end{aligned} \tag{6.3}$$

Response process model:

$$logit[R_{ij} = 1 | \theta_i] = (c_j + a\theta_i). \tag{6.4}$$

### 6.2.3 Two-Parameter Latent Trait Pattern-Mixture Mixed-Model

The fourth proposed model has the same format as the one-parameter LTPMMM except a two-parameter IRT formulation is used to represent the missingness mechanism. The level-1 and level-2 one-parameter LTPMMMs are:

Level-1: Occasions-level:

$$y_{ij} = b_{0i} + b_{1i}(Alone_{ij} - \overline{Alone_i}) + e_{ij}.$$

Level-2: Between-subjects:

$$\begin{aligned}
 b_{0i} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i + \beta_4 GPA_i \\
 &\quad + \beta_5 \overline{Alone_i} + \gamma\theta_i + v_{0i} \\
 b_{1i} &= \beta_6.
 \end{aligned}$$

The full two-parameter LTPMMM is written as:

$$\begin{aligned}
 y_{ij} &= \beta_0 + \beta_1 Smoker_i + \beta_2 GenderM_i + \beta_3 NegMoodReg_i \\
 &\quad + \beta_4 GPA_i + \beta_5 \overline{Alone_i} + \beta_6 (Alone_{ij} - \overline{Alone_i}) + \gamma\theta_i + v_{0i} + e_{ij}.
 \end{aligned} \tag{6.5}$$

Response process:

$$logit[R_{ij} = 1|\theta_i] = (c_j + a_j\theta_i). \tag{6.6}$$

The  $y_{ij}$  shown above correspond to level of positive affect (PA) or negative affect (NA) for individual  $i$  at time interval  $j$ . A subject may have repeated values of the model outcomes for two reasons. One is that more than one prompt may occur on the same day within a certain time-bin. Another reason is that if subjects participated in the study for more than seven days, these additional prompts collected after one week will just get added to the appropriate days and time-bin. In that way, the item characteristics can be studied for each day of the week.

In the IRT model shown above, thirty-five item difficulty parameters will be estimated. These correspond to the thirty-five time-bins created from the raw EMA data. Each day of the week will have five time-bins: from 3 a.m. to 8:59 a.m., from 9 a.m. to 2:59 p.m., from 3 p.m. to 5:59 p.m., from 6 p.m. to 8:59 p.m., and from 9 p.m. to 2:59 a.m. Further discussion of this bin structure will be provided in Section 8.2. Because the response patterns varied between days, the days will correspond to “Monday,” “Tuesday,” “Wednesday,” “Thursday,” “Friday,”

“Saturday,” and “Sunday”. The term  $a_j$  represents the item discrimination parameters, which, if the one-parameter LTPMMM is to be fit, will be equal for all time-bins. If the two-parameter LTPMMM is fit, all thirty-five discrimination parameters will be estimated.

As described in Chapter 5, identifiability issues can be a problem with IRT models. In fitting both the one- and two-parameter LTPMMMs, convergence issues arose while using fifty-six items, therefore the number of items was reduced to thirty-five. Also in the one- and two-parameter LTPMMM, some item difficulties were set equal to other so that the models would converge. This reduction was done by comparing item characteristic curves of the same time-bin across all study days. For instance, all difficulty parameters from the early morning time-bin from 3 a.m. until 8:59 a.m. were compared across days, if item characteristic curves were similar then the parameters were set to be equal. This method helped the LTPMMMs converge to a stable solution.

The proposed LTPMMM is presented using two separate models in a hierarchical structure; one model estimating the missingness process through the latent trait and a second model for the outcomes  $y_{ij}$  conditional on the latent trait  $\theta_i$ . The missingness model estimates latent trait or the “ability” of each participant ( $\theta_i$ ) of responding to the EMA device. The one-parameter IRT model will be modeled as:

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-(c_j + a\theta_i)]} \quad (6.7)$$

where all discrimination parameters among items are equal to  $a$  and the item-discrimination parameter  $c_j$  is equal to  $-ab_j$ . The two-parameter IRT model allows the discrimination terms ( $a_j$ ) to vary among items:

$$P(R_{ij} = 1|\theta_i) = \frac{1}{1 + \exp[-(c_j + a_j\theta_i)]} \quad (6.8)$$

and  $c_j = -a_jb_j$ . The outcomes will be fit using a mixed-model for the estimation of positive or negative affect with the estimated latent trait from Equation 6.8 and other subject-specific parameters such as gender. A longitudinal LTPMMM without interaction can be written as:

$$y_{ij} = x'_{ij}\beta + \gamma\theta_i + v_{0i} + e_{ij}. \quad (6.9)$$

The LTPMMM with interaction is written as:

$$y_{ij} = x'_{ij}\beta + (x'_{ij} * \theta_i)\beta_\theta + v_{0i} + e_{ij}. \quad (6.10)$$

The term  $x_{ij}$  refers the  $p \times 1$  vector of fixed effects for each individual and  $\beta$  represents a  $p \times 1$  vector of coefficients. As described previously, the subject's latent trait  $\theta_i$ , is measured by the Rasch or two-parameter IRT model and is distributed as  $\theta_i \sim N(0, \sigma_{\theta_i}^2)$ . The random effect  $v_{0i}$ , will allow for individuals to have unique intercepts and is distributed as  $v_{0i} \sim N(0, \sigma_{v_{0i}}^2)$ . The error terms  $e_{ij}$  are also assumed to be distributed as  $e_{ij} \sim N(0, \sigma_e^2)$ . The covariance matrix  $\Sigma_{v_{0i}, \theta_i}$  of the two random effects is assumed to be bivariate normal with the following structure:

$$\Sigma_{v_{0i}, \theta_i} \sim MVN \begin{bmatrix} \sigma_{v_{0i}}^2 & 0 \\ 0 & \sigma_{\theta_i}^2 \end{bmatrix}.$$

The covariance,  $\sigma_{v_{0i}\theta}$  is assumed to be zero due to the fact that both  $v_{0i}$  and  $\theta_i$  act as random intercepts, and the latter is included in the longitudinal model in Equation 6.9.

The proposed LTPMMM is similar to the model presented by Guo et al. (2004) in that each subject acts as their own pattern. Also, the proposed model shares features of selection models and pattern-mixture models as described in Guo et al. (2004). Furthermore, the proposed LTPMMM is a variation of a random-coefficient pattern-mixture model presented by Little (1995) where the latent trait for each subject acts as the random-coefficient. Each subject's latent trait will then play a role in estimating the two mood outcomes. This is a new approach fitting pattern-mixture models to intermittent missing data that have previously used latent classes to form patterns. Also, the LTPMMMs provide a novel technique to handle intermittent missingness that is frequently found with EMA data collection.

These two models can be estimated separately by first finding the latent trait in Equation 6.8 for each subject using (SAS, 2008) or the R package ltm (Rizopoulos, 2006). The second step can fit Equation 6.9 and Equation 6.10 and using standard mixed-model software. A more robust approach will estimate both outcomes and the missingness process as measured by the latent trait in a joint model. This modelling can easily be done using SAS PROC NLMIXED. The advantages of the joint model approach such as unbiased estimates are outlined in detail by Guo and Carlin (2004). This usually results because a parameter shared by both processes is linked together and estimated in one model. The full-likelihood derivation and estimation of the proposed model will be provided in the following chapter, with particular attention on how the latent trait is used as a shared parameter. Our approach is also unique in that the latent trait will be used as a covariate that has a relationship to negative and positive affect outcomes.

## CHAPTER 7

### RESEARCH PLAN

#### 7.1 Model Estimation

Maximum marginal likelihood estimation will be used to fit the proposed LTPMMM using the method described by Bock and Aitkin (1981). As shown by Liu (2008) and Liu and Hedeker (2006) the full-data likelihood needs to be averaged over the two random effects represented by the random-intercept  $v_{0i}$  and the latent trait  $\theta_i$ . The steps to formulate the full-data likelihood are shown as follows. The LTPMMM (with no interaction) can be written as:

$$f_1 = p(Y|b, \theta, R) = y_{ij} = x'_{ij}\beta + b_{0i} + e_{ij} \quad (7.1)$$

with error terms that are assumed to be normally distributed

$$e_{ij} \sim N(0, \sigma_e^2). \quad (7.2)$$

with standard deviation  $\sigma_e$ . If interaction terms of model covariates  $x'$  and  $\theta_i$  are included, the LTPMMM has the form  $f_1 = y_{ij} = x'_{ij}\beta + (x'_{ij} * \theta_i) * \beta_\theta + b_{0i} + e_{ij}$  with the same distribution for the error terms. The term  $b_{0i}$  includes the effect of the latent trait  $\theta_i$  and a random intercept term  $v_i$  and will be explained below. For ease of computation, the random intercept term can be written in standardized form as  $\sigma_v \xi_i$  where  $\xi_i$  follows a standard normal distribution. Let  $\gamma$

represent the effect of the latent trait  $\theta_i$  on  $y_{ij}$ . Therefore,  $b_{0i}$  is defined as the sum of  $\gamma\theta_i$  and  $\sigma_v\xi_i$ .

$$f_2 = p(b|\theta, R) = b_{0i} = \gamma\theta_i + \sigma_v\xi_i \quad (7.3)$$

$$\xi_i \sim N(0, 1) \text{ and } \theta_i \sim N(0, 1). \quad (7.4)$$

Including the standardized random effects in Equation 7.1 results in the following expression for the latent trait pattern mixture mixed-model:

$$f_{1,2} = y_{ij} = x'_{ij}\beta + \gamma\theta_i + \sigma_v\xi_i + e_{ij} \quad (7.5)$$

Since the probability density function of  $\xi$  is a standard normal with mean 0 and standard deviation 1 then:

$$p(\xi_i|\sigma_v) = (2\pi\sigma_v)^{1/2} \exp \left[ -\frac{1}{2\sigma_v^2}\xi_i^2 \right]. \quad (7.6)$$

The missingness or response mechanism of the joint model will be estimated by an IRT process. The probability of response for each subject  $i$  to a random prompt in time-interval  $j$  is represented by the one or two-parameter IRT model.

$$f_3 = p(R|\theta) = \text{logit}(R_{ij}) = c_j + a_j\theta_i = \Psi(\theta_i). \quad (7.7)$$

The logistic cumulative density function is denoted by  $\Psi$ . This equation can be rewritten in mixed-model format where  $\lambda_i$  represents the  $n_i \times 1$  vector of logits for each subject  $i$ :

$$\lambda_i = x_{ij}^{*'}c_j + z_{ij}^{*'}a_j\theta_i. \quad (7.8)$$

In this equation,  $x_{ij}^{*'} is the  $j \times j$  design matrix for the item indicators in the latent trait model and  $z_{ij}^{*'} is the  $j \times j$  design matrix for the random effects  $a$ . Since the vector  $a$  is equivalent to the standard deviation of random effects in an IRT model, the latent trait ( $\theta_i$ ) for the “ability” to respond is assumed to follow a standard normal distribution.$$

## 7.2 Longitudinal Model Derivations

Following the approach presented in Chapter 3, the marginal maximum likelihood solutions for a LTPMMM can be written as:

$$h_i(\mathbf{y}_i) = \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} f(\mathbf{y}_i | \boldsymbol{\theta}, \boldsymbol{\xi}; \boldsymbol{\beta}, \sigma_e^2) g(\boldsymbol{\theta}, \boldsymbol{\xi}; \boldsymbol{\Sigma}_{\boldsymbol{\theta}, \boldsymbol{\xi}}) d\boldsymbol{\theta} d\boldsymbol{\xi} \quad (7.9)$$

with probability density  $f(\mathbf{y}_i | \boldsymbol{\theta}, \boldsymbol{\xi}; \boldsymbol{\beta}, \sigma_e^2)$  equal to

$$(2\pi)^{-n_i/2} |\sigma_e^2 \mathbf{I}_{n_i}| \exp \left[ -\frac{1}{2} (\mathbf{y}_i - \mathbf{X}_i \boldsymbol{\beta} - \boldsymbol{\gamma} \boldsymbol{\theta}_i - \boldsymbol{\sigma}_v \boldsymbol{\xi}_i)' (\sigma_e^2 \mathbf{I}_{n_i})^{-1} (\mathbf{y}_i - \mathbf{X}_i \boldsymbol{\beta} - \boldsymbol{\gamma} \boldsymbol{\theta}_i - \boldsymbol{\sigma}_v \boldsymbol{\xi}_i) \right]$$

and the prior density for the random effects is a normal distribution written as:

$$g(\boldsymbol{\zeta}, \boldsymbol{\Sigma}_{\boldsymbol{\zeta}}) = (2\pi)^{-1} |\boldsymbol{\Sigma}_{\boldsymbol{\zeta}}|^{-1/2} \exp \left[ -\frac{1}{2} \boldsymbol{\zeta}' \boldsymbol{\Sigma}_{\boldsymbol{\zeta}}^{-1} \boldsymbol{\zeta} \right]. \quad (7.10)$$

In this case, the vector  $\boldsymbol{\zeta}$  contains the two standardized random effects  $\boldsymbol{\theta}$  and  $\boldsymbol{\xi}$  and  $g(\cdot)$  is a multivariate standard normal distribution. The maximum likelihood solution for the fixed-effects coefficient vector  $\boldsymbol{\beta}$  is derived as:

$$\begin{aligned} \log L &= \sum_{i=1}^N \log h_i(\mathbf{y}_i) \\ &= \sum_{i=1}^N \log \left[ \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} f_{1,2} \cdot g d\boldsymbol{\theta} d\boldsymbol{\xi} \right] \end{aligned}$$



$$\begin{aligned}
p_i &= p(\theta_i) \times p(\xi_i) \\
&= f_{1,2} \cdot g/h_i
\end{aligned}$$

Taking the derivative of both sides with respect to  $\beta$  results in:

$$\begin{aligned}
\frac{\partial \log L}{\partial \beta} &= \sum_{i=1}^N \frac{\partial \log h_i}{\partial \beta} \\
&= \sum_{i=1}^N \frac{1}{h_i} \frac{\partial \left[ \int_{\theta} \int_{\xi} f_{1,2} \cdot g \, d\theta d\xi \right]}{\partial \beta} \\
&= \sum_{i=1}^N \frac{1}{h_i} \int_{\theta} \int_{\xi} \frac{\partial f_{1,2}}{\partial \beta} g \, d\theta d\xi \\
&= \sum_{i=1}^N \int_{\theta} \int_{\xi} \frac{f_{1,2} \cdot g}{h_i} \frac{\partial \log f_i}{\partial \beta} \, d\theta d\xi \\
&= \sum_{i=1}^N \int_{\theta} \int_{\xi} p_i \mathbf{X}'_i (\sigma_e^2 \mathbf{I}_{n_i})^{-1} (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \theta_i - \sigma_v \xi_i) \, d\theta d\xi
\end{aligned}$$

Since the empirical Bayes estimate for the mean of the latent trait  $\theta_i$  is defined as

$$\tilde{\theta} = \int_{\theta} p(\theta_i) \, d\theta \quad (7.11)$$

and the empirical Bayes estimate for the mean of the random intercept  $\xi_i$  is defined as

$$\tilde{\xi} = \int_{\xi} p(\xi_i) \, d\xi \quad (7.12)$$

the above equation can be simplified to:

$$\frac{\partial \log L}{\partial \beta} = \sigma_e^2 \sum_{i=1}^N \mathbf{X}'_i (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\theta}_i - \sigma_v \tilde{\xi}_i) \quad (7.13)$$

Setting the derivative of  $\frac{\partial \log L}{\partial \beta}$  equal to 0 results in:

$$\sum_{i=1}^N \mathbf{X}_i' \mathbf{X}_i \beta = \sum_{i=1}^N \mathbf{X}_i' (\mathbf{y}_i - \gamma \tilde{\boldsymbol{\theta}}_i - \sigma_v \tilde{\boldsymbol{\xi}}_i).$$

Therefore, the marginal maximum likelihood solution for the fixed effects covariate vector  $\beta$  is:

$$\hat{\beta} = \left[ \sum_{i=1}^N \mathbf{X}_i' \mathbf{X}_i \right]^{-1} \left[ \sum_{i=1}^N \mathbf{X}_i' (\mathbf{y}_i - \gamma \tilde{\boldsymbol{\theta}}_i - \sigma_v \tilde{\boldsymbol{\xi}}_i) \right]. \quad (7.14)$$

The solution for the fixed-effects covariate matrix  $\beta$  in the proposed LTPMMM resembles the maximum-likelihood solution of the random-intercept mixed-effects model where the random effect terms are now modeled by:

$$\gamma \tilde{\boldsymbol{\theta}}_i + \sigma_v \tilde{\boldsymbol{\xi}}_i. \quad (7.15)$$

The maximum likelihood solution for the coefficient terms  $\gamma$  of the latent trait  $\boldsymbol{\theta}_i$  is derived as:

$$\begin{aligned} \frac{\partial \log L}{\partial \gamma} &= \sum_{i=1}^N \frac{\partial \log h_i}{\partial \gamma} \\ &= \sum_{i=1}^N \frac{1}{h_i} \frac{\partial \left[ \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} f_{1,2} \cdot g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \right]}{\partial \gamma} \\ &= \sum_{i=1}^N \frac{1}{h_i} \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{\partial f_{1,2}}{\partial \gamma} g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \end{aligned}$$

and using Equation 7.11 and Equation 7.12 results in:

$$\begin{aligned} &= \sum_{i=1}^N \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{f_{1,2} \cdot g}{h_i} \frac{\partial \log f_{1,2}}{\partial \gamma} g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \sum_{i=1}^N \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} p_i(\sigma_e^2 \mathbf{I}_{n_i})^{-1} (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \boldsymbol{\theta}_i - \sigma_v \boldsymbol{\xi}_i) \boldsymbol{\theta}_i' \, d\boldsymbol{\theta} d\boldsymbol{\xi} \end{aligned}$$

and setting this last equation equal to zero results in the marginal maximum likelihood solution for  $\hat{\gamma}$ ,

$$\begin{aligned}\frac{\partial \log L}{\partial \gamma} &= \sigma_e^2 \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\boldsymbol{\theta}}_i - \boldsymbol{\sigma}_v \tilde{\boldsymbol{\xi}}_i) \tilde{\boldsymbol{\theta}}_i' \\ \sum_{i=1}^N \gamma \tilde{\boldsymbol{\theta}}_i \tilde{\boldsymbol{\theta}}_i' &= \sum_{i=1}^N (\mathbf{y}_i - \gamma \tilde{\boldsymbol{\theta}}_i - \boldsymbol{\sigma}_v \tilde{\boldsymbol{\xi}}_i)\end{aligned}$$

which equals:

$$\hat{\gamma} = \left[ \sum_{i=1}^N \tilde{\boldsymbol{\theta}}_i \tilde{\boldsymbol{\theta}}_i' \right]^{-1} \left[ \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \boldsymbol{\sigma}_v \tilde{\boldsymbol{\xi}}_i) \right]. \quad (7.16)$$

The maximum likelihood solution for the coefficient terms  $\sigma_v$  of the standardized random effect  $\xi_i$  is derived as:

$$\begin{aligned}\frac{\partial \log L}{\partial \boldsymbol{\sigma}_v} &= \sum_{i=1}^N \frac{\partial \log h_i}{\partial \boldsymbol{\sigma}_v} \\ &= \sum_{i=1}^N \frac{1}{h_i} \frac{\partial \left[ \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} f_{1,2} \cdot g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \right]}{\partial \boldsymbol{\sigma}_v} \\ &= \sum_{i=1}^N \frac{1}{h_i} \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{\partial f_{1,2}}{\partial \boldsymbol{\sigma}_v} g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \sum_{i=1}^N \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{f_{1,2} \cdot g}{h_i} \frac{\partial \log f_{1,2}}{\partial \boldsymbol{\sigma}_v} g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \sum_{i=1}^N \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} p_i(\sigma_e^2 \mathbf{I}_{n_i})^{-1} (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \boldsymbol{\theta}_i - \boldsymbol{\sigma}_v \boldsymbol{\xi}_i) \boldsymbol{\sigma}_v' \, d\boldsymbol{\theta} d\boldsymbol{\xi}\end{aligned}$$

and using Equation 7.11 and Equation 7.12, results in:

$$\frac{\partial \log L}{\partial \boldsymbol{\sigma}_v} = \sigma_e^2 \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\boldsymbol{\theta}}_i - \boldsymbol{\sigma}_v \tilde{\boldsymbol{\xi}}_i) \boldsymbol{\sigma}_v'$$

The likelihood solution for  $\sigma_v$  is therefore derived after setting the last equation equal to 0 and solving:

$$\sum_{i=1}^N \sigma_v \xi_i \xi_i' = \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\theta}_i) \sigma_v$$

which is finally solved as:

$$\hat{\sigma}_v = \left[ \sum_{i=1}^N \tilde{\xi}_i' \tilde{\xi}_i \right]^{-1} \left[ \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\theta}_i) \right]. \quad (7.17)$$

The LTPMMM has the following error term  $\mathbf{e}_i$  defined as  $\mathbf{e}_i = \mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\theta}_i - \sigma_v \tilde{\xi}_i$ . The maximum likelihood solution of the error variance  $\sigma_e^2$  is:

$$\begin{aligned} \frac{\partial \log L}{\partial \sigma_e^2} &= \sum_{i=1}^N \frac{1}{h_i} \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{\partial f_{1,2}}{\partial \sigma_e^2} g \, d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \sum_{i=1}^N \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} \frac{f_{1,2} \cdot g}{h_i} \frac{\partial \log f_{1,2}}{\partial \sigma_e^2} \, d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \int_{\boldsymbol{\theta}} \int_{\boldsymbol{\xi}} p_i \left[ -\frac{n_i}{2} \sigma_e^2 + \frac{1}{2} \sigma_e^{-4} (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \boldsymbol{\theta}_i - \sigma_v \xi_i)' (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \boldsymbol{\theta}_i - \sigma_v \xi_i) \right] d\boldsymbol{\theta} d\boldsymbol{\xi} \\ &= \frac{1}{2} \sigma_e^{-4} \sum_{i=1}^N \left( -n_i \sigma_e^2 + \mathbf{e}_i' \mathbf{e}_i + \text{tr}[\gamma \sigma_v \Sigma_{\boldsymbol{\theta}, \boldsymbol{\xi} | y_i} \gamma \sigma_v'] \right). \end{aligned}$$

### 7.3 Missingness Model Derivations

The IRT component of the LTPMMM will be solved next. The binary outcome  $\mathbf{R}_{ij} = 1$  representing an answered prompt from subject  $i$  in time-bin  $j$  is modeled as a function of item difficulties, item discrimination parameters, and the latent traits:

$$\begin{aligned} \log \left[ \frac{R_{ij}}{1 - R_{ij}} \right] &= X_i \beta + 1_i \sigma_{v(r)} \theta_i \\ z_{ij} &= X_i \beta + 1_i \sigma_{v(r)} \theta_i \end{aligned}$$

