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Advancing Understanding Of Dynamic Mechanisms In Onset To Event Models: Discrete Time Survival Mediation With A Time Variant Mediator

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ADVANCING UNDERSTANDING OF DYNAMIC MECHANISMS IN ONSET TO EVENT MODELS: DISCRETE TIME SURVIVAL MEDIATION WITH A TIME VARIANT MEDIATOR

by

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ABSTRACT

Integrating discrete time survival and mediation analytic approaches, discrete-time survival mediation models (DTSM) help researchers elucidate the impact of predictors on the timing of event occurrence. Though application of this model has been gainful in various applied developmental and intervention research contexts, empirical work has yet to consider how DTSM models operate with a mediator that has a varying effect over time. The importance of examining this situation has important impacts for application of the model, given more complex statistical models are required, and subsequent interpretation of model parameters differ from the basic DTSM model. The overarching purpose of this dissertation was to understand how the addition of a mediator with a time variant effect impacts parameter estimation and fit of the DTSM model estimated in a mixture modeling framework. This investigation was done within the context of an applied example (Study One) to simultaneously inform applied considerations in timing to onset of youth alcohol use, as well as to evaluate statistical performance of the model in a related single-cell Monte Carlo study (Study Two) and an expanded simulation study (Study Three). Results are presented with discussion of future directions for this research and considerations for application of this modeling approach.

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CHAPTER ONE

INTRODUCTION

Outcomes of interest in the social sciences at times relate to the occurrence of an event, such as initiation of substance use, school dropout, or onset of mental health symptomatology. Conventionally, researchers have often used logistic regression to answer questions relating to event occurrence, helping to illuminate the likelihood of experiencing an event (Menard, 2018). However, moving beyond simple questions of "if" an event occurs (and with what probability) to investigating questions that consider "if" and "when" an event occurs allows for the consideration of how different risk and protective factors impact *timing* of event occurrence. Survival analysis provides one such methodological tool to evaluate these questions (for review see Allison, 1984; Miller, 2011). These models have widespread utility, especially when the timing of an event has critical ramifications, such as timing of youth alcohol use, where earlier onset of use is particularly problematic and is associated with higher risk for the development of alcohol abuse behaviors and dependence (Chou & Pickering, 1992; DeWit, Adlaf, Offord, & Ogborne, 2000).

In the same way that investigating timing of an event can provide more information than looking at incidence alone, investigating the underlying reasons why (or how) given risk and protective factors exert an influence on timing of event occurrence can help inform etiology of different phenomena, as well as provide a foundation to develop intervention programs that target critical outcomes. Mediation analysis provides

a means to answer these questions (see Hayes, 2017; MacKinnon, 2008). Mediation analysis explains how a mediator or mechanism of interest (M) indirectly conveys the effect of a predictor (X) on an outcome (Y). Mediation is utilized in numerous fields to answer questions related to mechanisms of change. In the social sciences, mediation analysis can lend insight into questions related to developmental pathways and understanding the etiology of risk behaviors; additionally, mediation analysis can contribute to the evaluation of prevention and intervention programs (Fairchild & MacKinnon, 2014; MacKinnon, 2008; MacKinnon, Fairchild, & Fritz, 2007).

Integrating these analytic approaches, discrete-time survival mediation models (*DTSM;* Fairchild, Abara, Gottschall, Tein, & Prinz, 2015; Fairchild, Cai, McDaniel, Masyn, & Gottschall, 2018) have the potential to help researchers elucidate the impact of predictors on the timing of a particular event occurrence. By simultaneously incorporating both mediation and discrete-time survival analysis, the model allows for the examination of direct and indirect effects of a predictor on the timing of occurrence of an event of interest (Fairchild et al., 2015; 2018). In applications, the model aims to illustrate the means by which a variable impacts the timing of an outcome. These models have been utilized to study how gang membership impacts incidences of pregnancy indirectly through partnership characteristics, contraceptive behaviors, and pregnancy intentions (Minnis et al., 2008), as well as how timing to university dropout is predicted by high school grade point average indirectly through college grades (Voelkle & Sander, 2008), and how putative mechanisms of action in an alcohol use prevention effort impact timing to onset of alcohol use (DeGarmo, Eddy, Reid, & Fetrow, 2009).

Though application of the DTSM model has been gainful in the aforementioned research contexts and others, no empirical work has considered how discrete time mediation models operate with covariates that have a time variant effect. It would bolster the utility of this methodological tool and subsequent applications to better understand how a mediator with a time variant effect impacts parameter estimation, type one error and power in models that combine mediation and discrete time survival analysis. Previous research has examined the DTSM model (Fairchild, PI, NIDA - R01DA030349; Fairchild, et al., 2018) in a Monte Carlo simulation study to evaluate the accuracy of DTSM model parameter estimates, power, and Type 1 error. This work focused on a time invariant mediator in line with the standard proportional hazard odds assumption in discrete-time survival models, however (Cox, 1972). Expanding consideration of DTSM models to include a mediator with a time-variant effect may elucidate how a mediator can impact onset to an event variably over time. Such information may be particularly relevant in developmental research in which predictors of outcomes can change over time.

As one application, the DTSM model could help social scientists better understand how dynamic mechanisms impact timing to onset of youth alcohol use. Historically adolescence has been coined a period of "storm and stress", given notable conflict, mood disruption, and risk-taking (Hall, 1904). Recent research suggests that this developmental period of risk-taking and conflict is normative and driven by contextual as well as biological factors (Arnett, 1999; Spear, 2000). However, while some risk-taking during this period can be viewed as positive, such as conflict with parents leading to increased autonomy, other risk-taking behaviors can be more problematic, such as

drinking alcohol (SAMHSA, 2014). Rates of drinking, and problematic drinking, are an especially critical issue in adolescence given that the brain is still developing and changing (Spear, 2000). Youth drinking is linked to a myriad of poor health, behavioral, and social outcomes such as use of tobacco and illicit substances, drunk driving, unprotected sex, school failure, and even death (e.g., NHTSA, 2013; SAMHSA, 2014; USDHHS, 2007). In addition to poor youth outcomes, there is a substantial associated public health burden. In 2010, costs attributed to excessive drinking in the United States were around $249 billion, with underage drinking accounting for $24.3 billion in costs (Sacks, Gonzales, Bouchery, Tomedi, & Brewer, 2015).

Early onset of alcohol use (i.e., alcohol use before 15), is particularly problematic and associated with higher risk for development of alcohol abuse and dependence while youth that start drinking later have lower rates of unhealthy drinking behaviors in the long run (Chou & Pickering, 1992; DeWit et al., 2000). There are known protective factors that may offset early onset alcohol use, to promote later onset of drinking behaviors and long term positive outcomes, such as good family functioning and positive parenting behaviors (e.g., parental monitoring; Anderson & Henry, 1994; Beyers, Toumbourou, Catalano, Arthur, & Hawkins, 2004; Resnick et al., 1997; Tildesley & Andrews, 2008). However, some scholars suggest that this impact of these predictors may vary over the course of child