The notation  $\sigma_{v(r)}$  is used to show that the variance of the random effect corresponds to the response process modeled by a random-effects logistic model. As was explained in Chapter 3, the response  $z_{ij}$  is linearly related to the predictors shown above through a logit link:

$$\begin{aligned} p_{ij} &= P(R_{ij} = 1 | \theta_i) = \Psi(z_{ij}) \\ \Psi(z_{ij}) &= \frac{1}{1 + \exp(-z_{ij})} \\ \ell(\mathbf{R}_i | \theta_i) &= \prod_{j=1}^{m_i} \Psi(z_{ij})^{R_{ij}} [1 - \Psi(z_{ij})]^{1-R_{ij}} \\ h(\mathbf{R}_i) &= \int_{\theta} \ell(\mathbf{R}_i | \theta) g(\theta) d\theta. \end{aligned}$$

The function  $\Psi(z_{ij})$  represents the conditional probability a prompt was answered  $R_{ij} = 1$  given  $\theta_i$ . Here  $g(\theta)$  represents the probability density function of the standardized random effect, which is distributed as a  $\sim N(0, 1)$  variable. Also notice that the total number of time-bins for each subject is denoted  $m_i$ .

$$\begin{aligned} L &= \prod_{i=1}^M h(\mathbf{R}_i) \\ \log L &= \sum_{i=1}^M \log h(\mathbf{R}_i) \end{aligned}$$

The total number of time-bins  $M$  is different than the total number of observations  $N$  because it is possible that multiple prompts were generated within a given time-bin  $j$ . We will now derive the solutions of the item difficulties  $a_j$  and item-intercept parameters  $c_j$  for the mixed-effects longitudinal logistic model. Let the vector of item intercepts be denoted  $\boldsymbol{\beta}$  and the vector of item-intercept parameters as  $\sigma_{v(r)}$ . The vector  $\boldsymbol{\eta}$  containing both these quantities will be solved

using marginal maximum-likelihood. This approach follows results presented by Hedeker and Gibbons (2006).

$$\begin{aligned}
\frac{\partial \log L}{\partial \boldsymbol{\eta}} &= \sum_{i=1}^M h^{-1}(\mathbf{R}_i) \frac{\partial h(\mathbf{R}_i)}{\partial \boldsymbol{\eta}} \\
\int_{\theta} l(\mathbf{R}_i | \theta) g(\theta) d\theta &= \int_{\theta} \left( \prod_{j=1}^{m_i} (\Psi(z_{ij}))^{R_{ij}} [1 - \Psi(z_{ij})]^{1-R_{ij}} \right) g(\theta) d\theta \\
&= \int_{\theta} [\exp(\log \sum_{i=1}^M \Psi(z_{ij})^{R_{ij}} [1 - \Psi(z_{ij})]^{1-R_{ij}})] g(\theta) d\theta \\
&= \int_{\theta} \exp \left[ \sum_{i=1}^M R_{ij} \log \Psi(z_{ij}) + (1 - R_{ij}) \log [1 - \Psi(z_{ij})] \right] g(\theta) d\theta \\
\frac{\partial h(\mathbf{R}_{ij})}{\partial \boldsymbol{\eta}} &= \int_{\theta} \sum_{i=1}^M R_{ij} \frac{R_{ij}}{\Psi(z_{ij})} \partial \Psi(z_{ij}) + \frac{1 - R_{ij}}{1 - \Psi(z_{ij})} (-\partial \Psi(z_{ij})) \ell_i g(\theta) d\theta \\
&= \int_{\theta} \sum_{i=1}^M \frac{R_{ij} - \Psi(z_{ij})}{\Psi(z_{ij})(1 - \Psi(z_{ij}))} \partial \Psi(z_{ij}) \frac{\partial z_{ij}}{\partial \boldsymbol{\eta}} \ell_i g(\theta) d\theta.
\end{aligned}$$

The quantity  $\partial z_{ij}$  is equal to probability density function  $\Psi(z_{ij}(1 - z_{ij}))$ ,

$$\frac{\partial \log L}{\partial \boldsymbol{\eta}} = \sum_{i=1}^M h^{-1}(\mathbf{R}_i) \int_{\theta} \sum_{i=1}^M R_{ij} - \Psi(z_{ij}) \ell_i g(\theta) d\theta$$

where,  $\frac{\partial z_{ij}}{\partial \beta} = \mathbf{x}'_{ij}$  and,  $\frac{\partial z_{ij}}{\partial \sigma_{v(r)}} = \theta$ . The solutions therefore are derived as:

$$\begin{aligned}
\frac{\partial \log L}{\partial \beta} &= \sum_{i=1}^M h^{-1}(\mathbf{R}_i) \int_{\theta} \sum_{i=1}^M R_{ij} - \Psi(z_{ij}) \mathbf{x}'_{ij} \ell_i g(\theta) d\theta \\
\frac{\partial \log L}{\partial \sigma_{v(r)}} &= \sum_{i=1}^M h^{-1}(\mathbf{R}_i) \int_{\theta} \sum_{i=1}^M R_{ij} - \Psi(z_{ij}) \theta \ell_i g(\theta) d\theta.
\end{aligned}$$

The full-likelihood for the proposed LTPMMM is formed by integrating the product of  $f_{1,2}f_3$  over the two random effects  $\xi_i$  and  $\theta_i$ :

$$\begin{aligned}
h_i &= \int_{\theta} \int_{\xi} f_{1,2} f_3 f(\xi) f(\theta) d\xi d\theta \\
h_i &= \int_{\theta} \int_{\xi} p(Y|b, \theta, R) p(b|\theta, R) p(R|\theta) f(\xi) f(\theta) d\xi d\theta. \\
\log L &= \sum_{i=1}^N \log(h_i) \\
\eta &= [c, a, \gamma, \sigma_v, \beta, \sigma_e^2].
\end{aligned}$$

The log-likelihood is then solved by the following system of equations. The derivatives with respect to parameters in  $\eta$  are:

$$\begin{aligned}
\frac{\partial \log L}{\partial \eta} &= \sum_{i=1}^N \frac{1}{h_i} \frac{\partial h_i}{\partial \eta} \\
\frac{\partial f_{1,2}}{\partial \beta} &= \sigma_e^2 \sum_{i=1}^N \mathbf{X}'_i (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\boldsymbol{\theta}} - \sigma_v \tilde{\boldsymbol{\xi}}) \\
\frac{\partial f_{1,2}}{\partial \gamma} &= \sigma_e^2 \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\boldsymbol{\theta}} - \sigma_v \tilde{\boldsymbol{\xi}}) \tilde{\boldsymbol{\theta}}'_i \\
\frac{\partial f_{1,2}}{\partial \sigma_v} &= \sigma_e^2 \sum_{i=1}^N (\mathbf{y}_i - \mathbf{X}_i \beta - \gamma \tilde{\boldsymbol{\theta}} - \sigma_v \tilde{\boldsymbol{\xi}}) \sigma'_v \\
\frac{\partial f_{1,2}}{\partial \sigma_e^2} &= \frac{1}{2} \sigma_e^{-4} \sum_{i=1}^N (-n_i \sigma_e^2 + \mathbf{e}' \mathbf{e} + \text{tr}[\gamma \sigma_v \Sigma_{\theta, \xi | y_i} \gamma \sigma'_v]) \\
\frac{\partial f_3}{\partial a} &= x'_{ij} \\
\frac{\partial f_3}{\partial \sigma_v(r)} &= \theta.
\end{aligned}$$

The  $x'_{ij}$  solution for  $\frac{\partial f_3}{\partial a}$  includes item indicators for the IRT model which are different than the fixed-effects covariate matrix  $\mathbf{X}_i$  used in the longitudinal model. In order to estimate the final pattern-mixture models, Gaussian quadrature will be used to determine the estimated coefficients. In the final fitted model, the coefficients  $\beta$  and  $\gamma$  have a subject-specific interpretation.

The fitted coefficients will also represent population-averaged (marginal) effects of covariates on the response, due to the assumption of normally distributed outcomes. Also, a linear-link is used to model the random effects in the proposed LTPMMs. Further discussion of this special case of the equality of subject-specific and population-averaged parameters is discussed in Fitzmaurice et al. (2009) and Heagerty and Zeger (2000).

Fisher's method of scoring can also be used to solve for  $\boldsymbol{\eta}$  the vector of all parameters. This is in an iterative method that involves the matrix of first and second derivatives of  $\log L$  with respect to  $\boldsymbol{\eta}$ :

$$\boldsymbol{\eta}_{i+1} = \boldsymbol{\eta}_i - \left[ E \left[ \frac{\partial^2 \log L}{\partial \boldsymbol{\eta}_i \partial \boldsymbol{\eta}_i'} \right] \right]^{-1} \frac{\partial \log L}{\partial \boldsymbol{\eta}_i} \quad (7.18)$$

The expectation of the matrix of second derivatives (information matrix) is defined as:

$$-E \left[ \frac{\partial^2 \log L}{\partial \boldsymbol{\eta}_i \partial \boldsymbol{\eta}_i'} \right] = E \left[ \sum_{i=1}^N h^{-2}(\mathbf{Y}_i) \frac{\partial h(\mathbf{Y}_i)}{\partial \boldsymbol{\eta}_i} \left( \frac{\partial h(\mathbf{Y}_i)}{\partial \boldsymbol{\eta}_i} \right)' \right] \quad (7.19)$$

Convergence occurs when the difference between successive values of  $\boldsymbol{\eta}_{i+1}$  and  $\boldsymbol{\eta}_i$  is quite small. This iterative method will usually require different starting values to check that the algorithm is working properly. Also, variance and covariance estimates of the maximum likelihood estimates are provided by the inverse of this information matrix. Standard errors are found by taking the square roots of the diagonal terms of the information matrix.



## CHAPTER 8

### DATA ANALYSIS

The data used in this dissertation are from the National Cancer Institute Adolescent Smoking Study (P01CA098262, PI: R. Mermelstein).

#### 8.1 Ecological Momentary Assessment Data Set

As described in Hedeker et al. (2008), EMA data with intermittent missing longitudinal values will be used with the proposed LTPMMs. In that study, 461 high school students were prompted at various times in a seven-day period for different psychological and behavioral measures. The adolescents were recruited as part of a much larger study of Social-Emotional Contexts of Adolescent Smoking patterns which recruited 1,263 subjects (Hedeker et al., 2009). Mood (as measured by both NA and PA) was one of the many outcomes collected over approximately one week with an average of 30 prompts per subject. The two psychological measures of PA and NA consist of an average of several mood items identified by factor analysis. The following items were included to determine PA: I felt happy, I felt relaxed, I felt cheerful, I felt confident, and I felt accepted by others. The following items were used to determine NA: I felt sad, I felt stressed, I felt angry, I felt frustrated, and I felt irritable.

Subject-level covariates collected at baseline in the data set include grade in high school (9th or 10th grade), gender, smoking status (yes or no), negative mood regulation (a measure of the students' ability to regulate negative moods), novelty seeking (a measure of novelty seeking), and grade point average (GPA) which was measured on a five-point scale (A=5.00). Smoking status was yes if a subject smoked at least one time during the collection period. These subject-level covariates were relatively uncorrelated with each other and no pairwise correlation coefficient was above 0.25. Since the baseline GPA was missing for nine students, these subjects

were removed from all analyses, resulting in a total of 452 observations. Approximately half of the subjects were smokers, the majority (57%) were female, and mean GPA was 3.637 ( $SD = 0.747$ ). The mean negative mood regulation was 2.447 ( $SD = 0.680$ ) at the baseline measurement. Preliminary fits of the models showed that the two covariates grade10 and novelty seekers were non-significant; therefore they were dropped from all subsequent models. As described in Chapter 7, all of the remaining covariates will be used as fixed-effects in a MAR mixed-effects model, a latent class pattern-mixture model, and the two proposed LTPMMs.

Also, during the collection process, students recorded if they were alone or not when they answered the prompting device. This variable was separated into a within-subject (AloneWS) and between-subject (AloneBS) value following the approach described in Hedeker et al. (2008). The between-subject value indicates the proportion of time that a subject was alone during the collection period and the within-subject value records deviation from this average at each time-interval. The within-subjects effect (AloneWS) is time-varying, therefore it will be entered into the occasions-level (or level-1) of the models.

The prompts data set contains a total of 13,835 occasion-level observations. The marginal mean of PA was 6.802 ( $SD = 1.931$ ) and the marginal mean of NA was 3.454 ( $SD = 2.249$ ) where the marginal means are computed by summing over the number of observations for each subject. The AloneBS variable had a mean of 0.512 ( $SD = 0.194$ ) meaning that students were alone on average during 51.2% of the collection period. The AloneWS variable had a mean of 0.000 with a standard deviation of 0.460.

## **8.2 Ecological Momentary Assessment Data Prompts**

The students carried a small hand-held computer that beeped when the student was prompted. After a prompt was received, a student had the option of entering behavior and smoking responses into the computer. The length of time that the students participated varied:

the mean number of days that the data were collected was 7.7 days with a standard deviation 1.2 days. For the majority of students, the period of data collection lasted 8 days (54.4%) or 7 days (30.9%). However, this data collection period lasted for three days for one subject and seventeen days for another. The prompts data contained an indicator for the day of the week and the time that a prompt was generated. It also had an indicator if this prompt was answered or not. The mean response rate for all subjects was 77.6% over the course of the study. This response rate varied quite a bit among the 452 students participating in the study, the standard deviation was 16.3%, the minimum response rate was 9.8%, and the maximum was 100%. The latent trait may be highly correlated with the response rate, but hopefully it should provide a richer interpretation of the relationship with mood outcomes by using it in the proposed LTPMMM.

Initially, in the prompts data set, each twenty-four day was divided into eight three-hour intervals starting at 3 a.m. Due to the sparseness of data, some of the three-hour bins were combined resulting in five bins. These five bins divide the day into meaningful periods for analysis. The time-bin from 3 a.m. to 8:59 a.m. will be denoted as “early-morning”; the time-bin from 9 a.m. to 2:59 p.m. will be denoted as “mid-day”; the time-bin from 3 p.m. to 5:59 p.m. denoted as “afternoon”; the time-bin from 6 p.m. to 8:59 p.m. denoted as “evening”; and the time-bin from 9 p.m. to 2:59 a.m. denoted as “late evening.”

Since the length of the data collection period was close to a week for the majority of students, a total of thirty-five time periods (seven days multiplied by five daily time periods) were created. Also, having the same days and times as indicators in an IRT model allows for all subjects’ response patterns to be represented in a consistent manner. For instance, students who have less than or more than seven days of data collection can be included in the IRT model. For students with more than seven days of EMA data collected, repeat observations can easily

be used by including this prompt information in the appropriate day and time it was generated. This is only one of many ways to analyze this EMA data set with this intermittent structure. The following is a sample response pattern from one subject in the EMA data set. The length of this response vector is thirty-five corresponding to the number of formed response-periods. For example, the response vector  $R_{ij}$  for the first subject is structured as

$$R_{1j} = [..11...111..111..111.00.1..10..1001] \quad (8.1)$$

In this response vector, the 1's represent time-intervals when the EMA prompts were answered, the 0's represent time-intervals when an EMA prompt was not answered, and any periods (.) represent times when no prompts were made. These missing observations usually occurred at the late-night or early morning bins throughout the data collection period, but they can occur at any time during the day since they were generated by an EMA process.

Thus, the first day and time-bin for each subject becomes the first item in the IRT model. The items formed in this way allow for multiple responses from each subject. The multiple responses can arise via two mechanisms. One is that multiple random beeps occur within a time-bin. Secondly, if a subject has the EMA device for more than one week, these additional responses occurring after Sunday are simply added to the corresponding day and time-bin after the last bin. For example, suppose a student carried the EMA device for eight days starting on a Monday. On those two Mondays, prompts were generated to that student. If the student responds to the device on the second Monday and time-bin 1, this response is simply combined into time-bin 1 on Monday. In the model proposed here, this is the first item in the IRT representation of the latent trait pattern-mixture mixed model. The final structure of the bins is shown below in Table I.

Within each day during the study, most of the random prompts were generated from 9 a.m. to 2:59 p.m. The two-bins from 3 p.m. to 5:59 p.m. and from 6 p.m. to 8:59 p.m. also generated a substantial number of prompts. The early morning bin from 3 a.m. to 8:59 a.m. and the late night bin from 9 p.m. to 2:59 a.m. had the similar number of prompts generated except on the two weekend days of Saturday and Sunday. It is also interesting to note that response rates vary depending on when the prompt was made, with the lowest rates seen on Saturday and Sunday between 3 a.m. and 8:59 p.m. Therefore, an IRT model is worth pursuing with this EMA data set because of the nature of the different response rates (both between days and between time-intervals) and also varying rates for each student.

The initial data set formed from the random responses contained eight time bins per day that were three hours long. Some time bins had small amounts of responses, so these bins were combined with adjacent bins. Although this collapsing method did improve the estimation times for the joint models considerably, the two-parameter LTPMMMs did not always converge to a stable solution. Therefore, a decision was made by looking at item response curves and estimated difficulty parameters that were similar, and set difficulties for those time-bins to be equal. This process was only done for item difficulty parameters, so that all item discrimination parameters could be estimated in the two-parameter LTPMMMs. The item difficulty parameters were constrained to be equal for the following time-bins: early morning time-bin (from 3 a.m. to 8:59 a.m.) on Monday, Wednesday, Thursday, and Friday; time-bin from 9 a.m. to 2:59 p.m. from Monday through Friday; time-bin from 9 a.m. to 2:59 p.m. on Saturday and Sunday; afternoon time-bin (from 3 p.m. to 5:59 p.m.) on Monday, Tuesday, Wednesday, and Friday; afternoon bin (from 3 p.m. to 5:59 p.m.) on Wednesday and Sunday; evening time bin (from 6 p.m. to 8:59 p.m.) Monday through Friday and Sunday; evening time bin (between 6 p.m. and 8:59 p.m.) on Friday and Saturday; and late-evening time-bin (between

9 p.m. and 2:59 a.m.) on Tuesday, Wednesday, Thursday, and Sunday; and late-evening time-bin (between 9 p.m. and 2:59 a.m.) on Saturday and Sunday. This process reduced the number of item difficulty parameters from thirty-five to fourteen, which allowed all model runs to converge to stable solutions.

### 8.3 Fitted Models

The models shown in Table II have NA as the outcome; models in Table V have PA as the outcome. The first fit in each set is a MAR random-intercept model which does not model the missingness mechanism in any way (Equation 6.1). The next model is a latent class pattern-mixture model and uses three latent classes as patterns in a pattern-mixture mixed model (Equation 6.2). These latent classes were formed using the poLCA package from R statistical software (Linzer and Lewis, 2007). The latent classes are formed to assess the missingness mechanism as was done in Lin et al. (2004). The response vector for each subject  $R_i$  was used as input in the poLCA package with latent class models with one, two, three, four, five, and six classes. The response vector  $R_i$  has missing values corresponding to time-bins where no prompts were made. The three class latent class model was chosen because it had the lowest BIC among these six models. The two indicators *LatentClass*<sub>2</sub> and *LatentClass*<sub>3</sub> were used as covariates in the model where *LatentClass*<sub>1</sub> is the reference category.

Of the 452 subjects in the EMA study, 337 subjects are in latent class 1, 58 are in latent class 2, and 57 are in latent class 3. Latent class 2 includes students who missed most of the prompts in the first half of the study, latent class 3 includes students who miss most of the prompts in the last half of the study, and latent class 1 includes the remaining students. In terms of the model covariates, male gender is the only baseline measure that differs among the latent classes. A higher proportion of subjects in latent class 3 (57.0 %) and latent class 2 (53.3%) are males as compared to latent class 1 (39.7%). These proportions are significantly

different from the latent class 1 value at the significance level of 0.05. This possible relationship of missingness with gender will also be explored with simulations of all of the proposed models and is described in Chapter 10.

The third model uses latent traits formed from each subject as a random effect in a longitudinal mixed-model for outcomes( Equation 6.3). In this model, all item discrimination parameters are constrained to be equal. The fourth model is a two-parameter LTPMMM with varying difficulties and discrimination parameters( Equation 6.5). All model types were fit using PROC NLMIXED in SAS.

The two LTPMMMs jointly estimated the IRT parameters and the mixed-model for the longitudinal outcomes by linking the latent trait  $\theta_i$  in each model. The advantages of this joint approach are described in Guo and Carlin (2004) in which a model for longitudinal outcomes is fit concurrently with a model for survival outcomes. Mainly, estimated standard errors for model coefficients are lower with the joint model approach than with a separate or two-stage estimation approach. Also, the joint approach offers an improvement in model fit for both processes. The LTPMMMs were initially run using a two-stage approach by first fitting the one- or two-parameter IRT model to the prompts data set. The fitted latent traits  $\hat{\theta}_i$  were then used as a model covariate in the full latent trait pattern-mixture model shown in Equation 6.9. The joint models had lower estimated standard errors for the error variances  $\sigma_e^2$  than the two-stage model technique. Also, the joint model had slightly different regression coefficients. The two-stage model took much less time to fit using SAS software, but the joint-model reflects a better statistical fit due to reduced standard errors.

Fixed model covariates used in all models shown in Table II and Table V included genderM (indicator for male gender), sbeepy (smoker=yes or no), negative mood regulation, grade

point average (GPA) and AloneBS (between-subject). The time-varying covariate aloneWS (within-subject) was also included in all models.

All interactions between the latent traits and other covariates in the LTPMMM's were insignificant ( $p > 0.05$ ) so they are not presented in the results. It was hoped that some would be significant, because the interactions would reveal interesting effects of how the ability to respond to random prompts and model covariates work in conjunction. Therefore, no models with interaction terms will be simulated, but this is worth further investigation in later work. Chapter 12 will discuss some of the ways that LTPMMMs with interaction terms can be explored and simulated.

### 8.3.1 Negative Affect: Fitted Model Results

When NA is the outcome, the MAR, latent class, and latent trait pattern-mixture models do not differ significantly in terms of coefficient estimates for the smoker (yes or no), alone (within-subject), and alone (between-subject) effects. Also, the estimated standard errors and p-values for these effects did not differ considerably across the four model types. The estimates for the alone effect (between-subjects) differed in the two LTPMMM's which also had slightly lower standard errors than the MAR and latent class pattern-mixture model. However, the four models did differ significantly for the gender, negative mood regulation, and GPA covariate effects. The effect of male gender on NA outcomes was increased when the latent class pattern-mixture model and the two LTPMMMs were fit to the data. The two LTPMMMs also had higher coefficient estimates for GPA, whereas the coefficient estimate for the negative mood regulation was strengthened in the negative direction. The p-values for gender were reduced considerably with the two LTPMMM's as compared to the MAR model. Another advantage of the proposed LTPMMMs is that the variance of the random intercept terms  $\sigma_v^2$



was reduced when the LTPMMs were fit to negative affect outcomes. The estimates for the variance of the error terms  $\sigma_e^2$  was identical across the four models.

In the latent class pattern-mixture model, the latent classes were fit using latent class 1 as the reference level. Only the third latent class differs significantly from latent class 1, latent class 2 is insignificant. It was hoped that both indicators would be significant; this would be evidence that individuals in the three latent classes would have different average levels of the NA outcome after controlling for other variables in the models. This may mean that a latent class pattern-mixture model with three classes may not be the best model for this intermittent missing data structure. A more robust model would have latent classes that reveal clearly distinct response patterns and that would be significantly different.

The latent trait measuring each student's "ability" to respond to the random prompts is statistically significant in both the one- and two-parameter LTPMMs. If NA is the outcome, students who respond more have decreased negative affect. Thus, subjects who are more responsive as determined by the Rasch model, have better mood measured by negative affect. The significant p-values are strong evidence that the missingness process as measured by the latent trait is not MCAR and possibly not MAR.

Both the one- and two-parameter LTPMMM's have some interesting results for the estimated  $\gamma$  coefficient. This effect is negative with both models. Therefore, subjects who respond more to the EMA prompting device have better moods as measured by the decreased level of the negative affect. It is important to note that the estimates and standard errors differ. The two-parameter estimate of  $\gamma$  is less than the one-parameter model estimate and the standard error of the estimate is lower. These findings will be explored by comparing model fits from the one- and two-parameter LTPMMM's with simulated data.

Covariate effects in both the one-parameter and two-parameter latent trait pattern-mixture mixed models are all significant at  $p < 0.05$ . Subjects who are smokers have an increased level of negative affect (or lower moods) as compared to non-smokers. On average, males in the study have lower negative affect outcomes than females. Students who have higher levels of negative mood regulation also have decreased levels of the negative affect variable. Student's with higher GPA's had higher negative affect over the collection period. If the majority of times a student is alone is increased (AloneBS), then negative affect will increase as well. The alone within-subject effect measures each student's deviation with respect to the average time alone; a higher change in this deviation also causes negative affect to increase. On average, if a subject is more responsive to the EMA prompting device, they have lower average negative affect.

In order to compare the fit of the four models, the deviance statistic ( $-2 \times \log\text{-likelihood}$ ), Akaike Information Criteria (AIC) (Akaike, 1973), and Bayesian information criteria (BIC) (Read and Cressie, 1988) are presented in Table II. The deviances of the MAR mixed-model and LC pattern-mixture model are on the same scale, since the MAR model is nested in the LC pattern mixture model. Therefore, these two models will be compared. The one- and two-parameter LTPMMs will be compared to each other, since the one-parameter model is nested in the two parameter model.

In terms of model fit, the LC pattern-mixture model and the MAR mixed-model did differ considerably when comparing likelihood ratio deviance statistics, the  $\chi^2$  statistic of 7 is significant at  $p = 0.03$ . Also, the AIC favors the LC pattern-mixture model to the simpler MAR mixed-model. The BIC for the LC pattern-mixture model shows a poorer model fit than a MAR model. Therefore, the LC pattern-mixture model does add some benefit as compared to the MAR model, but not markedly so. Also, the third latent class significantly differed from

the first latent class, but the second latent class did not. This may be evidence that this latent class pattern-mixture model with three classes may not be appropriate with this EMA data set because the only one of the latent classes significantly differed from the reference class. The likelihood ratio test for the two-parameter LTPMMM compared to the one-parameter latent trait pattern-mixture mixed- model reveals a  $\chi^2$  statistic of 57 on 34 degrees of freedom, which is significant at  $p < 0.008$ . The 34 degrees of freedom correspond to the additional discrimination parameters that are estimated in the two-parameter LTPMMM. Therefore, having these additional discrimination parameters in the model improve overall fit and is a more realistic assumption of how the ability to respond differs by various time-intervals.

Although the likelihood ratio test results are encouraging for use of the two-parameter LTPMMM, the AIC and BIC statistics do not show an improved model over the one-parameter model. The AIC for the two-parameter model is arguably close to the one-parameter model, but the BIC is higher by a value of 150.

### **8.3.2 Positive Affect: Fitted Model Results**

When PA is the outcome, the MAR, latent class, and latent trait pattern-mixture models do not noticeably differ in terms of coefficient estimates for the smoker (yes or no), alone (within-subject), and alone (between-subject) effects. Also, the estimated standard errors and p-values for these effects did not differ considerably across the four model types. As was seen in the model for NA, the alone (between-subject) effect in the two LTPMMMs had smaller standard errors than the MAR model. However, the four models did differ for the gender, negative mood regulation, and GPA covariate effects. The effect of male gender was increased when the two LTPMMMs were fit to the data and is significant at  $p < 0.05$ . The coefficient estimate for NMR increased in the positive direction in the LTPMMMs, whereas the coefficient estimate for the GPA was strengthened in the negative direction. Also, the variance of the random

intercept terms  $\sigma_v^2$  was reduced when the LTPMMs were fit to positive affect outcomes, but this difference was only found when comparing terms to the MAR mixed-model. The estimates for the variance of the error terms  $\sigma_e$  was identical across the four models.

As was seen in the LTPMMs fit to NA, the estimates and standard errors for the covariate effect of the latent trait are different. The estimate of the latent trait effect is lower in the two-parameter LTPMMM and the standard error is lower as well. Since the estimated  $\gamma$  coefficient for the latent trait is positive, subjects who respond more to the EMA prompting device have better moods as measured by the increase level of the positive affect. These results coincide with the findings from the LTPMMs fit to NA. Therefore, this shows that the missingness due to unanswered prompts is related to the outcome, positive affect. Students who are more responsive (or have a higher latent trait  $\theta_i$ ) have better moods as measured by PA.

Covariate effects in both the one-parameter and two-parameter latent trait pattern-mixture mixed models are significant at  $p < 0.05$ . Subjects who are smokers have a reduced level of positive affect as compared to nonsmokers. On average, males in the study have higher positive affect outcomes than females. Students who have higher levels of negative mood regulation also have increased levels of the positive affect variable. Student's with higher GPA's had lower positive affect over the collection period. If the majority of times a student is alone is increased, then positive affect will decrease as well. If a subject is more responsive to the EMA prompting device, they have a higher mean positive affect.

Table V provides the deviance statistic ( $-2 \times \log\text{-likelihood}$ ), Akaike Information Criteria (AIC) (Akaike, 1973), and Bayesian information criteria (BIC) (Read and Cressie, 1988) for the positive affect outcomes. As was done with NA as the outcomes, the MAR mixed-model and LC pattern-mixture model will be compared based on these fit statistics. Also, the one-

and two-parameter LTPMMs will be compared, since the one-parameter model is nested in the two parameter model.

When comparing model fits, the LC pattern-mixture model and the MAR mixed-model did differ considerably in their likelihood ratio statistics, the  $\chi^2$  statistic of 8 is significant at  $p = 0.018$ . Also, the Akaike Information Criteria (AIC) favors the LC pattern-mixture model to the simpler MAR mixed-model. Bayesian information criteria (BIC) for the LC pattern-mixture model shows a poorer model fit than a MAR model. These results were also found in the latent class pattern-mixture model fit to NA outcomes. This is some evidence that a latent class pattern-mixture model with three classes may not be the best model with this EMA data set since the BIC statistic is higher than that from the MAR model.

The likelihood ratio test for the two-parameter latent trait pattern mixture model compared to the one-parameter latent trait pattern-mixture mixed model reveals a  $\chi^2$  statistic of 55 on 34 degrees of freedom which is significant at  $p < 0.012$ . The 34 degrees of freedom correspond to the additional discrimination parameters that are estimated in the two-parameter LTPMMM. Therefore, having these additional parameters in the model improve overall fit. This also improves interpretation of the model since varying discrimination parameters are a more realistic assumption of how the ability to respond differs by each time-bin.

Although the improved model fit of the two-parameter LTPMMM exists with the deviance (-2LogL) statistic, contradictory evidence is shown for the Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) statistics, which are both higher in the two-parameter models. These results were seen in models fitting negative affect and positive affect and may need to be evaluated to determine the appropriate choice between the one-parameter and two-parameter LTPMMM.

## 8.4 Item Parameters, Negative Affect

### 8.4.1 Difficulty Parameters, One-Parameter Model

The one-parameter LTPMMM fit to NA outcomes reveal the following about item difficulty parameters: All item difficulties were significant at  $p < 0.001$  except the two early-morning bins (3 a.m. to 8:59 a.m.) on Saturday and Sunday. The significant parameters ranked from -1.149 to -1.859 showing that it was not very difficult for the students to respond at most times through out the study. The two insignificant bins had the two highest difficulties of response among the thirty-five time-bins. The Saturday early morning bin (3 a.m. to 8:59 p.m.) had a difficulty of -0.489 and the Sunday time-bin at the same time-interval had a difficulty of 0.566. This is not unexpected because these occur on the weekend when students may be out with their friends or asleep. The time-bin with the lowest difficulty estimate was the same for Monday, Tuesday, Wednesday, Thursday, and Sunday and occurred between 6 p.m. and 8:59 p.m. This is intuitive because students probably have the most free time in these intervals. On Friday and Saturday, the time-bin occurring from 9 a.m. to 2:59 p.m. had the lowest estimated difficulty. Therefore, item difficulties vary between days with Monday through Thursday having similar difficulty parameters for the morning bins and Friday, Saturday, and Sunday having similar difficulty parameters for the evening time-bins. Within a given day, time-bins in the early morning (3 a.m. to 8:59 a.m.) and the late evening (9 p.m. to 2:59 a.m.) had the highest estimated difficulties. Comparison of these item difficulty parameters for each day and time-bin are shown in Figure 1.

The common item discrimination parameter for the thirty-five time-bins was estimated to be 0.912 for the one-parameter LTPMMM fit to negative affect outcomes. The standard error was estimated to be 0.045, therefore the item discrimination parameter was significant

( $p < 0.001$ ). The intraclass correlation coefficient for this discrimination parameter is 0.202, which shows that the proportion of unexplained variance that is at the subject level is 20%.

#### **8.4.2 Difficulty Parameters, Two-Parameter Model**

The following information about item difficulty parameters was found after fitting the two-parameter LTPMMM to negative affect outcomes. All item difficulties were significant at  $p < 0.001$  except the two early morning bins (3 a.m. until 8:59 a.m.) on Saturday and Sunday. This early-morning bin was significant at  $p < 0.01$  on Saturday but was insignificant on Sunday. As in the one-parameter LTPMMM, these two bins had the highest difficulty of response. This is not unexpected because these are weekend time-bins where students may not want to answer a prompt. Also, as seen in the one-parameter LTPMMM, the time-bin with the lowest difficulty estimate was the same on Monday, Tuesday, Wednesday, Thursday, and Sunday and occurred between 6 p.m. and 8:59 p.m. This is intuitive because students probably have the most free time in these time-intervals. The two-parameter LTPMMM estimates for these time-bins was lower than the one-parameter LTPMMM. For days Thursday and Friday, the time-bin between 9 a.m. and 2:59 p.m. had the lowest difficulty of response. Therefore, item difficulties vary between days with days Monday, Tuesday, Wednesday, Thursday, and Sunday having similar parameters and Friday and Saturday having similar difficulties. As seen in the one-parameter LTPMMM the early morning (from 3 a.m. to 8:59 p.m.) and late evening (9 p.m. to 2:59 a.m.) time-bins have the highest difficulties within each day, since these intervals are typically used for sleeping.

#### **8.4.3 Discrimination Parameters, Two-Parameter Model**

All thirty-five item discriminations were significant at  $p < 0.001$  except for the two early-morning intervals from 3 a.m. to 8:59 a.m. on Saturday and Sunday, which were significant at  $p < 0.01$ . Item discriminations ranged from 0.645 (Friday, 9 a.m. to 2:59 p.m.) to 2.073

(Saturday, 3 a.m. to 8:59 a.m. ). Patterns of discrimination parameters differed between days, with Saturday and Sunday having the biggest within day ranges. These item discrimination parameters from the two-parameter LTPMMM vary widely from the estimated discrimination parameter from the one-parameter LTPMMM which is fixed at 0.912 for all thirty-five items. Except for Mondays, the time-bin with the highest discrimination estimate occurred during late-night bin from 9 p.m. to 2:59 a.m. (Tuesday, Wednesday, Thursday, Friday, and Sunday), and during the early-morning bin on Saturday. On Monday, the time-bin with the highest discrimination estimate occurred between 3 p.m. and 5:59 p.m. Therefore, the two-parameter model captures the differing item discriminations better than the one-parameter model. Plots of the discrimination and difficulty parameters are shown in Figure 2 and Figure 3.

The one- and two-parameter models both represent the varying difficulties across each day. Both models have the identical time-bins assigned to the highest and lowest difficulty estimates across the days. The benefit of the two-parameter LTPMMM is that it estimates separate discrimination parameters allowing for a more realistic fit of the data. As was noted above when looking at the overall fits of the two models, the additional item discrimination parameters do not improve model fit in terms of AIC and BIC fit statistics. This contradictory evidence for use of the two-parameter LTPMMM versus the one-parameter LTPMMM will be investigated by comparing simulation performance in Chapter 10.

## **8.5 Item Parameters, Positive Affect**

### **8.5.1 Difficulty Parameters, One-Parameter Model**

After fitting the one-parameter LTPMMM to positive affect outcomes, the item difficulty parameters revealed similar effects to the same model fit to NA outcomes. All item difficulties were significant at  $p < 0.001$  except the two early-morning bins (3 a.m. to 8:59 a.m.) on Saturday and Sunday. These two insignificant bins had the highest difficulty of response. This



is not unexpected because these are weekend days and a small number of prompts were generated at these time-bins and the students generally did not answer the prompts at these times. The time-bin with the lowest difficulty estimate was the same on Monday, Tuesday, Wednesday and Thursday and occurred between 6 p.m. and 8:59 p.m. This is intuitive because students probably have the most free time in these time-intervals. On Friday and Saturday, the time-bin between 9 a.m. and 2:59 p.m. had the lowest difficulty of response. On Sunday, the time bin with the lowest difficulty of response occurred in the afternoon between 3 p.m. and 5:59 p.m. This differs from the results shown from the one-parameter LTPMMM with negative affect as the outcome. Therefore, item difficulties vary between days with Monday through Thursday having similar parameters and Friday through Sunday having varied difficulty parameters. Time-bins in the early morning (3 a.m. to 8:59 a.m.) and the late evening (9 p.m. to 2:59 a.m.) did not always have the highest estimated difficulties with-day as seen in the one-parameter LTPMMM for negative affect. Comparison of these item difficulty parameters from the two-parameter models for each time-bin are shown in Figure 2.

The common discrimination parameter for the thirty-five time-bins from the one-parameter model was estimated as 0.916 with a standard error of 0.045. This parameter was significant at  $p < 0.001$ . In terms of the intraclass correlation coefficient, this quantity is expressed as 0.203 and means that the proportion of unexplained variation at the subject level is approximately one-fifth of the total. The estimated discrimination parameter from the one-parameter model for positive affect outcomes did not vary significantly from the discrimination parameter estimated from the one-parameter LTPMMM for negative affect which was 0.912.

### **8.5.2 Difficulty Parameters, Two-Parameter Model**

The two-parameter LTPMMM fit to PA outcomes had the following results about item difficulty parameters. All item difficulties were significant at  $p < 0.001$  except the two early

morning bins (3 a.m. to 8:59 a.m.) on Saturday and Sunday. This early morning bin was significant at  $p < 0.01$  on Saturday but was insignificant on Sunday. As in the one-parameter LTPMMM, these two bins had the highest difficulty of response. This is not unexpected because these are weekend days and a small number of prompts were generated at these times. The time-bin with the lowest difficulty estimate was the same for Monday through Thursday, and Sunday and occurred between 6 p.m. and 8:59 p.m. This is intuitive because students probably have the most free time in these time-intervals. The two-parameter LTPMMM difficulty estimates for these time-bins were lower than estimates from the one-parameter LTPMMM. On Friday and Saturday, the time-bin between 9 a.m. and 2:59 p.m. had the lowest difficulty of response. Therefore, item difficulties vary between days with Monday through Thursday, and Sunday having similar difficulty parameters and Friday and Saturday having similar difficulties. The item difficulty parameters across days are shown in Figure 2.

### 8.5.3 Discrimination Parameters, Two-Parameter Model

All thirty-five item discriminations were significant at  $p < 0.001$  except the two time-bins occurring between 9 a.m. and 2:59 p.m. on Saturday and Sunday which were significant at  $p < 0.01$ . Item discriminations ranged from 0.689 (Wednesday, 3 p.m. to 5:59 p.m.) to 2.073 (Saturday, 3 a.m. to 8:59 a.m.). As was seen in the two-parameter LTPMMM fit to negative affect, all days except for Monday had the most discriminating time-bin occur in the early morning (3 a.m. to 8:59 a.m.) or late-evening (9 p.m. to 2:59 a.m.). Patterns of discrimination parameters differed between days, with Saturday and Sunday having the biggest within-day ranges. Plots of the discrimination and difficulty parameters are shown in Figure 3.

Throughout the collection days, the highest and lowest difficulties occurred in the same time-bins for both the one-and two-parameter models fit to positive affect. Varying discrimination parameters in the two-parameter LTPMMM allow for a more realistic representation

of the relationship of the latent traits in the separate time-bins. As was noted above when looking at the overall fits of the two models, the additional item discrimination parameters do not improve model fit in terms of AIC and BIC statistics. The likelihood ratio test showed that the two-parameter model dramatically improves fit ( $\chi^2 = 55, p < 0.012$ ). This contradictory evidence for use of the two-parameter LTPMMM will be investigated and explored in terms of simulation performance in Chapter 10.

#### **8.5.4 Correlation of Item Parameters**

When comparing the item difficulty parameters from the one-parameter LTPMMM across negative and positive affect outcomes, the difficulty parameters are virtually identical between the two models. This relationship is also true when comparing across the one- and two-parameter latent trait pattern-mixture models. The Pearson correlation coefficient was computed with the two vectors of difficulty parameters (each having length 35) across the one- and two-parameter LTPMMMs. Table VIII summarizes these results across the four possible models (two models for PA or NA and two models for the one-parameter LTPMMM or the two-parameter LTPMMM). All of these six Pearson product-moment correlations are significant ( $p < 0.0001$ ). As expected these correlations are all close to 1 because the same response vector was used for both NA and PA outcomes. This is evidence that the process used to model the missing-data mechanism through a latent trait approach is working properly. If the difficulty and or the discrimination parameters varied widely among the two latent trait models, this would be cause for concern in terms of model fit and estimation.

**TABLE I: BIN STRUCTURE**

Proportion (and n) of prompts answered by time-interval and day

3 a.m.-8:59 a.m.	70.7 (215)	68.8 (234)	69.2 (250)	74.5 (235)	71.6 (232)	43.8 (80)	21.2 (66)
9 a.m.-2:59 p.m.	81.5 (697)	79.0 (728)	77.5 (728)	77.5 (711)	77.2 (733)	76.5 (620)	78.5 (586)
3 p.m.-5:59 p.m.	77.8 (361)	78.0 (359)	75.3 (377)	81.3 (356)	77.8 (369)	73.8 (401)	82.0 (395)
6 p.m.-8:59 p.m.	80.4 (392)	79.8 (396)	82.9 (386)	77.0 (382)	74.9 (382)	75.6 (381)	82.0 (394)
9 p.m.-2:59 a.m.	75.1 (245)	75.4 (268)	73.4 (263)	81.2 (259)	69.9 (306)	68.5 (352)	77.4 (314)

$$n_i = 35$$

5 time-intervals  $\times$  7 days = 35 items

**TABLE II: NEGATIVE AFFECT — COMPARISON OF MIXED MODELS**

	MAR	Latent Class	Latent Trait (1P)	Latent Trait (2P)
Intercept	4.150 ***	4.003 ***	4.039 ***	4.095 ***
	0.423	0.423	0.420	0.420
Sheepy	0.353 **	0.347 **	0.345 **	0.342 **
	0.131	0.130	0.130	0.130
GenderM	-0.424 ***	-0.472 **	-0.475 ***	-0.473 ***
	0.136	0.136	0.136	0.136
NegMoodReg	-0.809 ***	-0.801 ***	-0.824 ***	-0.826 ***
	0.099	0.098	0.098	0.098
GPA	0.233 **	0.247 **	0.273 ***	0.268 **
	0.089	0.089	0.089	0.089
AloneWS	0.385 ***	0.385 ***	0.384 ***	0.385 ***
	0.031	0.031	0.031	0.031
AloneBS	0.952 **	0.984 **	0.962 **	0.954 **
	0.334	0.333	0.331	0.332
Latent Class 2		0.170		
		0.195		
Latent Class 3		0.530 **		
		0.198		
Latent Trait $\theta$			-0.242 **	-0.219 **
			0.085	0.076
$\sigma_{v_0}^2$	1.752 ***	1.723 ***	1.701 ***	1.708 ***
	0.123	0.121	0.121	0.122
$\sigma_e^2$	2.839 ***	2.839 ***	2.839 ***	2.839 ***
	0.035	0.035	0.035	0.035
-2LogL	55034	55027	68255	68198
AIC	55052	55049	68305	68316
BIC	55089	55094	68408	68558

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05

**TABLE III:** ITEM PARAMETERS, ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL, NEGATIVE AFFECT, ESTIMATE (STANDARD ERROR)

Item	Day	Time	Difficulty	Discrimination
1	Monday	3 a.m.-8:59 a.m.	-1.337(0.097) ***	0.912(0.045) ***
2	Monday	9 a.m.-2:59 p.m.	-1.701(0.069) ***	0.912(0.045) ***
3	Monday	3 p.m.-5:59 p.m.	-1.605(0.087) ***	0.912(0.045) ***
4	Monday	6 p.m.-8:59 p.m.	-1.859(0.082) ***	0.912(0.045) ***
5	Monday	9 p.m.-2:59 a.m.	-1.555(0.174) ***	0.912(0.045) ***
6	Tuesday	3 a.m.-8:59 a.m.	-1.149(0.168) ***	0.912(0.045) ***
7	Tuesday	9 a.m.-2:59 p.m.	-1.701(0.069) ***	0.912(0.045) ***
8	Tuesday	3 p.m.-5:59 p.m.	-1.605(0.087) ***	0.912(0.045) ***
9	Tuesday	6 p.m.-8:59 p.m.	-1.859(0.082) ***	0.912(0.045) ***
10	Tuesday	9 p.m.-2:59 a.m.	-1.635(0.095) ***	0.912(0.045) ***
11	Wednesday	3 a.m.-8:59 a.m.	-1.337(0.097) ***	0.912(0.045) ***
12	Wednesday	9 a.m.-2:59 p.m.	-1.701(0.069) ***	0.912(0.045) ***
13	Wednesday	3 p.m.-5:59 p.m.	-1.383(0.104) ***	0.912(0.045) ***
14	Wednesday	6 p.m.-8:59 p.m.	-1.859(0.082) ***	0.912(0.045) ***
15	Wednesday	9 p.m.-2:59 a.m.	-1.635(0.095) ***	0.912(0.045) ***
16	Thursday	3 a.m.-8:59 a.m.	-1.337(0.097) ***	0.912(0.045) ***
17	Thursday	9 a.m.-2:59 p.m.	-1.701(0.069) ***	0.912(0.045) ***
18	Thursday	3 p.m.-5:59 p.m.	-1.605(0.087) ***	0.912(0.045) ***
19	Thursday	6 p.m.-8:59 p.m.	-1.859(0.082) ***	0.912(0.045) ***
20	Thursday	9 p.m.-2:59 a.m.	-1.635(0.095) ***	0.912(0.045) ***
21	Friday	3 a.m.-8:59 a.m.	-1.337(0.097) ***	0.912(0.045) ***
22	Friday	9 a.m.-2:59 p.m.	-1.701(0.069) ***	0.912(0.045) ***
23	Friday	3 p.m.-5:59 p.m.	-1.605(0.087) ***	0.912(0.045) ***
24	Friday	6 p.m.-8:59 p.m.	-1.423(0.106) ***	0.912(0.045) ***
25	Friday	9 p.m.-2:59 a.m.	-1.200(0.108) ***	0.912(0.045) ***
26	Saturday	3 a.m.-8:59 a.m.	-0.489(0.265)	0.912(0.045) ***
27	Saturday	9 a.m.-2:59 p.m.	-1.584(0.092) ***	0.912(0.045) ***
28	Saturday	3 p.m.-5:59 p.m.	-1.383(0.104) ***	0.912(0.045) ***
29	Saturday	6 p.m.-8:59 p.m.	-1.423(0.106) ***	0.912(0.045) ***
30	Saturday	9 p.m.-2:59 a.m.	-1.200(0.108) ***	0.912(0.045) ***
31	Sunday	3 a.m.-8:59 a.m.	0.566(0.339)	0.912(0.045) ***
32	Sunday	9 a.m.-2:59 p.m.	-1.584(0.092) ***	0.912(0.045) ***
33	Sunday	3 p.m.-5:59 p.m.	-1.839(0.151) ***	0.912(0.045) ***
34	Sunday	6 p.m.-8:59 p.m.	-1.859(0.082) ***	0.912(0.045) ***
35	Sunday	9 p.m.-2:59 a.m.	-1.635(0.095) ***	0.912(0.045) ***

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05

**TABLE IV:** ITEM PARAMETERS, TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL, NEGATIVE AFFECT, ESTIMATE (STANDARD ERROR)

Item	Day	Time	Difficulty	Discrimination
1	Monday	3 a.m.-8:59 a.m.	-1.337(0.147) ***	0.803(0.143) ***
2	Monday	9 a.m.-2:59 p.m.	-2.015(0.158) ***	0.833(0.087) ***
3	Monday	3 p.m.-5:59 p.m.	-1.601(0.154) ***	0.973(0.136) ***
4	Monday	6 p.m.-8:59 p.m.	-2.090(0.195) ***	0.724(0.094) ***
5	Monday	9 p.m.-2:59 a.m.	-1.636(0.335) ***	0.846(0.195) ***
6	Tuesday	3 a.m.-8:59 a.m.	-1.259(0.299) ***	0.765(0.176) ***
7	Tuesday	9 a.m.-2:59 p.m.	-2.015(0.158) ***	0.778(0.083) ***
8	Tuesday	3 p.m.-5:59 p.m.	-1.601(0.154) ***	0.921(0.127) ***
9	Tuesday	6 p.m.-8:59 p.m.	-2.090(0.195) ***	0.760(0.101) ***
10	Tuesday	9 p.m.-2:59 a.m.	-1.381(0.114) ***	1.358(0.206) ***
11	Wednesday	3 a.m.-8:59 a.m.	-1.337(0.147) ***	0.911(0.155) ***
12	Wednesday	9 a.m.-2:59 p.m.	-2.015(0.158) ***	0.689(0.073) ***
13	Wednesday	3 p.m.-5:59 p.m.	-1.365(0.175) ***	0.908(0.137) ***
14	Wednesday	6 p.m.-8:59 p.m.	-2.090(0.195) ***	0.811(0.104) ***
15	Wednesday	9 p.m.-2:59 a.m.	-1.381(0.114) ***	1.157(0.176) ***
16	Thursday	3 a.m.-8:59 a.m.	-1.337(0.147) ***	0.984(0.161) ***
17	Thursday	9 a.m.-2:59 p.m.	-2.015(0.158) ***	0.766(0.077) ***
18	Thursday	3 p.m.-5:59 p.m.	-1.601(0.154) ***	0.872(0.119) ***
19	Thursday	6 p.m.-8:59 p.m.	-2.090(0.195) ***	0.795(0.105) ***
20	Thursday	9 p.m.-2:59 a.m.	-1.381(0.114) ***	1.197(0.177) ***
21	Friday	3 a.m.-8:59 a.m.	-1.337(0.147) ***	0.872(0.148) ***
22	Friday	9 a.m.-2:59 p.m.	-2.015(0.158) ***	0.645(0.067) ***
23	Friday	3 p.m.-5:59 p.m.	-1.601(0.154) ***	0.879(0.119) ***
24	Friday	6 p.m.-8:59 p.m.	-1.309(0.161) ***	1.032(0.159) ***
25	Friday	9 p.m.-2:59 a.m.	-1.033(0.124) ***	1.186(0.186) ***
26	Saturday	3 a.m.-8:59 a.m.	-0.542(0.168) **	2.073(0.637) **
27	Saturday	9 a.m.-2:59 p.m.	-1.816(0.211) ***	0.762(0.107) ***
28	Saturday	3 p.m.-5:59 p.m.	-1.365(0.175) ***	0.909(0.141) ***
29	Saturday	6 p.m.-8:59 p.m.	-1.309(0.161) ***	0.982(0.143) ***
30	Saturday	9 p.m.-2:59 a.m.	-1.033(0.124) ***	1.058(0.155) ***
31	Sunday	3 a.m.-8:59 a.m.	1.006(0.825)	0.766(0.351) **
32	Sunday	9 a.m.-2:59 p.m.	-1.816(0.211) ***	0.760(0.101) ***
33	Sunday	3 p.m.-5:59 p.m.	-1.844(0.311) ***	0.936(0.180) ***
34	Sunday	6 p.m.-8:59 p.m.	-2.090(0.195) ***	0.860(0.115) ***
35	Sunday	9 p.m.-2:59 a.m.	-1.381(0.114) ***	1.262(0.172) ***

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05

**TABLE V: POSITIVE AFFECT — COMPARISON OF MIXED-MODELS**

	MAR	Latent Class	Latent Trait (1P)	Latent Trait (2P)
Intercept	6.449***	6.563***	6.501***	6.495***
	0.342	0.342	0.341	0.341
Sheepy	-0.189	-0.188	-0.182	-0.182
	0.106	0.105	0.105	0.105
GenderM	0.218*	0.255*	0.252*	0.252*
	0.110	0.110	0.111	0.110
NegMoodReg	0.625***	0.618***	0.636***	0.637***
	0.080	0.079	0.080	0.080
GPA	-0.133	-0.141*	-0.158*	-0.158*
	0.072	0.072	0.073	0.073
AloneWS	-0.514***	-0.514***	-0.517***	-0.514***
	0.028	0.028	0.028	0.028
AloneBS	-1.397***	-1.439***	-1.399***	-1.402***
	0.271	0.269	0.269	0.269
Latent Class 2		-0.026		
		0.158		
Latent Class 3		-0.456**		
		0.160		
Latent Trait $\theta$			0.162*	0.151*
			0.069	0.062
$\sigma_{v_0}^2$	1.134***	1.114***	1.114***	1.114***
	0.081	0.079	0.080	0.080
$\sigma_e^2$	2.252***	2.252***	2.252***	2.252***
	0.028	0.028	0.028	0.028
-2LogL	51742	51734	64963	64908
AIC	51760	51756	65013	65026
BIC	51797	51801	65116	65269

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05



**TABLE VI:** ITEM PARAMETERS, ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL, POSITIVE AFFECT, ESTIMATE (STANDARD ERROR)

Item	Day	Time	Difficulty	Discrimination
1	Monday	3 a.m. - 8:59 a.m.	-1.342(0.098) ***	0.916(0.045) ***
2	Monday	9 a.m. - 2:59 p.m.	-1.702(0.069) ***	0.916(0.045) ***
3	Monday	3 p.m. - 5:59 p.m.	-1.603(0.087) ***	0.916(0.045) ***
4	Monday	6 p.m. - 8:59 p.m.	-1.851(0.082) ***	0.916(0.045) ***
5	Monday	9 p.m. - 2:59 a.m.	-1.579(0.175) ***	0.916(0.045) ***
6	Tuesday	3 a.m. - 8:59 a.m.	-1.173(0.169) ***	0.916(0.045) ***
7	Tuesday	9 a.m. - 2:59 p.m.	-1.702(0.069) ***	0.916(0.045) ***
8	Tuesday	3 p.m. - 5:59 p.m.	-1.603(0.087) ***	0.916(0.045) ***
9	Tuesday	6 p.m. - 8:59 p.m.	-1.851(0.082) ***	0.916(0.045) ***
10	Tuesday	9 p.m. - 2:59 a.m.	-1.639(0.095) ***	0.916(0.045) ***
11	Wednesday	3 a.m. - 8:59 a.m.	-1.342(0.098) ***	0.916(0.045) ***
12	Wednesday	9 a.m. - 2:59 p.m.	-1.702(0.069) ***	0.916(0.045) ***
13	Wednesday	3 p.m. - 5:59 p.m.	-1.388(0.105) ***	0.916(0.045) ***
14	Wednesday	6 p.m. - 8:59 p.m.	-1.851(0.082) ***	0.916(0.045) ***
15	Wednesday	9 p.m. - 2:59 a.m.	-1.639(0.095) ***	0.916(0.045) ***
16	Thursday	3 a.m. - 8:59 a.m.	-1.342(0.098) ***	0.916(0.045) ***
17	Thursday	9 a.m. - 2:59 p.m.	-1.702(0.069) ***	0.916(0.045) ***
18	Thursday	3 p.m. - 5:59 p.m.	-1.603(0.087) ***	0.916(0.045) ***
19	Thursday	6 p.m. - 8:59 p.m.	-1.851(0.082) ***	0.916(0.045) ***
20	Thursday	9 p.m. - 2:59 a.m.	-1.639(0.095) ***	0.916(0.045) ***
21	Friday	3 a.m. - 8:59 a.m.	-1.342(0.098) ***	0.916(0.045) ***
22	Friday	9 a.m. - 2:59 p.m.	-1.702(0.069) ***	0.916(0.045) ***
23	Friday	3 p.m. - 5:59 p.m.	-1.603(0.087) ***	0.916(0.045) ***
24	Friday	6 p.m. - 8:59 p.m.	-1.427(0.106) ***	0.916(0.045) ***
25	Friday	9 p.m. - 2:59 a.m.	-1.204(0.108) ***	0.916(0.045) ***
26	Saturday	3 a.m. - 8:59 a.m.	-0.490(0.265)	0.916(0.045) ***
27	Saturday	9 a.m. - 2:59 p.m.	-1.583(0.092) ***	0.916(0.045) ***
28	Saturday	3 p.m. - 5:59 p.m.	-1.388(0.105) ***	0.916(0.045) ***
29	Saturday	6 p.m. - 8:59 p.m.	-1.427(0.106) ***	0.916(0.045) ***
30	Saturday	9 p.m. - 2:59 a.m.	-1.204(0.108) ***	0.916(0.045) ***
31	Sunday	3 a.m. - 8:59 a.m.	0.457(0.332)	0.916(0.045) ***
32	Sunday	9 a.m. - 2:59 p.m.	-1.583(0.092) ***	0.916(0.045) ***
33	Sunday	3 p.m. - 5:59 p.m.	-1.865(0.152) ***	0.916(0.045) ***
34	Sunday	6 p.m. - 8:59 p.m.	-1.851(0.082) ***	0.916(0.045) ***
35	Sunday	9 p.m. - 2:59 a.m.	-1.639(0.095) ***	0.916(0.045) ***

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05

**TABLE VII:** ITEM PARAMETERS, TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL, POSITIVE AFFECT, ESTIMATE (STANDARD ERROR)

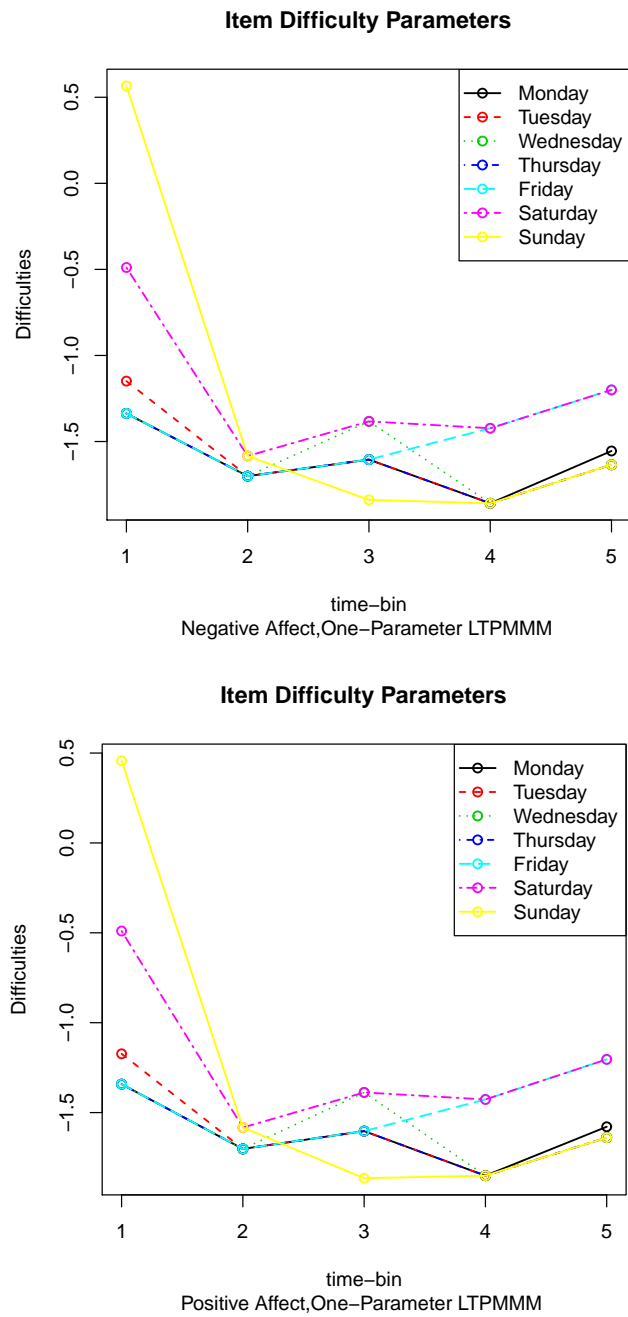
Item	Day	Time	Difficulty	Discrimination
1	Monday	3 a.m. - 8:59 a.m.	-1.333(0.146) ***	0.808(0.143) ***
2	Monday	9 a.m. - 2:59 p.m.	-2.017(0.158) ***	0.833(0.087) ***
3	Monday	3 p.m. - 5:59 p.m.	-1.608(0.155) ***	0.968(0.135) ***
4	Monday	6 p.m. - 8:59 p.m.	-2.106(0.198) ***	0.718(0.094) ***
5	Monday	9 p.m. - 2:59 a.m.	-1.648(0.338) ***	0.838(0.194) ***
6	Tuesday	3 a.m. - 8:59 a.m.	-1.272(0.304) ***	0.757(0.176) ***
7	Tuesday	9 a.m. - 2:59 p.m.	-2.017(0.158) ***	0.778(0.083) ***
8	Tuesday	3 p.m. - 5:59 p.m.	-1.608(0.155) ***	0.918(0.127) ***
9	Tuesday	6 p.m. - 8:59 p.m.	-2.106(0.198) ***	0.753(0.100) ***
10	Tuesday	9 p.m. - 2:59 a.m.	-1.384(0.114) ***	1.351(0.205) ***
11	Wednesday	3 a.m. - 8:59 a.m.	-1.333(0.146) ***	0.916(0.156) ***
12	Wednesday	9 a.m. - 2:59 p.m.	-2.017(0.158) ***	0.688(0.073) ***
13	Wednesday	3 p.m. - 5:59 p.m.	-1.378(0.178) ***	0.895(0.135) ***
14	Wednesday	6 p.m. - 8:59 p.m.	-2.106(0.198) ***	0.806(0.104) ***
15	Wednesday	9 p.m. - 2:59 a.m.	-1.384(0.114) ***	1.155(0.176) ***
16	Thursday	3 a.m. - 8:59 a.m.	-1.333(0.146) ***	0.984(0.160) ***
17	Thursday	9 a.m. - 2:59 p.m.	-2.017(0.158) ***	0.766(0.077) ***
18	Thursday	3 p.m. - 5:59 p.m.	-1.608(0.155) ***	0.868(0.119) ***
19	Thursday	6 p.m. - 8:59 p.m.	-2.106(0.198) ***	0.788(0.104) ***
20	Thursday	9 p.m. - 2:59 a.m.	-1.384(0.114) ***	1.193(0.176) ***
21	Friday	3 a.m. - 8:59 a.m.	-1.333(0.146) ***	0.872(0.147) ***
22	Friday	9 a.m. - 2:59 p.m.	-2.017(0.158) ***	0.645(0.067) ***
23	Friday	3 p.m. - 5:59 p.m.	-1.608(0.155) ***	0.872(0.118) ***
24	Friday	6 p.m. - 8:59 p.m.	-1.313(0.161) ***	1.030(0.159) ***
25	Friday	9 p.m. - 2:59 a.m.	-1.029(0.124) ***	1.198(0.188) ***
26	Saturday	3 a.m. - 8:59 a.m.	-0.536(0.173) **	1.982(0.595) **
27	Saturday	9 a.m. - 2:59 p.m.	-1.812(0.211) ***	0.765(0.107) **
28	Saturday	3 p.m. - 5:59 p.m.	-1.378(0.178) ***	0.897(0.141) ***
29	Saturday	6 p.m. - 8:59 p.m.	-1.313(0.161) ***	0.981(0.143) ***
30	Saturday	9 p.m. - 2:59 a.m.	-1.029(0.124) ***	1.060(0.155) ***
31	Sunday	3 a.m. - 8:59 a.m.	0.920(0.758)	0.805(0.355) **
32	Sunday	9 a.m. - 2:59 p.m.	-1.812(0.211) ***	0.763(0.102) ***
33	Sunday	3 p.m. - 5:59 p.m.	-1.823(0.303) ***	0.950(0.181) ***
34	Sunday	6 p.m. - 8:59 p.m.	-2.106(0.198) ***	0.850(0.114) ***
35	Sunday	9 p.m. - 2:59 a.m.	-1.384(0.114) ***	1.257(0.172) ***

\*\*\* p&lt;0.001, \*\* p&lt;0.01, \* p&lt;0.05

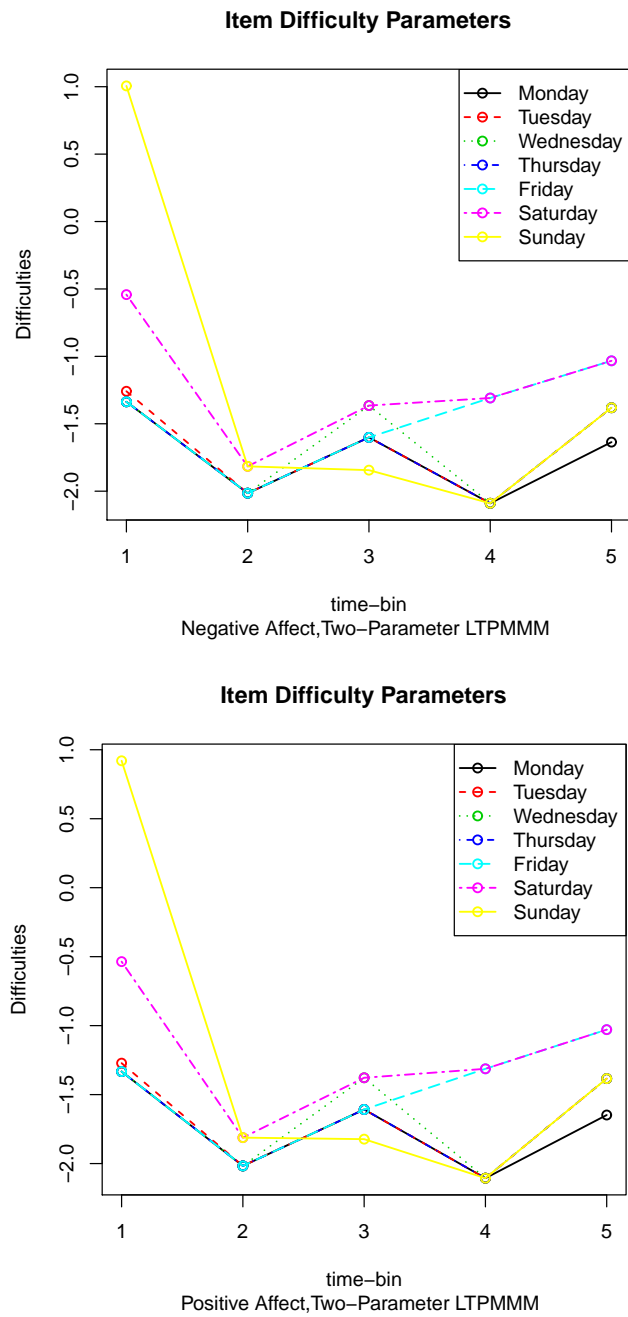
**TABLE VIII:** PEARSON CORRELATION COEFFICIENTS OF ITEM DIFFICULTY PARAMETERS

	1P, NA	1P, PA	2P, NA
1P, NA			
1P, PA	1.000		
2P, NA	0.955	0.954	
2P, PA	0.953	0.952	1.000

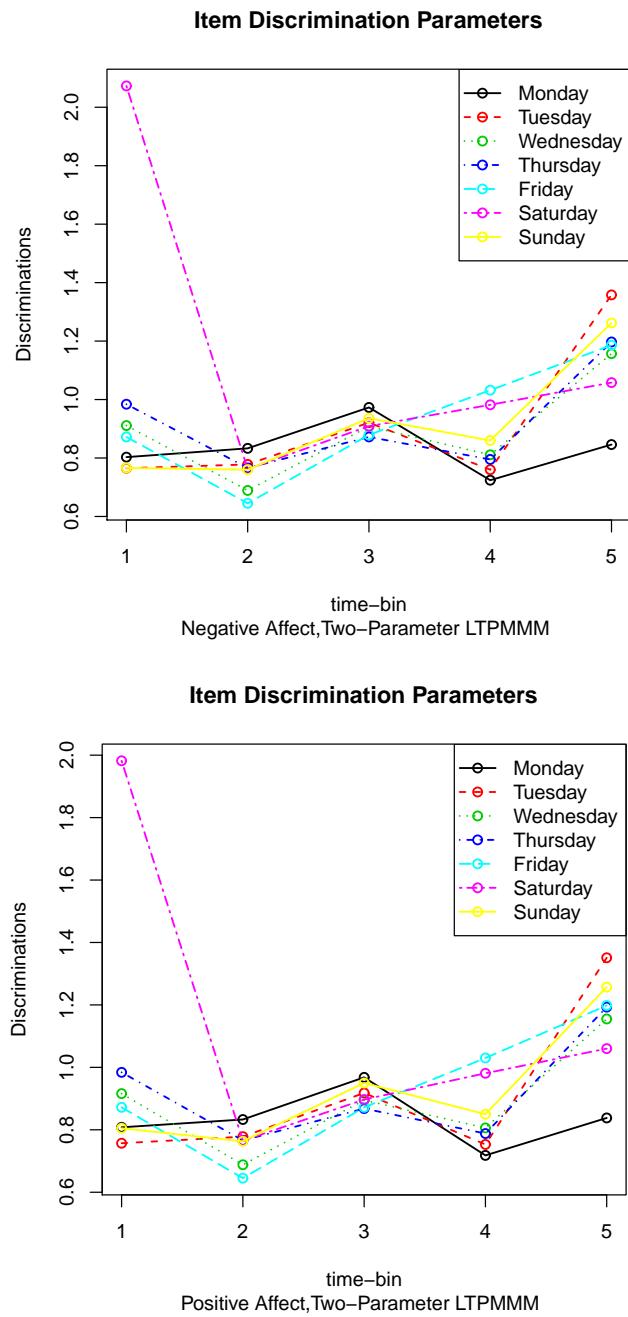
1P, NA = One-Parameter LTPMMM, Negative Affect  
 1P, PA = One-Parameter LTPMMM, Positive Affect  
 2P, NA = Two-Parameter LTPMMM, Negative Affect  
 2P, PA = Two-Parameter LTPMMM, Positive Affect



**Figure 1:** Item difficulty parameters, one-parameter latent trait pattern-mixture mixed-models, negative and positive affect.



**Figure 2:** Item difficulty parameters, two-parameter latent trait pattern-mixture mixed-models, negative and positive affect.



**Figure 3:** Item discrimination parameters, two-parameter latent trait pattern-mixture mixed-models, negative and positive affect.

## CHAPTER 9

### SIMULATION PLAN

The following simulation plan was implemented with the fitted models shown in Table II and Table V in Chapter 8. Estimated coefficients ( $\hat{\beta}$ ), error variance ( $\hat{\sigma}_e^2$ ), random intercepts ( $\hat{v}_{0i}$ ), latent traits ( $\hat{\theta}_i$ ), and the variance-covariance matrix of the two random effects ( $\hat{\Sigma}_{v_{0i}\theta_i}$ ) were used to draw simulated outcomes. The first step in the process was to simulate data sets assuming that the MAR random intercept mixed-model was the true model. In the next step, all four model types (MAR mixed-model, latent class pattern-mixture model, one-parameter LTPMMM, and two-parameter LTPMMM) were fit to the data generated by the MAR model. This process was continued assuming that latent class pattern-mixture model was the true model and all model types were be fit to the simulated data. Continuing this process for the one-parameter LTPMMM and the two-parameter LTPMMM resulted in the necessary simulations for both positive and negative affect.

The estimated regression coefficient for the gender effect and negative mood regulation were compared across the four model types, since fitted models in Table II and Table V showed some differences among the models. The estimated coefficient of the latent trait effect was compared between the one-parameter and two-parameter LTPMMM. All of the relevant results are shown in Chapter 10.

All simulated data sets had a total of 15,820 observations ( $452 \text{ subjects} \times 35 \text{ time-bins}$ ) and were simulated 1,000 times. The 452 subjects were chosen to represent the sample size of subjects used to fit the models in Table II and Table V. In order to evaluate the effectiveness and performance of the four modelling scenarios, a random 20% of the simulated outcome values for males was set to missing. This caused the latent trait for each subject  $\theta_i$  to be correlated

with male gender in the simulated data sets. The next section outlines the simulation process in a step-by-step manner that was used for the four simulation scenarios. The quantity  $\mathbf{Y}_i^S$  is used to indicate the simulated outcome vector where  $i$  represents data from the  $i^{th}$  simulation.

### 9.1 Simulation Scenarios

1. **MAR** model with EMA data set. A random-intercept mixed-model with the EMA data set was fit using model covariates shown in Table II and negative affect as the outcome.
2. **Saved** fitted covariate regression coefficients  $\hat{\beta}$ , fitted covariance matrix of the two random effects  $\hat{\Sigma}_{v_{0i}\theta_i}$  and variance of the fitted error terms  $\hat{\sigma}_e^2$ .
3. **Saved** the probability  $\hat{p}_{ij}$  that subject  $i$  answered a prompt in a time-bin  $j$ . This probability was computed as  $\sum_{j \in 1} R_{ij} / \sum R_{ij}$  and was determined from the observed data. The term in the numerator is the total number of answered prompts for subject  $i$  and the denominator is the total number prompts for subject  $i$ . In the MAR model this probability did not vary at each iteration.
4. **Generated** outcomes  $\mathbf{Y}_i^S$  from a multivariate normal distribution  $\mathbf{Y}_i^S \sim N(\hat{\mathbf{X}}_\beta, \hat{\Sigma}_{v_{0i}\theta_i} + \hat{\sigma}_e^2)$  using values saved from step 2. Data were generated from the marginal distribution of  $\mathbf{Y}_i^S$ . As stated above, the total number of subject-observations ( $\sum n_i$ ) was 15,820.
5. **Created** missingness vector  $\mathbf{R}_i$  for each subject by a random draw from a binomial distribution with  $p = \hat{p}_{ij}$  from step 3.  $\mathbf{Y}_i^S$  was set equal to “.” where  $\mathbf{R}_{ij} = 0$ .
6. **Set** an additional 20% of simulated  $\mathbf{Y}_i^S$  to missing for males. This was done at each step of the simulation.
7. **Fit** simulated data  $\mathbf{Y}_i^S$  using true covariate data  $\mathbf{X}$  with a MAR mixed-model, latent-class pattern-mixture mixed-model, one-parameter LTPMMM, and two-parameter LTPMMM.



8. **Saved** regression coefficient estimates ( $\hat{\beta}^S$ ) and standard errors for gender and NMR fixed-effects.
9. **Repeated** 1,000 times.
10. **Compared** average estimate, standard error, raw bias, percentage bias, standardized bias, root mean squared error, coverage rates, fraction of missing information and average width of 95% confidence interval for gender and NMR coefficients across the four simulated data sets. These comparisons are shown in the next chapter.
11. **Repeated** steps 1–10 using positive affect as the outcome.
12. **Repeated** steps 1–11 using latent class pattern-mixture model with three latent classes as true model. In step 3, the probability of missingness for subject  $i$  at time-bin  $j$ ,  $\hat{p}_{ij}$ , was determined from the fitted latent trait pattern-mixture model at each step of the iteration.
13. **Repeated** steps 1–11 using the one-parameter latent trait pattern-mixture model as the true model. In step 3, the probability of missingness for subject  $i$  at time-bin  $j$ ,  $\hat{p}_{ij}$  was determined by the fitted one-parameter IRT model at each step of the iteration. The coefficient estimates  $\hat{\beta}_\theta$  and standard errors for  $\theta_i$  were saved in step 8.
14. **Repeated** steps 1–11 using two-parameter latent trait pattern-mixture model as true model. In step 3, the probability of missingness for subject  $i$  at time-bin  $j$ ,  $\hat{p}_{ij}$  was determined by the fitted two-parameter IRT model at each step of the iteration. As was done with the one-parameter LTPMMM, the coefficient estimates  $\hat{\gamma}$  and standard errors for  $\theta_i$  were saved in step 8.
15. **Evaluated** sensitivity of LTPMMM using the IRT approach. Compare fitted coefficients  $\hat{\beta}$ , standard errors, convergence properties, and model fits among simulated data from the

MAR model, the latent class pattern-mixture model, and the LTPMMM. The full results are presented in the next chapter.

## 9.2 Performance Measures

The following measures for the estimated coefficients were used to compare the different mixed-models fit to the one-thousand simulated data sets. They are the average estimate, standard error, raw bias, percentage bias, standardized bias, root mean squared error (RMSE), coverage rate, fraction of missing information, and the average width of the 95% confidence intervals for the true value. The average estimate, raw bias, percentage bias, and standardized bias provide a sense of the accuracy of the coefficient estimate from mixed-models fit the simulated data sets. The raw bias, percentage bias, standardized bias should all be relatively low. The standard error and average width provide a measure of the precision of the model estimates. Smaller versus larger values of the standard error and average width are desired. The root mean squared error provides an assessment of both accuracy and precision; it should also be low. Coverage rates are defined as the percentage of time that the true parameter value is contained in the confidence interval (Demirtas et al., 2009). Like the RMSE, the coverage rate is a combined measure that assesses both accuracy and precision of an estimator. Higher values of coverage rates correspond to a better performance measure. The fraction of missing information is the proportionate increase in variance of the estimator due to the missing values (Li et al., 1991) and it should be low.

Let  $\beta_i^S$  represent the coefficient estimate for a covariate  $X$  in the linear model fit to the data in imputation  $i$ ,  $U_m$  be the standard error of  $\beta_i^S$ , and  $\beta^T$  represent the true estimate of the regression coefficient. In this illustration,  $i$  represents the  $i^{th}$  imputation from the  $m = 1,000$  imputed data sets. The following performance diagnostics were computed for all modelling scenarios.

- **Average Estimate** computed as

$$\frac{1}{m} \sum_{i=1}^m \beta_i^S = \overline{\beta_m^S}. \quad (9.1)$$

- **Standard Error** of the average estimate. Denote the vector of standard errors from the 1,000 simulations as  $U_m$ . The standard error of the average estimate is computed by first obtaining the within-imputation variance of  $U$  which is

$$\overline{U} = \frac{1}{m} \sum_{i=1}^m U_i. \quad (9.2)$$

and the between-imputation variance ( $B$ ) computed as

$$B = \frac{1}{m-1} \sum_{i=1}^m (\hat{\beta}_i^S - \overline{\beta_i^S})^2. \quad (9.3)$$

Computing the quantity  $T$  where

$$T = \overline{U} + \left(1 + \frac{1}{m}\right) B \quad (9.4)$$

and taking the  $\sqrt{T}$  results in the overall standard error of the estimate  $\beta_m^S$ .

- **Raw Bias** computed as  $\beta^T - \overline{\beta_m^S}$ .
- **Percentage Bias** computed as  $100 \times \frac{\beta^T - \overline{\beta_m^S}}{\beta^T}$ .
- **Standardized Bias** computed as the raw bias divided by the standard error shown above.
- **Root Mean Squared Error (RMSE)** computed as  $\frac{1}{m} \sum \sqrt{(\beta_m^S - \beta^T)^2}$ .
- **Coverage Rate** Number of times the estimated value  $\beta_m^S$  is contained in the true confidence interval for  $\overline{\beta^T}$ . The 95% confidence intervals for  $\beta^T$  are computed as  $\beta^T \pm 1.96 \times SE$   
The SE is used from the calculation shown above.

- **Fraction of Missing Information** ( $\gamma$ ) computed as:

$$\begin{aligned}\gamma &= \frac{r + 1/(df + 3)}{r + 1} \\ r &= \frac{(1 + m^{-1})B}{\bar{U}} \\ df &= (m - 1) \left( 1 + \frac{m\bar{U}}{(m + 1)B} \right)^2\end{aligned}$$

where  $B$  and  $U$  are defined above.

- **Average width** computed as the average width of 1,000 95% confidence intervals for  $\overline{\beta_m^S}$ .

The average width of the intervals is the absolute value of

$$\frac{1}{m}(\beta_m^S + 1.96 \times SE) - (\beta_m^S + 1.96 \times SE). \quad (9.5)$$

- **Estimated 95% Confidence Intervals** computed as:  $\overline{\beta} \pm 1.96 \times \overline{SE}$ . These were computed for the estimated gender regression coefficient, negative mood regulation regression coefficient, and latent trait  $\theta_i$  regression coefficient.

Table IX outlines the different mixed-models that were simulated using the EMA data set. For simulation purposes, only models without interaction terms were analyzed. This is due to the fact that all interaction terms of covariates with the latent trait ( $\theta_i$ ) were statistically insignificant ( $p > 0.05$ ) in the one-parameter LTPMMM and two-parameter LTPMMM for both NA and PA outcomes.

**TABLE IX: MODEL SCENARIOS**

Model #	Simulate
2	Latent Class Pattern-Mixture
3	One-Parameter LTPMMM
4	Two-Parameter LTPMMM

4 Models  $\times$  2 outcomes (PA and NA) = 8 models

LTPMMM = Latent Trait Pattern-Mixture Mixed-Model

## CHAPTER 10

### SIMULATION RESULTS

In order to test the validity and fits of the proposed LTPMMs, the simulation analysis described in Chapter 9 was conducted. In the data creation, 20% of the observations for males were randomly set to missing at each iteration. This was done to induce correlation between the males and the estimated latent trait. As was explained previously, four models were estimated to the simulated data under different scenarios. In the first scenario, the MAR model was assumed to be the true model and its performance will be compared to a latent class pattern-mixture model, a one-parameter LTPMMM, and a two-parameter LTPMMM. The second scenario assumed that the latent class mixture model was the correct model and its performance will be compared performance to the other three models. The third and fourth scenarios repeated the simulation process for the one-parameter LTPMMM and the two-parameter LTPMMM assuming that they were the true models. These simulation results should also determine if the LTPMMs modeled the outcomes more accurately than the LC pattern-mixture and the MAR models, when data were generated assuming a latent trait process for the missingness mechanism. In order to determine if the model performance is superior with the LTPMMs, bias and precision measures for the estimated regression coefficients of gender and negative mood regulation will be compared across all four simulation scenarios. After the one- and two-parameter LTPMMs are simulated, bias and precision values for the estimate of the latent trait regression coefficient will be compared from the two LTPMMs.

#### 10.1 Missing at Random Mixed Model

This section shows the results from MAR models fit to the EMA data. In the MAR model simulations, the missingness process for the EMA prompts were not modeled in any way.

The MAR model included random intercept terms and the model covariates gender, smoker, negative mood regulation, alone (within-subjects effect), alone (between-subjects effect) and grade point average (GPA). Bias and precision measures for the regression coefficient of gender on NA will be examined first and measures for the regression coefficient of NMR on NA will be presented last.

#### **10.1.1 Negative Affect**

As was done with all simulations, twenty percent of observed values for males were set as missing at each simulation run. The MAR model was assumed to be the true model and its performance will be compared to a latent class pattern-mixture model with three latent classes, the one-parameter LTPMMM, and the two-parameter LTPMMM.

#### **10.1.2 Gender Regression Coefficient Estimates**

In Table X under the column heading for gender, no significant differences in the regression coefficient for gender are seen across the four models when the true model was assumed to be a MAR model. The raw bias, percentage bias, and standardized bias of the gender coefficient estimates are all low and comparable among the four models. The two LTPMMMs have the highest percentage bias, but they are both less than 1%. The model precision measures of standard error, RMSE, fraction of missing information, and average width of the estimated 95% confidence intervals are close when the LC pattern-mixture model and the two LTPMMMs were fit to the simulated data. The MAR model has a clear advantage over the other three models for standard error, RMSE, coverage rate and average width.

#### **10.1.3 Negative Mood Regulation Regression Coefficient Estimates**

Table X under the column titled negative mood regulation shows that no significant differences are seen in the four models when estimating the NMR regression coefficient on negative affect when the true model was assumed to be a MAR model. The NMR coefficient

estimates are comparable: the average estimates are identical across the four models and the raw bias, percentage bias, and standardized bias measures are also similar. The precision measures for the NMR coefficient are not significantly different; standard error, fraction of missing information, and average widths of the 95% confidence intervals do not show a definite “best” model. The two hybrid assessment measures coverage rates and RMSE are comparable among the four model scenarios. The LTPMMMs are virtually the same in terms of bias and precision for the estimated regression coefficient of NMR on negative affect. It is interesting to note that the MAR model has the lowest coverage rate when it was assumed to be the true model, instead of being noticeably higher than the other three models.

#### **10.1.4 Positive Affect**

Table XI show the results of 1,000 simulations assuming that the true model was a MAR mixed-model fitting positive affect to our model covariates. The MAR model has the same format as the model fit to negative affect outcomes and is shown in Equation 6.1.

#### **10.1.5 Gender Regression Coefficient Estimates**

Gender regression coefficient estimates for the four models are shown in Table XI on the left-hand side of the table. If the true model was assumed to be a MAR mixed-effect model with random-intercept terms, it performs best among the four models in terms of precision of the estimate: the standard error, RMSE, and average width of the 95% confidence intervals are the lowest. In terms of model bias the gender coefficient, the MAR model has a slight edge in raw bias, percentage bias, and standardized bias. The two LTPMMMs offer the best coverage rates and lowest fraction of missing information among the four models in terms of estimating the gender coefficient.



### 10.1.6 Negative Mood Regulation Regression Coefficient Estimates

Negative mood regulation regression coefficient estimates assuming that the MAR model was the true model are shown in Table XI in the right-hand side of the table. No drastic differences in bias of the estimates are seen among the models when the true model is a MAR random-intercept model. The two LTPMMs have a slight edge over the latent class pattern-mixture and the MAR models in terms of percentage bias; raw bias and standardized bias are virtually identical across the four models. Also, the precision measures of the estimate are comparable; no one model outperforms the others in terms of standard error and fraction of missing information. The two hybrid measures assessing both bias and precision (RMSE and coverage rates) are close as well. This is to be expected since the true model assumes that positive affect outcomes are MAR.

In summary, model performance was not extremely different among the four models when the true model was assumed to be a MAR mixed-model. Also, the MAR mixed-model does not outperform the other models in a consistent manner based on these bias and precision measures.

## 10.2 Latent Class Pattern-Mixture Model

Using a similar approach shown above for the MAR random-intercept models, correlation was induced between the gender regression coefficient and the latent classes. This was done by determining latent class membership that was based on each subjects response vector  $\mathbf{R}_i$  and their gender. The latent class variables were then fit into a mixed-model as:

$$y_{ij} = x'_{ij}\beta + v_{0i} + e_{ij} \quad (10.1)$$

where  $\beta$  includes indicator variables for latent class membership,  $x'_{ij}$  contains all model covariates mentioned previously and  $y_{ij}$  refers to negative or positive affect. In all simulations, a latent class pattern-mixture model with three latent classes was used.

### 10.2.1 Negative Affect

Performance measures among the four models using NA as the outcome will be examined first. In this scenario, the true model was assumed to be a latent class pattern-mixture model. The results for the two regression coefficients of gender and negative mood regulation are shown in Table XII.

### 10.2.2 Gender Regression Coefficient Estimates

As shown in Table XII, the latent class pattern-mixture model with three latent classes performs best in terms of bias measures of the effect of gender on the negative affect outcome variable. Raw bias, percentage bias, and standardized bias of the gender regression coefficient are lowest when using the LC pattern-mixture model. But in terms of model precision of the estimate, the LC pattern-mixture model does not outperform the two LTPMMs and the MAR model which has the lowest standard error among the four models. The RMSE of the estimate is the highest using the LC pattern-mixture model and the average width of the 95% confidence intervals for the regression coefficient is the widest. No clear advantage is seen when using the latent class pattern-mixture model to fit the EMA data. The two LTPMMs can be used as an alternative to the latent class mixed-model because of these favorable differences in model precision of the gender estimate.

### 10.2.3 Negative Mood Regulation Regression Coefficient Estimates

The estimates among the models do not differ drastically when comparing the regression coefficient of negative mood regulation across the four simulated models; this is seen in Table XII. The two LTPMMs are virtually performing the same as the true latent class

pattern-mixture model in terms of bias of the estimate, the percentage and standardized bias. Also, in terms of model precision the two LTPMMs are very close to the MAR and LC pattern-mixture models in terms of standard error, RMSE, fraction of missing information and average width of 95% confidence intervals for the regression coefficient. The LC pattern-mixture model does not offer a drastic improvement in model performance compared to the MAR mixed-model and the two LTPMMs. As was seen when analyzing the coefficient estimates for gender, this lends support to use the LTPMMM for EMA data even when the true model used to simulate data sets was the latent class pattern-mixture model.

#### **10.2.4 Positive Affect**

The same procedure used to simulate the latent class pattern-mixture model with negative affect as the outcome is now used to simulate a latent class model pattern-mixture model with positive affect as the outcome. The estimates for the gender regression coefficient are shown next.

#### **10.2.5 Gender Regression Coefficient Estimates**

The left hand-side of Table XIII presents the results of estimating the gender regression coefficient across the four models when the true model is a latent class pattern-mixture model with three classes. The latent class pattern-mixture model performs best in terms of model fit, raw bias, percentage bias, and standardized bias of the gender coefficient estimate; all of these measures are low with the LC pattern-mixture model. For precision measures, the LC pattern-mixture model performs the worst in standard error, RMSE, and the average width of the 95% confidence intervals. The average width is especially high with the LC pattern-mixture model ( $\approx 0.61$ ), whereas the other models are no higher than 0.50. The LC pattern-mixture model has the best coverage rate as well, but this due to the higher standard error. Both the

one-parameter and two-parameter LTPMMs perform well in terms of bias and precision, and are preferred over the true LC pattern-mixture model based on RMSE and average width.

### 10.2.6 Negative Mood Regulation Regression Coefficient Estimates

No big difference in model performance of the NMR regression coefficient is seen in Table XIII when the latent class pattern-mixture model is assumed to be the true model. The model fits for the NMR coefficient estimate as measured by raw bias, percentage bias, and standardized bias are similar across the four models. Also, model precision does not differ based on the RMSE, coverage rate, fraction of missing information, and average width of the 95% across the four models. When the true model is a latent class pattern-mixture model, it does not clearly outperform the MAR mixed model. As was seen with negative affect as the outcome, the LTPMMs are matching the performance from the latent class pattern-mixture model for the coefficient estimate of NMR.

In conclusion, the two LTPMMs offer a clear advantage in model precision over the latent class pattern mixture-model when estimating the effect of gender on both NA and PA outcomes. No clear advantage exists among the models in estimating the effect of NMR on the two mood (negative and positive affect) outcomes.

### 10.3 One-Parameter Latent Trait Pattern-Mixture Mixed-Model

The one-parameter LTPMMM should outperform the two-parameter LTPMMM, latent class, and MAR models when the one-parameter LTPMMM is the “true” model. This will be checked by looking at the two outcome measures of positive affect and negative affect and by comparing estimates from the gender regression coefficient and negative mood regulation regression coefficient.

### 10.3.1 Negative Affect

The one-parameter LTPMMM was fit using the missingness process explained above with negative affect as the outcome. The model included a random-intercept term for each subject, the model covariates smoker, gender, negative mood regulation, alone (within-subjects), alone (between-subjects) and the estimated latent trait of response. The results of the simulations estimating the coefficients for gender, negative mood regulation and the latent trait ( $\theta_i$ ) are shown in Table XIV.

### 10.3.2 Gender Regression Coefficient Estimates

The left-hand side of Table XIV shows the results of estimating the gender regression coefficient in the one-parameter LTPMMM. If the true model is the one-parameter LTPMMM, the one- and two-parameter LTPMMMs perform best compared to the latent class pattern-mixture model and the MAR linear mixed-model in terms of bias and precision of the estimated coefficient. The fraction of missing information is lower with the one- and two-parameter LTPMMMs. The two LTPMMMs outperform the other models in terms of raw bias, percentage bias, standardized bias, and RMSE. The latent class pattern-mixture model also performs well with the simulated data sets, but the bias in the gender estimate is roughly five percent. It also interesting to note that the results are very comparable between the one- and two-parameter latent trait pattern-mixture mixed models in terms of bias, root mean squared error, and coverage rates. One may consider the one-parameter LTPMMM in cases where the two-parameter has convergence problems or very long run times. The MAR model definitely performs the worst in terms of bias and coverage rates even though the average width of the 95% confidence intervals for the estimated gender regression coefficient is the smallest across these four models. The 91.8% coverage rate of the MAR model is at a level that may be too low, since it is below 95%.

### 10.3.3 Negative Mood Regulation Regression Coefficient Estimates

The right columns of Table XIV shows the results of estimating the regression coefficient of NMR in the one-parameter LTPMMM. When looking at the estimated coefficient of negative mood regulation, a difference was seen in model performance in terms of bias with the four models. The latent class and MAR mixed-models have the highest bias. The one- and two-parameter latent trait pattern-mixture models performed best in terms of raw bias, percentage bias, and standardized bias compared to the MAR model and latent class pattern-mixture model. The estimated RMSE for the NMR coefficient was slightly lower for the two LTPMMMs. No significant differences in model precision was found across the four models; standard errors, coverage rates, fraction of missing information, and average widths of the 95% confidence intervals were all virtually identical.

### 10.3.4 Latent Trait ( $\theta_i$ ) Regression Coefficient ( $\hat{\gamma}$ ) Estimates

In order to compare the performance of the one-parameter LTPMMM with the two-parameter LTPMMM, the estimates for the latent trait coefficient ( $\gamma$ ) in the mixed-models is presented in Table XV. The one-parameter LTPMMM clearly outperforms the two-parameter LTPMMM in terms of raw bias, percentage bias, standardized bias, and coverage rates of this estimate. It is curious to note that the two-parameter LTPMMM has a lower standard error, RMSE and average width. Therefore, the two-parameter LTPMMM outperforms the one-parameter LTPMMM in terms of precision; the additional estimated item discrimination parameters reduced the variability of the latent trait coefficient estimate. Even though the two models have different advantages, the lower bias may warrant the use of a one-parameter LTPMMM because the bias from the two-parameter model is quite high.

### 10.3.5 Positive Affect

Performance for the one-parameter LTPMMM with positive affect as the outcome is shown in Table XVI.

### 10.3.6 Gender Regression Coefficient Estimates

Results for 1,000 simulations for the gender regression coefficient when the true model is a one-parameter LTPMMM are shown in Table XVI. The one-parameter LTPMMM performs best in terms of bias and precision of the estimated regression coefficient for gender. The RMSE and coverage rates are best with the two LTPMMMs, therefore these two models are also more precise and less biased than the other two fits. As expected, the latent class pattern-mixture model and MAR random-intercept model perform the worst in terms of bias and precision because the correlation between the males and the missingness is not modeled in any way. In these simulations for the regression coefficient of male gender on positive affect, the two LTPMMMs are preferred over the MAR and latent class pattern-mixture models, which on average show a lower estimate than the true gender regression coefficient. As was seen the simulations for NA when the true model was a one-parameter LTPMMM, the MAR model provides a coverage rate that is the lowest among the models and is below 95% (93.7%).

### 10.3.7 Negative Mood Regulation Regression Coefficient Estimates

As shown in Table XVI the one- and two-parameter LTPMMMs perform best in terms of bias of the NMR regression coefficient as measured by raw bias, percentage bias, and standardized bias, but these improvements are only slight. In terms of model precision, the standard errors, RMSE, fraction of missing information, and average widths are very similar across the models. All four models are acceptable in terms of biases, standard errors, RMSE, and coverage rates. It is interesting to note that the MAR model had the highest coverage rate among the models, but not noticeably higher than the other three models.

### 10.3.8 Latent Trait ( $\theta_i$ ) Regression Coefficient ( $\hat{\gamma}$ ) Estimates

Results of 1,000 simulations for the latent trait ( $\theta_i$ ) regression coefficient estimates are shown in Table XVII. If the true model used to simulate positive affect is the one-parameter LTPMMM, a two-parameter LTPMMM is shown to be biased when estimating the latent traits ( $\theta_i$ ) for each subject. This may be due to estimation of separate item discrimination parameters when the true model only includes one item discrimination parameter. The one-parameter LTPMMM outperforms the two-parameter LTPMMM in terms of raw bias, standardized bias, and coverage rates, but the two-parameter LTPMMM generates estimates that are more precise. This is seen by comparing standard error, RMSE and average width which are lower in the two-parameter LTPMMM. Although these are desirable reasons to use the two-parameter LTPMMM, the one-parameter LTPMMM is probably preferred because the two-parameter LTPMMM induces too much bias (-22.1%).

## 10.4 Two-Parameter Pattern-Mixture Mixed-Model

In this section, the two-parameter LTPMMM is assumed to be the true model. The model includes the same covariates and form as the one-parameter LTPMMM except separate discrimination parameters are estimated for the thirty-five time-bins in the model. As was done with the one-parameter model in this chapter, results for the gender regression coefficient, negative mood regulation, and the  $\theta_i$  regression coefficient will be compared for both negative and positive affect outcomes. Results of the 1,000 simulations across the four models are shown in Table XVIII.

### 10.4.1 Negative Affect

The next section shows the results of 1,000 estimates of the estimated gender regression coefficient if the two-parameter LTPMMM is the true model.



#### **10.4.2 Gender Regression Coefficient Estimates**

As seen in Table XVIII on the left-hand-side of the table, the one- and two-parameter LTPMMMs have the best performance in terms of model fit: the raw bias, percentage bias, and standardized bias are lowest with these models. Also, the two LTPMMMs outperform the other models in terms of precision and bias of the gender estimate, as shown by the hybrid measures RMSE and coverage rates. The latent class pattern-mixture model performance is much better than the MAR model which has the highest percentage bias and lowest coverage rate. The MAR model has unacceptable bias and coverage rates compared to the other models; less than 90% of the estimated confidence intervals for the true effect of male gender on positive affect contain the true value. Although the MAR model generates confidence intervals that are the narrowest among the simulated models, it underestimates the true gender regression coefficient by a large margin. Once again, the two LTPMMMs outperform the MAR and LC pattern-mixture models, when the true model is a two-parameter LTPMMM.

#### **10.4.3 Negative Mood Regulation Regression Coefficient Estimates**

Results are shown in the right columns of Table XVIII. As seen in the one-parameter LTPMMM simulations for negative affect, the models are comparable in terms of model performance when estimating the coefficient for negative mood regulation. The biases of the estimators are extremely small across the four models, with the one-parameter model having the smallest raw bias, percentage bias, and standardized bias. Although the one-parameter LTPMMM was not the true model simulated here, it does differ in overall fit and precision with the two-parameter LTPMMM. In terms of model precision, the four models have comparable standard errors, RMSE, and fraction of missing information values. The MAR model has the largest average width, but it is not noticeably different from the other three mixed models.

#### 10.4.4 Latent Trait ( $\theta_i$ ) Regression Coefficient ( $\hat{\gamma}$ ) Estimates

If the true model is a two-parameter LTPMMM, the one-parameter LTPMMM is biased for the estimate of  $\gamma$  as shown in the right-hand side of Table XIX. Bias, standard error, raw bias, percentage bias, standardized bias, RMSE, and average width are all increased when using the one-parameter model. This may be a result of not having the additional item discrimination parameters for each time-interval. The percentage bias for the one-parameter LTPMMM is quite high (14.2%). The two-parameter LTPMMM is the more precise model as seen by the lower standard error, RMSE, fraction of missing information, and average width of 95% confidence intervals.

#### 10.4.5 Positive Affect

#### 10.4.6 Gender Regression Coefficient Estimates

The LTPMMMs performed best in terms of estimating the regression coefficient of gender on the outcome. Results are presented in Table XX on the left-hand side of the table. This is true when comparing the fit of the models; the two LTPMMMs have the lowest raw bias, percentage bias, and standardized bias for the gender effect. Two LTPMMMs have the best precision as measured by RMSE, but they do not outperform the LC pattern-mixture and MAR random-intercept models in terms of standard error, fraction of missing information, and average width. The one-parameter LTPMMM is adequate in predicting the regression coefficient of NMR on positive affect when the true model is a two-parameter LTPMMM, overall the two models do not differ. The MAR model provided the smallest average width of 95% confidence intervals among the models, but this increased gain in precision is hampered by the high percentage bias in the downward direction (-22.7%). It is also curious to note that none of the four models had a coverage rate that was higher than 95%, this may need further investigation.

#### 10.4.7 Negative Mood Regulation Regression Coefficient Estimates

The models are performing in a comparable manner in terms of overall fit and precision of the coefficient estimate of NMR; this is seen in the right columns of Table XX. The four models have similar bias; the average estimates, raw bias, percentage bias, and standardized bias are all comparable. This is also seen when comparing the precision measures for the models, the standard errors are identical, and RMSE, coverage rates, fraction of missing information are close as well. One troubling observation is that the coverage rates for the four models seem low, a similar result was found in the performance measures for the gender regression coefficient. The two-parameter LTPMMM does not have higher coverage rates than the other models when it is the true model; this may need further exploration.

#### 10.4.8 Latent Trait ( $\theta_i$ ) Regression Coefficient ( $\hat{\gamma}$ ) Estimates

Results for simulations comparing the one- and two-parameter LTPMMMs in estimating the latent trait regression coefficient are presented in Table XXI. The two-parameter LTPMMM performs better than the one-parameter LTPMMM in terms of model fit: raw bias, percentage bias, and standardized bias are all equal to zero in the two-parameter model. In terms of model precision the standard error, RMSE, and average width of the 95% confidence intervals are all lower than the one-parameter LTPMMM. Coverage rates happen to be higher with the one-parameter LTPMMM, but not considerably so. Since the true model in contains more additional discrimination parameters, the one-parameter model is biased upwards and does not accurately estimate the  $\theta$  coefficient with 1,000 simulations. The percentage bias (14.2%) from the one-parameter model is quite high.

In summary, the one- and two-parameter LTPMMMs clearly outperform the MAR and latent class mixed-models for both PA and NA outcomes. This was especially true for the estimated gender regression coefficient when the true model was either a one- or two-parameter

LTPMMM, since correlation was induced between gender and the estimated latent traits. The NMR regression coefficient estimates also showed some differences among the models, the most noticeable was when the data were generated from a LC pattern-mixture model and in this case, the two-LTPMMMs outperformed the true assumed LC pattern-mixture model. The two-parameter LTPMMM has an advantage over the one-parameter LTPMMM model when estimating the regression coefficient of the latent trait. This may be due to the fact that the additional item discrimination parameters allow the two-parameter LTPMMM to better estimate the latent trait of response for each subject.

### **10.5 Ninety-Five Percent Confidence Intervals**

Figure 4 and Figure 5 compare the 95% confidence intervals of the gender regression coefficient for the four simulated models when negative affect is the outcome. The one-parameter and two-parameter LTPMMMs have an unbiased estimate for the gender regression coefficient as compared to latent class pattern-mixture and MAR mixed-models. This occurs when the true model is a one-parameter LTPMMM or a two-parameter LTPMMM and the latent trait is correlated with gender. If the true model is a latent class pattern-mixture model, the LC pattern-mixture model performs the worst in terms of precision of the estimate. The MAR only performs best when the true model is the MAR mixed model.

Similar results are found when comparing the 95% confidence intervals of the gender regression coefficient for the four simulated models when positive affect is the outcome. These are shown in Figure 6 and Figure 7.

No particular differences are seen in model performance when estimating the regression coefficient of NMR in the four models. The 95% confidence intervals are virtually identical between the four models with the different data generation scenarios. This is true when both

positive and negative affect is the outcome. These results are presented in Figure 8, Figure 9, Figure 10, and Figure 11.

Based on the simulation results from the one-parameter and two-parameter LTPMMM, the two models' confidence intervals do not differ much in terms of model performance based on the gender regression coefficient. When looking at the regression coefficient of the latent trait estimate  $\theta_i$  across the two models, the extra parameters used in the two-parameter LTPMMM decrease the size of the confidence interval and also reduces the bias if the two-parameter LTPMMM is the true model. This applies with the two model outcomes NA and PA. Therefore, the two-parameter model is preferred for over the one-parameter LTPMMM due to the increase in efficiency. These results can be found in Figure 12 and Figure 13.

These differences in the latent trait distributions from the one- and two-parameter LTPMMM are presented in Figure 14. These figures contain the estimated latent traits ( $\theta_i$ ) from the fitted LTPMMM referenced in Table II and Table V. The two-parameter LTPMMM is able to estimate a wider distribution of latent traits and the distribution looks less skewed, this may also mean that the additional item discrimination parameters greatly improve the two-parameter model's precision.

In summary, the 95% confidence intervals for the estimated gender, negative mood regulation, and latent trait regression coefficients all show some noticeable differences between the models. Overall, for both positive and negative outcomes, both the one- and two-parameter LTPMMM outperform the LC pattern-mixture and MAR mixed-models. The tightest confidence intervals were seen in the gender coefficient estimates for the two LTPMMMs, the other model approaches typically were biased. These differences in the confidence intervals were not as striking for the NMR regression coefficient, but results showed that the LC pattern-mixture model had much wider confidence intervals than the other approaches, even when data were

generated assuming the LC pattern-mixture model was the true model. Lastly, the differences in confidence intervals for the latent trait regression coefficient were noticeable, especially if data were generated assuming that the two-parameter LTPMMM model was the true model, and if simulated data were fit with a one-parameter LTPMMM. These 95% confidence interval results along with the bias and accuracy measures shown previously, provide strong evidence that the proposed LTPMMMs are a better alternative than the LC pattern-mixture models for use with EMA data.

**TABLE X:** GENDER AND NEGATIVE MOOD REGULATION REGRESSION COEFFICIENT ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: MISSING AT RANDOM MIXED MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	-0.425	-0.425	-0.425	-0.425	-0.809	-0.809	-0.809	-0.809
Average Estimate	-0.422	-0.422	-0.425	-0.425	-0.814	-0.814	-0.814	-0.814
Standard Error	0.247	0.246	0.246	0.191	0.140	0.140	0.140	0.140
Raw Bias	0.003	0.003	0.000	0.000	-0.004	-0.004	-0.004	-0.004
Percentage Bias	-0.725	-0.691	0.004	0.000	0.539	0.540	0.528	0.529
Standardized Bias	0.012	0.012	0.000	0.000	-0.031	-0.031	-0.031	-0.031
RMSE	0.172	0.171	0.170	0.134	0.099	0.099	0.100	0.099
Coverage Rate	0.957	0.957	0.954	0.960	0.946	0.946	0.947	0.942
Fraction of Missing Information	0.485	0.485	0.482	0.492	0.505	0.505	0.507	0.505
Average Width	0.694	0.693	0.692	0.534	0.385	0.385	0.385	0.385

**TABLE XI:** GENDER AND NEGATIVE MOOD REGULATION REGRESSION COEFFICIENT ESTIMATES, POSITIVE AFFECT, TRUE MODEL: MISSING AT RANDOM MIXED MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	0.213	0.213	0.213	0.213	0.625	0.625	0.625	0.625
Average Estimate	0.211	0.211	0.212	0.213	0.629	0.629	0.629	0.629
Standard Error	0.200	0.200	0.202	0.156	0.112	0.112	0.112	0.112
Raw Bias	-0.002	-0.002	-0.001	0.000	0.004	0.004	0.004	0.004
Percentage Bias	-1.086	-0.941	-0.418	0.000	0.564	0.566	0.570	0.571
Standardized Bias	-0.012	-0.010	-0.004	0.000	0.032	0.032	0.032	0.032
RMSE	0.140	0.140	0.143	0.111	0.079	0.079	0.079	0.079
Coverage Rate	0.948	0.950	0.943	0.944	0.942	0.943	0.941	0.943
Fraction of Missing Information	0.489	0.488	0.501	0.504	0.497	0.497	0.497	0.496
Average Width	0.561	0.561	0.559	0.432	0.311	0.311	0.311	0.311



**TABLE XII:** GENDER AND NEGATIVE MOOD REGULATION REGRESSION COEFFICIENT ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: LATENT CLASS PATTERN-MIXTURE MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	-0.532	-0.532	-0.532	-0.532	-0.801	-0.801	-0.801	-0.801
Average Estimate	-0.535	-0.532	-0.532	-0.455	-0.810	-0.811	-0.807	-0.807
Standard Error	0.221	0.221	0.272	0.193	0.140	0.140	0.140	0.140
Raw Bias	0.018	-0.003	0.000	0.077	-0.009	-0.009	-0.005	-0.005
Percentage Bias	-3.404	-0.514	0.000	-14.562	1.077	1.138	0.681	0.662
Standardized Bias	0.082	-0.012	0.000	0.401	-0.062	-0.065	-0.039	-0.038
RMSE	0.156	0.163	0.190	0.154	0.098	0.098	0.098	0.098
Coverage Rate	0.959	0.959	0.972	0.938	0.953	0.954	0.956	0.957
Fraction of Missing Information	0.492	0.493	0.490	0.477	0.488	0.489	0.490	0.487
Average Width	0.617	0.617	0.758	0.547	0.393	0.393	0.393	0.394

**TABLE XIII:** GENDER AND NEGATIVE MOOD REGULATION REGRESSION COEFFICIENT ESTIMATES, POSITIVE AFFECT, TRUE MODEL: LATENT CLASS PATTERN-MIXTURE MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	0.293	0.293	0.293	0.293	0.618	0.618	0.618	0.618
Average Estimate	0.284	0.297	0.293	0.240	0.628	0.628	0.625	0.625
Standard Error	0.176	0.176	0.217	0.158	0.112	0.112	0.112	0.112
Raw Bias	-0.009	0.004	0.000	-0.053	0.010	0.010	0.007	0.007
Percentage Bias	-2.934	1.226	0.000	-17.935	1.611	1.639	1.205	1.189
Standardized Bias	-0.049	0.020	0.000	-0.333	0.088	0.090	0.066	0.065
RMSE	0.124	0.124	0.152	0.124	0.080	0.080	0.079	0.079
Coverage Rate	0.954	0.952	0.969	0.928	0.947	0.948	0.946	0.950
Fraction of Missing Information	0.497	0.496	0.490	0.508	0.497	0.497	0.496	0.495
Average Width	0.490	0.490	0.605	0.434	0.313	0.312	0.312	0.313

**TABLE XIV:** GENDER AND NEGATIVE MOOD REGULATION ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	-0.548	-0.548	-0.548	-0.548	-0.824	-0.824	-0.824	-0.824
Average Estimate	-0.548	-0.548	-0.520	-0.449	-0.815	-0.815	-0.812	-0.806
Standard Error	0.248	0.248	0.249	0.237	0.169	0.169	0.169	0.169
Raw Bias	0.000	0.000	0.028	0.099	0.009	0.009	0.012	0.018
Percentage Bias	0.000	-0.062	-5.043	-18.054	-1.091	-1.119	-1.408	-2.157
Standardized Bias	0.000	0.001	0.111	0.418	0.053	0.054	0.069	0.105
RMSE	0.175	0.175	0.179	0.194	0.119	0.119	0.120	0.120
Coverage Rate	0.959	0.957	0.957	0.918	0.953	0.953	0.952	0.953
Fraction of Missing Information	0.498	0.499	0.506	0.502	0.497	0.497	0.496	0.495
Average Width	0.688	0.688	0.686	0.655	0.471	0.471	0.471	0.472

**TABLE XV:** LATENT TRAIT REGRESSION COEFFICIENT ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

Final Results	Latent Trait	
	LT1P	LT2P
Truth	-0.238	-0.238
Average Estimate	-0.238	-0.187
Standard Error	0.188	0.148
Raw Bias	0.000	0.051
Percentage Bias	0.000	-21.280
Standardized Bias	0.000	0.341
RMSE	0.131	0.115
Coverage Rate	0.966	0.939
Fraction of Missing Information	0.487	0.487
Average Width	0.526	0.416

**TABLE XVI:** GENDER AND NEGATIVE MOOD REGULATION ESTIMATES, POSITIVE AFFECT, TRUE MODEL: ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	0.303	0.303	0.303	0.303	0.636	0.636	0.636	0.636
Average Estimate	0.303	0.302	0.285	0.237	0.634	0.634	0.633	0.628
Standard Error	0.218	0.218	0.218	0.206	0.149	0.149	0.150	0.149
Raw Bias	0.000	0.000	-0.017	-0.065	-0.002	-0.002	-0.003	-0.008
Percentage Bias	0.000	-0.147	-5.745	-21.618	-0.266	-0.288	-0.543	-1.216
Standardized Bias	0.000	-0.002	-0.080	-0.317	-0.011	-0.012	-0.023	-0.052
RMSE	0.155	0.155	0.157	0.160	0.107	0.107	0.107	0.107
Coverage Rate	0.956	0.953	0.947	0.937	0.944	0.944	0.944	0.950
Fraction of Missing Information	0.508	0.507	0.513	0.505	0.510	0.510	0.511	0.508
Average Width	0.600	0.600	0.598	0.569	0.410	0.410	0.410	0.410

**TABLE XVII:** LATENT TRAIT REGRESSION COEFFICIENT ESTIMATES, POSITIVE AFFECT, TRUE MODEL: ONE-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

Final Results	Latent Trait	
	LT1P	LT2P
Truth	0.165	0.165
Average Estimate	0.165	0.128
Standard Error	0.166	0.130
Raw Bias	0.000	-0.036
Percentage Bias	0.000	-22.132
Standardized Bias	0.000	-0.281
RMSE	0.116	0.097
Coverage Rate	0.935	0.920
Fraction of Missing Information	0.488	0.487
Average Width	0.465	0.364

**TABLE XVIII:** GENDER AND NEGATIVE MOOD REGULATION ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	-0.564	-0.564	-0.564	-0.564	-0.826	-0.826	-0.826	-0.826
Average Estimate	-0.561	-0.564	-0.538	-0.458	-0.824	-0.824	-0.822	-0.816
Standard Error	0.247	0.248	0.251	0.233	0.168	0.168	0.168	0.169
Raw Bias	0.003	0.000	0.027	0.107	0.001	0.002	0.003	0.010
Percentage Bias	-0.561	0.000	-4.769	-18.940	-0.144	-0.188	-0.396	-1.166
Standardized Bias	0.013	0.000	0.107	0.460	0.007	0.009	0.019	0.057
RMSE	0.178	0.178	0.183	0.197	0.121	0.121	0.121	0.121
Coverage Rate	0.951	0.954	0.944	0.899	0.951	0.949	0.952	0.951
Fraction of Missing Information	0.520	0.520	0.525	0.510	0.516	0.516	0.516	0.515
Average Width	0.670	0.673	0.676	0.638	0.458	0.458	0.458	0.460

**TABLE XIX:** LATENT TRAIT REGRESSION COEFFICIENT ESTIMATES, NEGATIVE AFFECT, TRUE MODEL: TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

Final Results	Latent Trait	
	LT1P	LT2P
Truth	-0.194	-0.194
Average Estimate	-0.221	-0.194
Standard Error	0.166	0.146
Raw Bias	-0.027	0.000
Percentage Bias	14.174	0.000
Standardized Bias	-0.165	0.000
RMSE	0.122	0.104
Coverage Rate	0.952	0.947
Fraction of Missing Information	0.512	0.509
Average Width	0.455	0.401

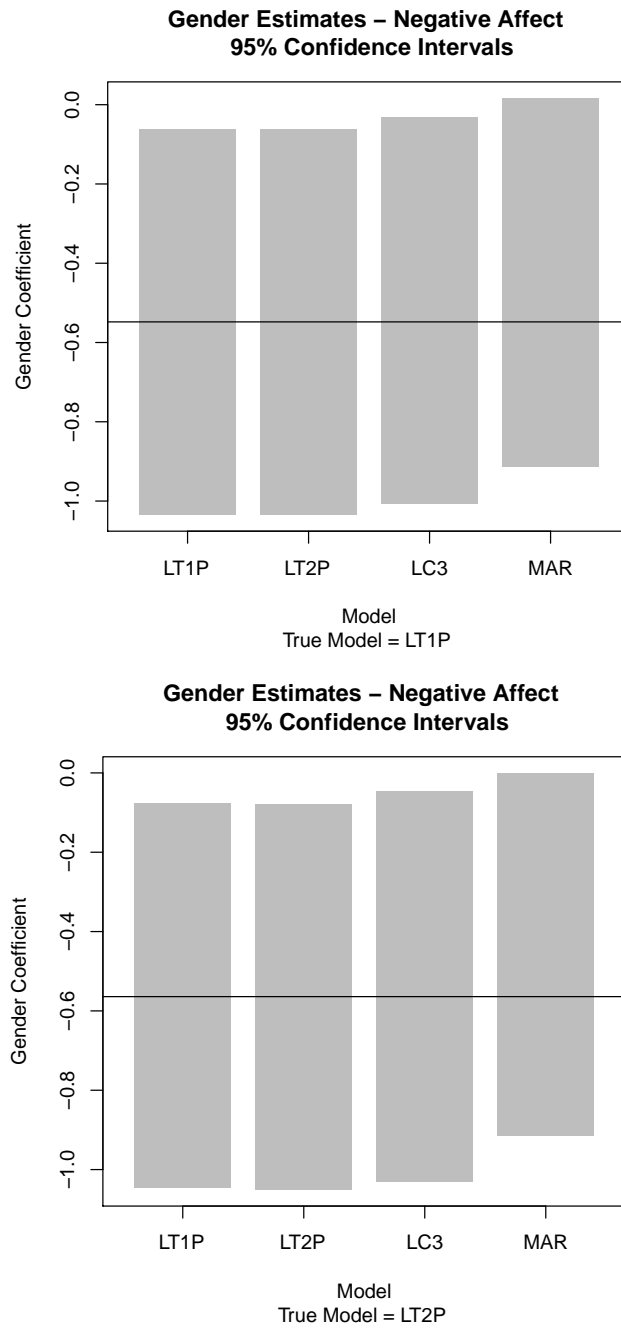


**TABLE XX:** GENDER AND NEGATIVE MOOD REGULATION ESTIMATES, POSITIVE AFFECT, TRUE MODEL: TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

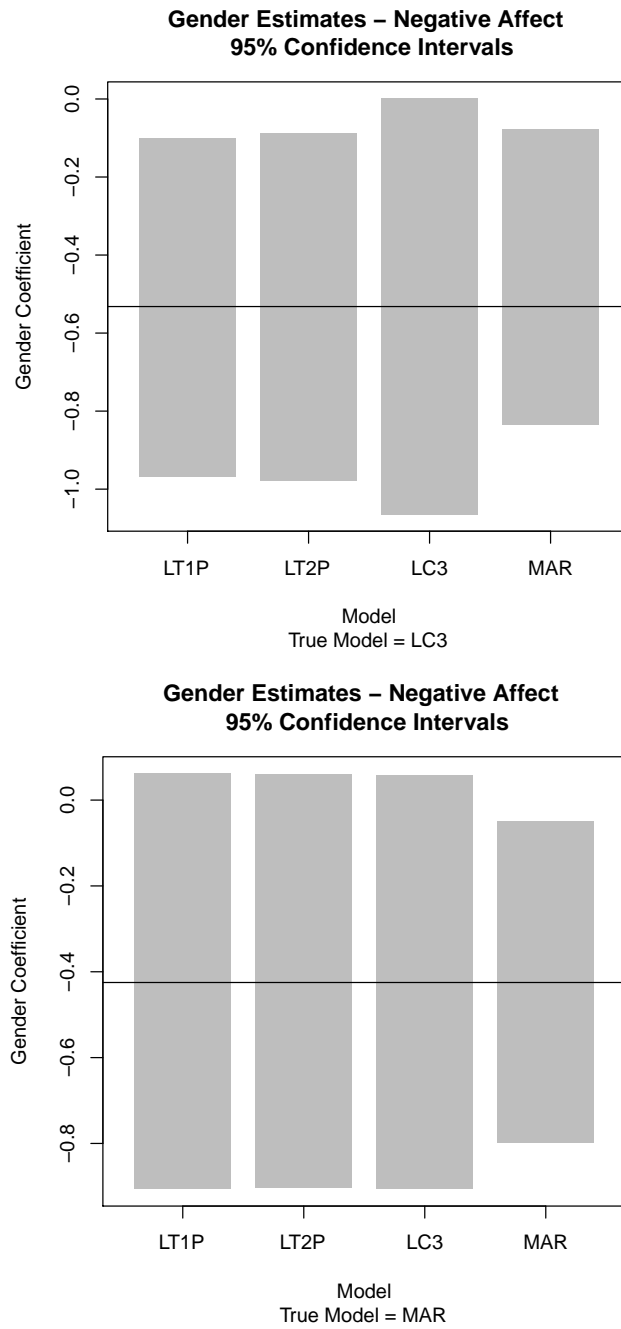
	Gender				Negative Mood Regulation			
Final Results	LT1P	LT2P	LC3	MAR	LT1P	LT2P	LC3	MAR
Truth	0.316	0.316	0.316	0.316	0.637	0.637	0.637	0.637
Average Estimate	0.314	0.316	0.296	0.244	0.632	0.632	0.631	0.626
Standard Error	0.211	0.212	0.212	0.200	0.147	0.147	0.147	0.147
Raw Bias	-0.002	0.000	-0.019	-0.072	-0.005	-0.005	-0.006	-0.011
Percentage Bias	-0.653	0.000	-6.108	-22.731	-0.762	-0.800	-0.955	-1.701
Standardized Bias	-0.010	0.000	-0.091	-0.360	-0.033	-0.035	-0.041	-0.074
RMSE	0.150	0.150	0.151	0.158	0.106	0.106	0.107	0.107
Coverage Rate	0.924	0.921	0.924	0.897	0.913	0.915	0.910	0.914
Fraction of Missing Information	0.503	0.504	0.500	0.498	0.522	0.523	0.523	0.520
Average Width	0.583	0.585	0.588	0.554	0.399	0.399	0.399	0.400

**TABLE XXI:** LATENT TRAIT REGRESSION COEFFICIENT ESTIMATES, POSITIVE AFFECT, TRUE MODEL: TWO-PARAMETER LATENT TRAIT PATTERN-MIXTURE MIXED-MODEL

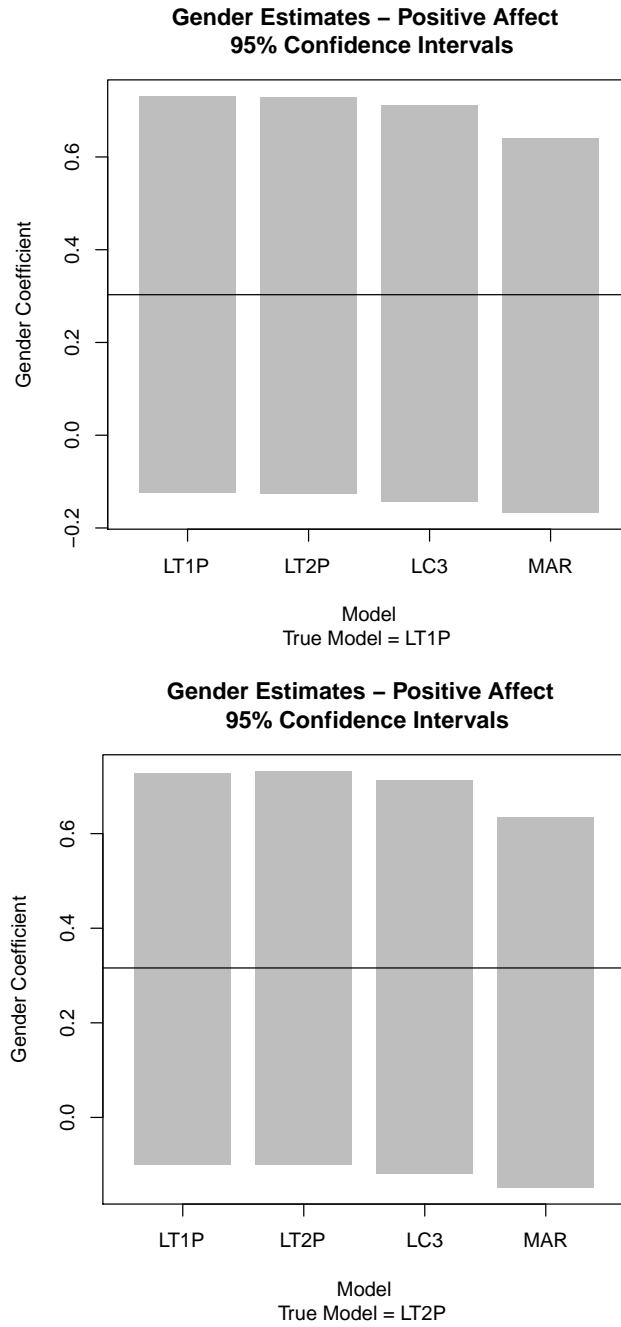
Final Results	Latent Trait	
	LT1P	LT2P
Truth	0.133	0.133
Average Estimate	0.152	0.133
Standard Error	0.144	0.126
Raw Bias	0.019	0.000
Percentage Bias	14.248	0.000
Standardized Bias	0.132	0.000
RMSE	0.104	0.089
Coverage Rate	0.961	0.958
Fraction of Missing Information	0.506	0.501
Average Width	0.396	0.349



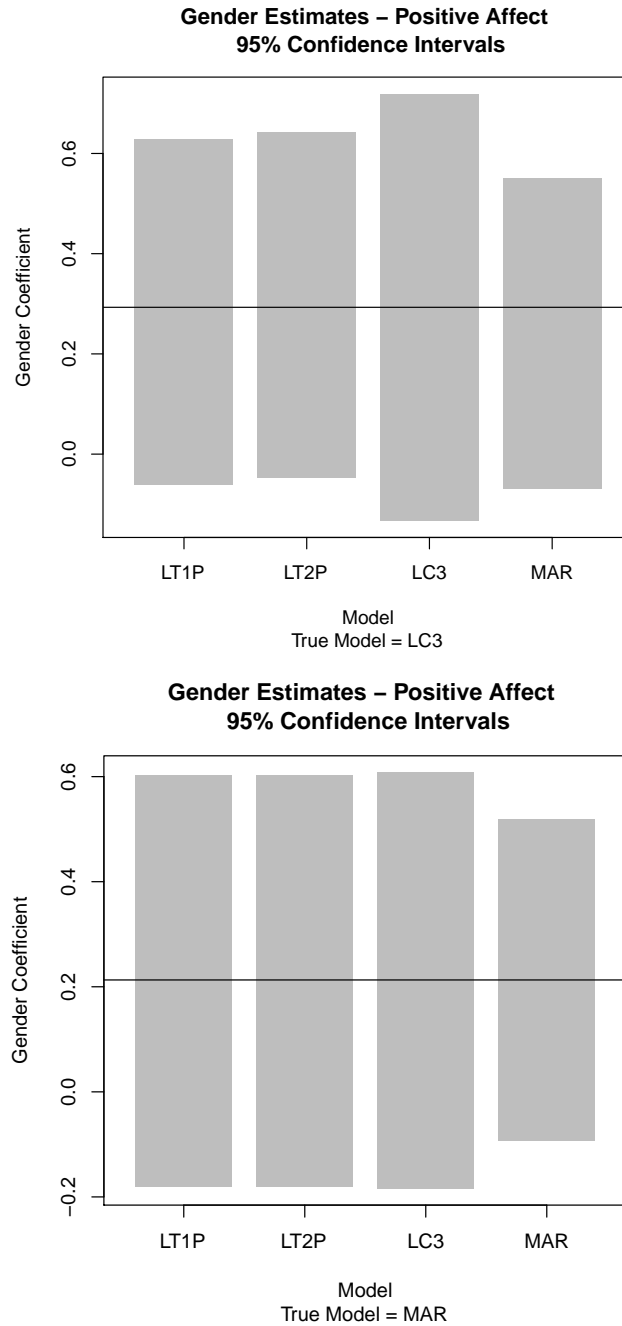
**Figure 4:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for gender regression coefficient estimate, negative affect.



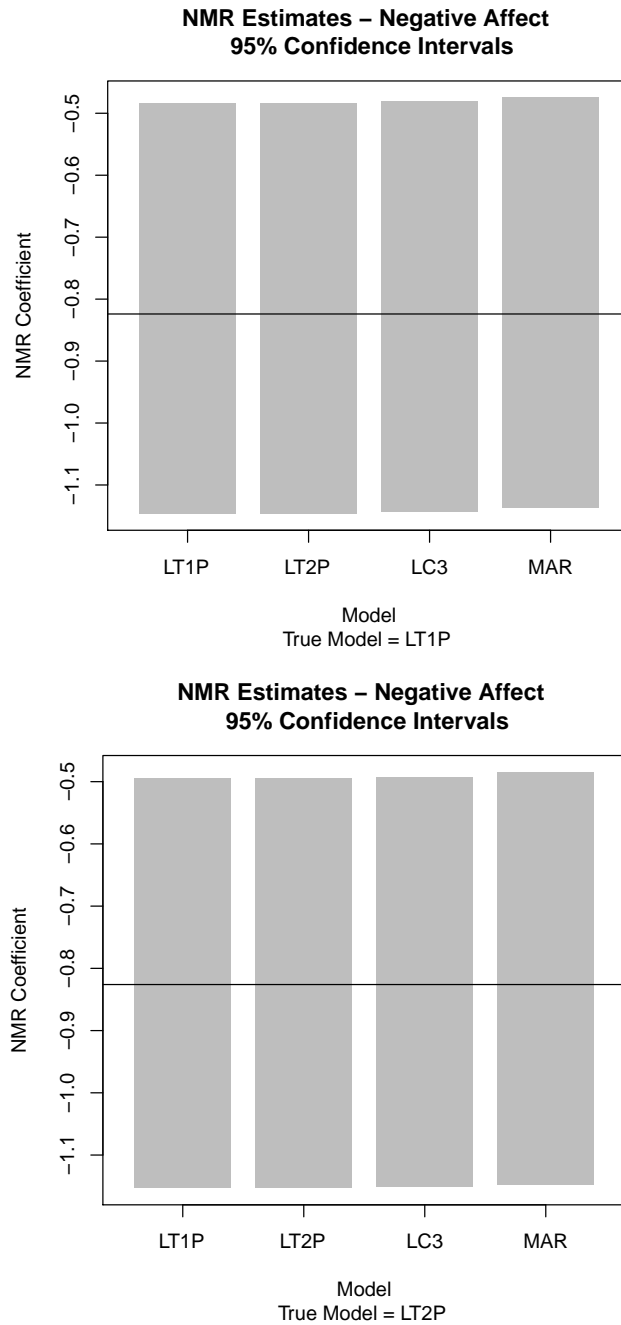
**Figure 5:** Latent class pattern-mixture and missing at random mixed-models, 1000 simulations, 95% confidence intervals for gender regression coefficient estimate, negative affect.



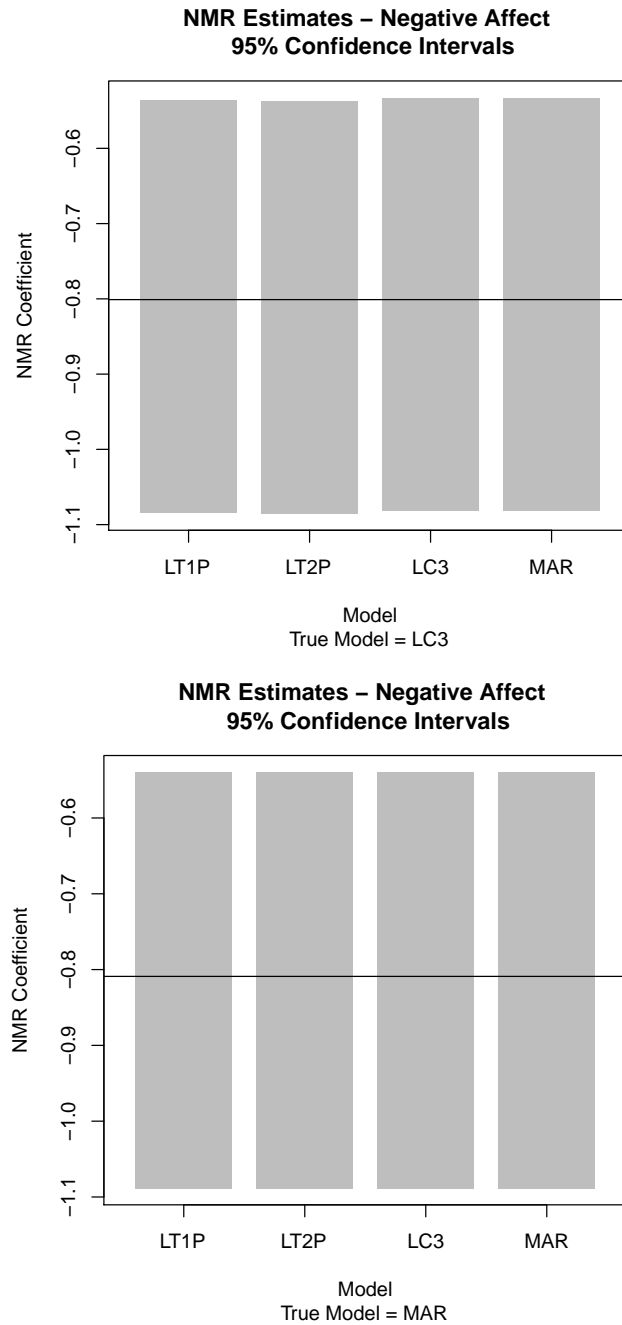
**Figure 6:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for gender regression coefficient estimate, positive affect.



**Figure 7:** Latent class pattern-mixture and missing at random mixed-models, 1000 simulations, 95% confidence intervals for gender regression coefficient estimate, positive affect.

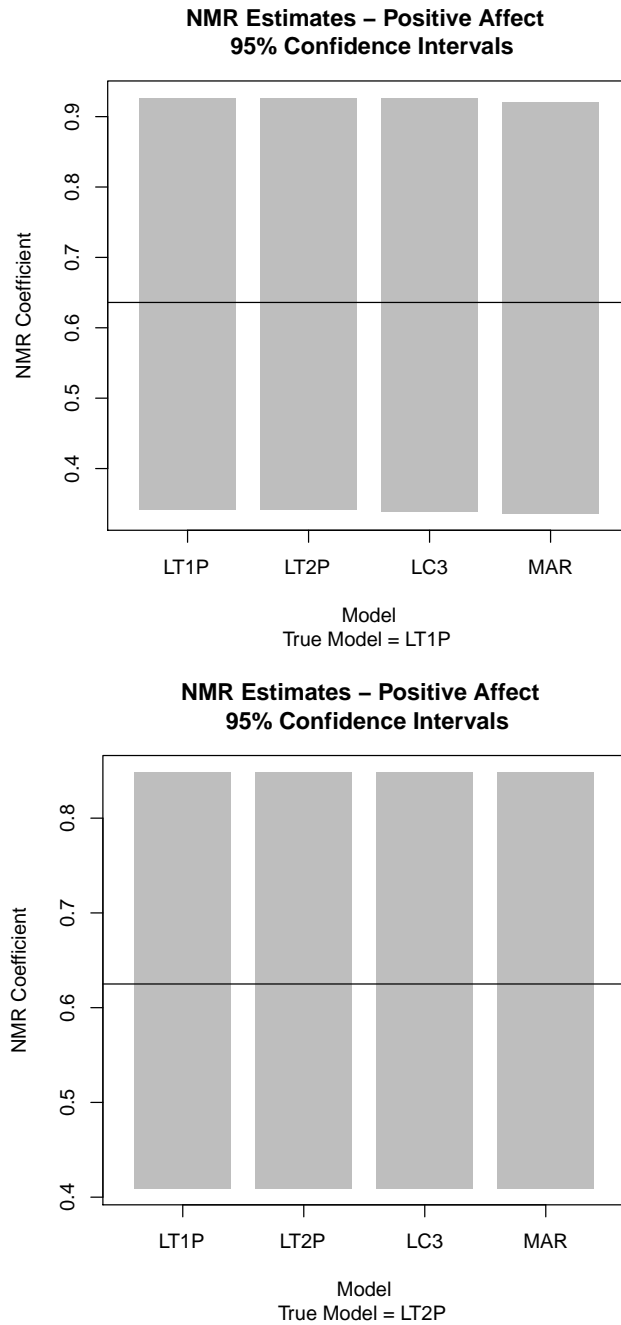


**Figure 8:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for negative mood regulation regression coefficient estimate, negative affect.

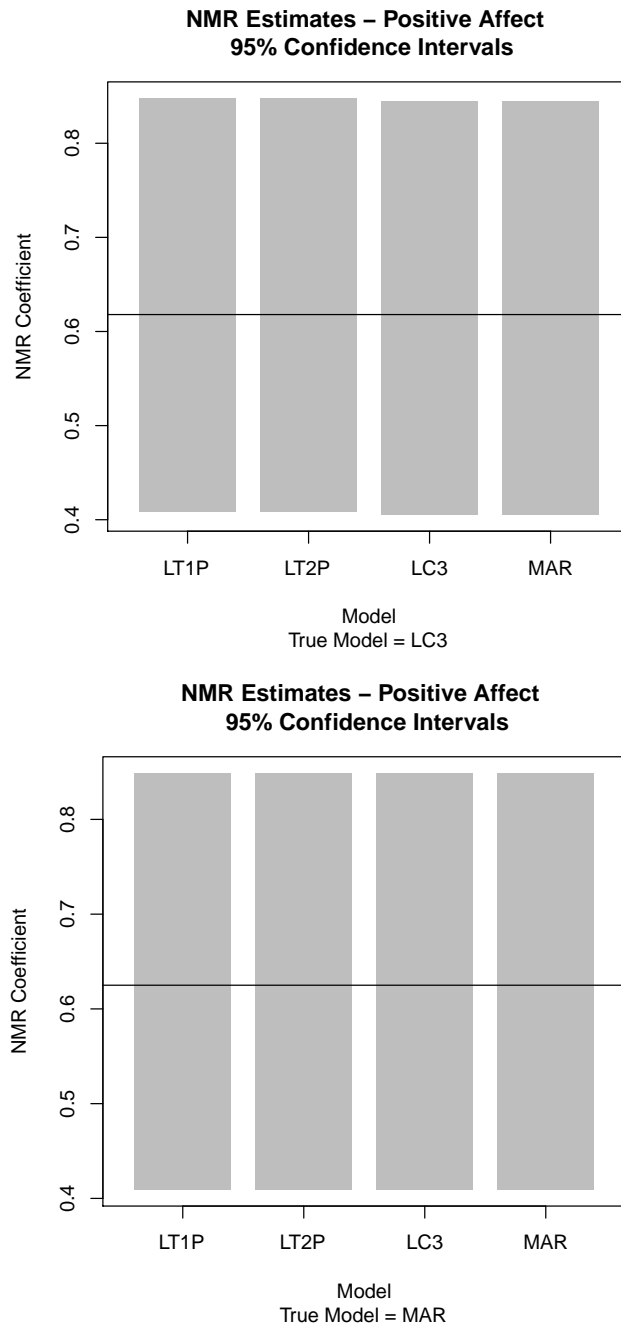


**Figure 9:** Latent class pattern-mixture and missing at random mixed-models, 1000 simulations, 95% confidence intervals for negative mood regulation regression coefficient estimate, negative affect.

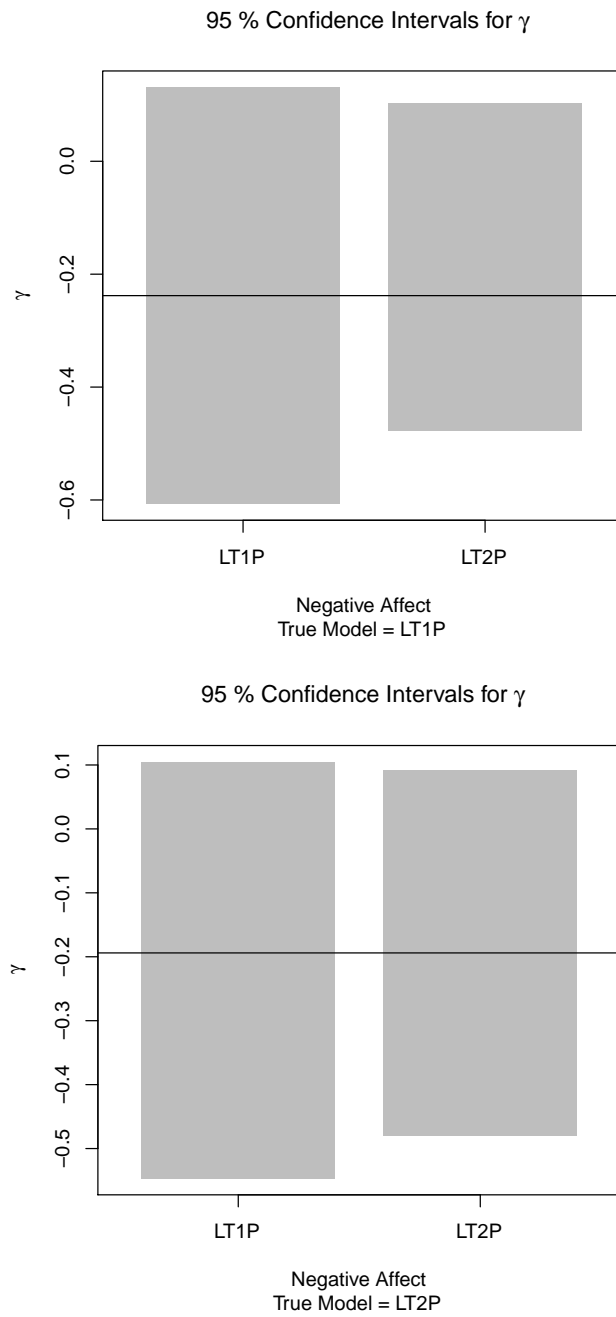




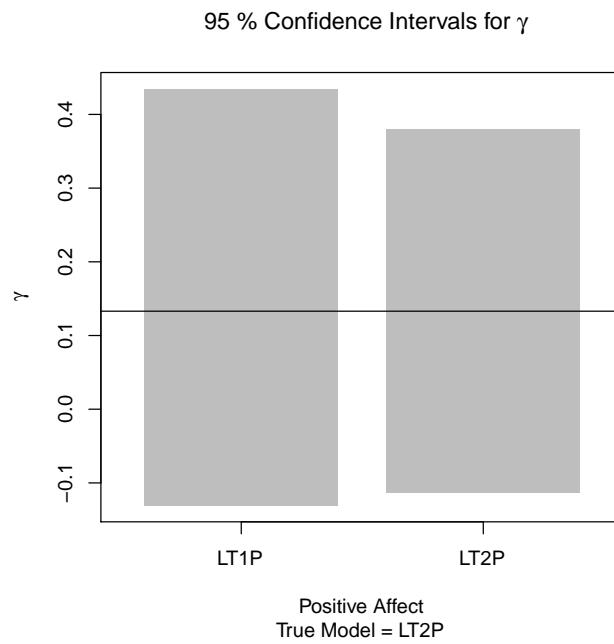
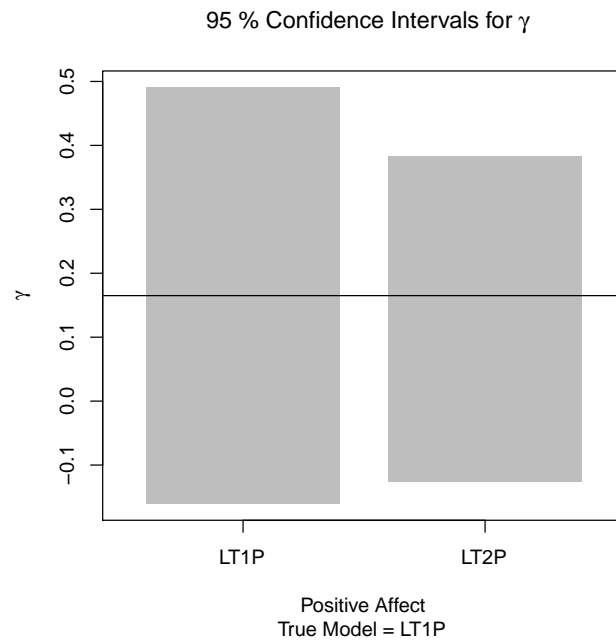
**Figure 10:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for negative mood regulation regression coefficient estimate, positive affect.



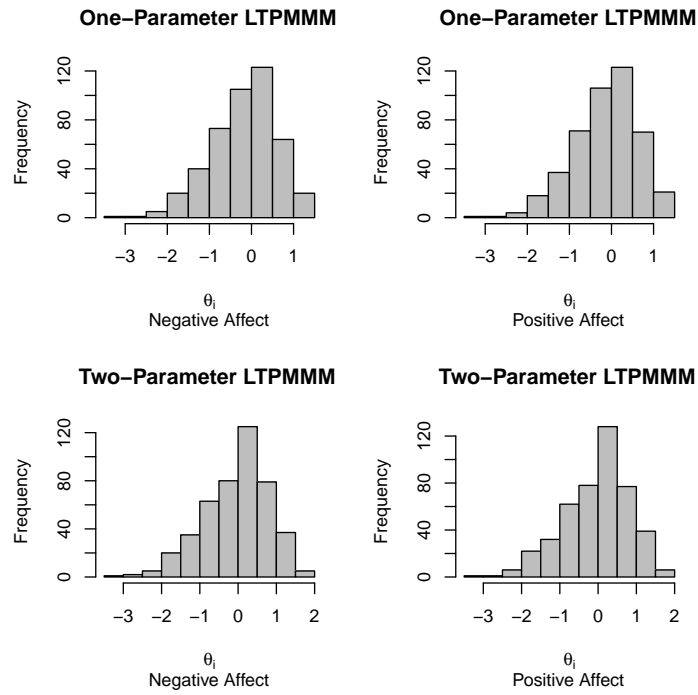
**Figure 11:** Latent class and missing at random mixed-models, 1000 simulations, 95% confidence intervals for negative mood regulation regression coefficient estimate, positive affect.



**Figure 12:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for latent trait ( $\theta_i$ ) regression coefficient estimate ( $\hat{\gamma}$ ), negative affect.



**Figure 13:** One- and two-parameter latent trait pattern-mixture mixed-models, 1000 simulations, 95% confidence intervals for latent trait ( $\theta_i$ ) regression coefficient estimate ( $\hat{\gamma}$ ), positive affect.



**Figure 14:** Histograms of latent traits ( $\theta_i$ ), one- and two-parameter latent trait pattern-mixture mixed-models

## CHAPTER 11

### CONCLUSIONS

#### 11.1 The Latent Trait Pattern-Mixture Mixed-Model

The proposed LTPMMMs are an important development in the area of EMA and missing-data analysis techniques. As explained in this work, research in EMA has mentioned the need to have missing-data analysis performed (Schwartz and Stone, 2007; Munsch et al., 2009; Walls et al., 2007), but very few papers have presented these techniques. Research by Holman and Glas (2005) introduced methods to model non-ignorable missing-data mechanisms with IRT models. The two LTPMMMs introduced here combine longitudinal mixed-effects models and IRT in a meaningful way. These models provide a starting point that can be used to model missing EMA data in the future.

The LTPMMMs provide a novel way to analyze longitudinal data with an intermittent structure. Previous models dealing with longitudinal intermittent missing data have applied latent class pattern-mixture models to group participants into similar response patterns. These latent classes usually have a meaningful interpretation such as “early” and “late” responders and are related to the research question in some manner. These latent classes are easy to form when subjects share some patterns based on fixed response times. When data are collected through EMA, typically many response patterns exist, so the latent class pattern-mixture model may not be appropriate. Also, data obtained through EMA methods do not typically have fixed collection times. We have proposed LTPMMMs combining ideas from IRT and pattern-mixture models to handle these intermittent data issues. Both one- and two-parameter logistic forms of IRT models were fit jointly with a longitudinal mixed-model to study PA and NA mood outcomes collected through EMA.

The one-parameter and two-parameter LTPMMMs were fit using standard statistical software. For both NA and PA outcomes, the proposed models offer increased efficiency of estimated regression coefficients for gender compared to a random intercept mixed-model and a latent class pattern-mixture model. Also, both LTPMMMs showed that the latent trait for response was significantly related to mood outcome. Increasing moods as measured by increased PA or decreased NA occurred if a student was more responsive to the EMA prompting device. The latent class pattern-mixture models formed using the same EMA data set did not find significant relationships between all latent classes and the two mood outcomes.

### **11.2 Latent Class and Latent Trait Plots**

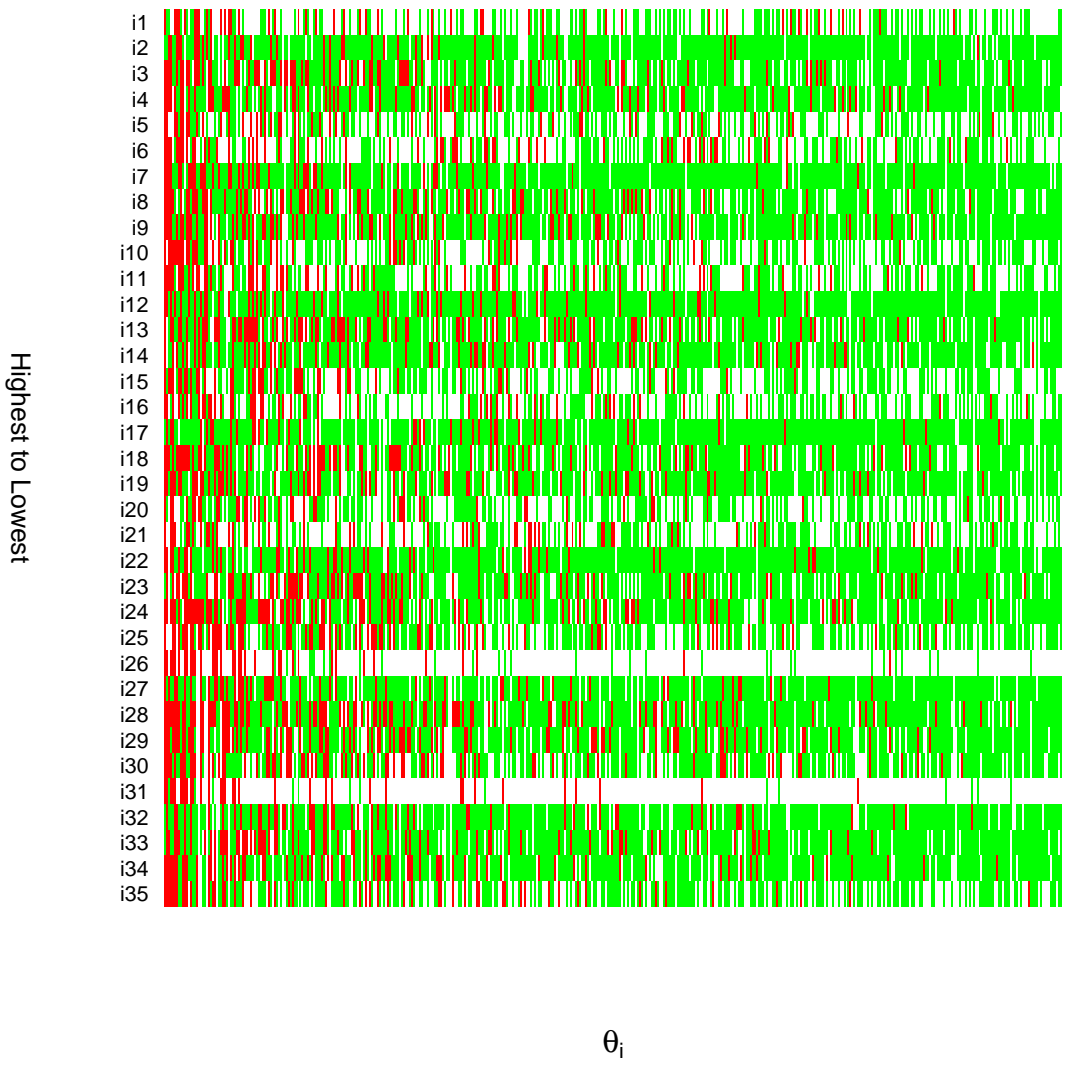
The LTPMMMs formed a unique latent variable representing each subjects' missingness process based on their responses to the EMA device. Figure 15 shows the unique response patterns for each subject using the formed thirty-five response-bins. The green color represents bins where a prompt was answered, the red color represents bins where a prompt was not answered, and white represents bins where a prompt was not made or the EMA device was turned off. The figure is sorted from highest to lowest based on the estimated subject latent traits. As expected, subjects that respond to more prompts have higher latent traits. There is a clear relationship between subjects with the most green bins and the latent trait. Conversely, as shown in Figure 16, the same subjects formed into three latent classes have much different patterns. Subjects in latent class 2 and latent class 3 have the most unanswered prompts, but some students in the first latent class also have more than a few unanswered prompts. The response patterns of students in this first latent class look comparable to the response patterns in the other two latent classes. This is some evidence that the latent class approach did not find meaningful and distinct classes that were related to the two outcomes.

The LTPMMMs also allowed questions to be investigated concerning the patterns of responses over time. Throughout the length of the study, students responded more in the time-interval from 9 a.m. to 3 p.m. and weekday responses were more common than weekend responses. The item discrimination parameters estimated from the two-parameter LTPMMM gave a better fit than the one-parameter LTPMMM, and provided more information on what time periods were more influential in estimating responsiveness among the subjects.

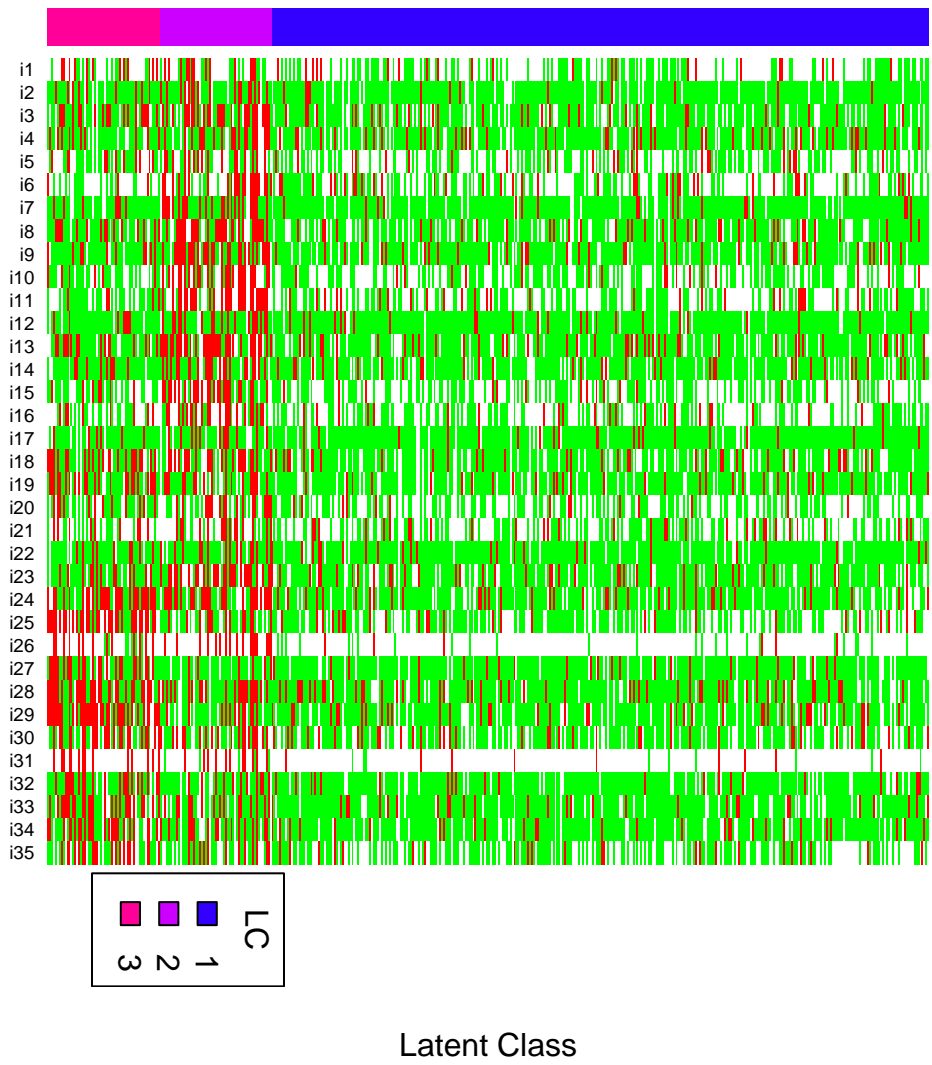
The proposed LTPMMMs offer an exciting and new alternative to fitting pattern-mixture models with missing data that has a complex and non-monotone structure. In the work presented here, model regression coefficients varied as compared to MAR and latent class pattern mixture models. This was true for both models having negative and positive affect as the outcome. The simulated LTPMMMs outperformed the MAR and latent class pattern-mixture models in terms of bias and coverage rates for the true model coefficients for gender and the latent trait  $\theta_i$ . This was especially true for the estimated regression coefficient of gender across models when correlation was induced between gender and the latent trait variable ( $\theta_i$ ). This difference was quite striking and supports the use of the LTPMMMs for intermittent data structures.

Even though the two-parameter LTPMMM took more time to fit and converge, it outperformed the one-parameter LTPMMM in terms of bias and standard error of the estimated regression coefficient of the latent trait. It may be that the two-parameter LTPMMM was more appropriate for the EMA data used in this work. Thus, the full use of the two proposed LTPMMMs should depend on situations that warrant specifying unique discrimination parameters or not. For EMA data containing many response patterns, both the one- and two-parameter LTPMMMs show definite improvement from latent class pattern-mixture models that were previously used for intermittent missing data.





**Figure 15:** Response patterns and latent traits.



**Figure 16:** Response patterns and latent classes.

## CHAPTER 12

### FUTURE WORK

Many possibilities for future research exist with the proposed LTPMMMs. They involve convergence issues, model specification, time-bin formation, interactions of the latent trait with model covariates, the missingness mechanism, conditional independence, and other statistical techniques to fit the models.

Although the results of the proposed LTPMMMs were promising, the models were not trivial to fit due the large number of parameters. All of the joint models needed at least three hours of computer time to converge using SAS PROC NLMIXED. In some cases the two-parameter LTPMMM needed eight hours of computing time. The full use and acceptance of LTPMMMs will need these convergence issues resolved. Model solutions including regression coefficients and variance parameters should be verified as well; all estimates should be checked that they occur at the true maximum values and not at local maximums.

The LTPMMMs presented here included random intercepts and latent traits due to intra-subject correlation. The models did not include a covariate for the time variable per se; time-bins were modeled as items in the IRT portion of the joint model. Additional model fits can be tested that include the effect of time and random slope terms as well since the data were collected longitudinally. Also, the LTPMMMs were modeled assuming that the two random effects were from a joint normal distribution, this assumption can be modified so that other distribution types can be fit. The error variance was also assumed to be normally distributed; autoregressive or moving average covariance structures can be modeled and compared to the proposed models presented here.

In the IRT component of the proposed models, the items were originally formed by creating three-hour time bins over a weekly period resulting in fifty-six total bins. This required an additional fifty-six parameters in the one-parameter LTPMMM and one-hundred twelve additional parameters in the two-parameter LTPMMM. After some difficulty in fitting joint models with a high number of parameters, the models were modified to five bins per day instead of eight bins per day. Further work can study if an optimal number of bins exists that will still provide reliable estimates for the mixed-model regression estimates, the latent trait of response for each subject, and the item parameters in the IRT component of the model. The goal will be to optimize performance of the models while reducing the number of parameters so as to decrease the long computing times.

As was stated earlier, the proposed latent trait pattern-mixture mixed models did not have any significant interactions of model covariates and the latent trait when fit to the EMA data set. However, models with interactions can be simulated using the approaches shown in this work. One approach is to make the coefficients of these interactions significant after fitting LTPMMMs with interactions to the data. This can be done by artificially inflating interaction terms in the model and assuming these are the true effects.

Another topic for further work will be to investigate the nature of the missingness mechanism with EMA data. For instance, the response rate for this study was high (76.6% of prompts were answered) and a very large range of latent traits was not seen (min = -3.1, max = 1.4). It is feasible to vary these parameters using the same simulation approach conducted in this study and investigate the model fit and precision under various modelling scenarios. One way to do this is by increasing the amount of missing observations and evaluate the performance of the various models. In this work, 20% of simulated observations for males was set to missing, this percentage can be increased by 10% increments until the models do

not converge to a stable solution. This will help determine situations in which the model may not be appropriate. Future plans will also investigate the missingness properties of other model covariates and explore settings where the proposed models do not converge.

In a latent class models explored by Guo et al. (2004) and Lin et al. (2004), the conditional independence assumption between the missingness mechanism and model outcomes are tested and verified. Guo et al. (2004) tested this assumption by computing the correlation coefficient between the residuals from a dropout model to the residuals from a longitudinal model; the resulting correlation was quite low. Lin et al. (2004) tested the conditional independence assumption by checking if outcomes were related to the visit process. Further work can be done to test the conditional independence assumption with the proposed LTPMMM, by forming a similar method based on these two approaches.

Other statistical methods to fitting the proposed models can be investigated. Bayesian methods such as Markov chain Monte Carlo or data augmentation can be pursued. The EM algorithm provides another avenue to find the LTPMMM parameters. The LTPMMMs used the logistic form of the IRT model, this can be adapted to a probit model as well. Another possible technique is to see if the LTPMMMs can be fit with more than one latent trait.

Although our proposed models performed well with the data set presented here, the models may not be appropriate with all types of EMA data. For instance, the LTPMMMs may not be an improvement over latent class pattern-mixture models if the number of time intervals is small. The situations where LTPMMMs are not desirable with intermittent data patterns will be explored by fitting the proposed models on other EMA data sets as they become available. The hope is that the proposed LTPMMMs will be a valuable tool that should be considered when analyzing EMA data in the near future.

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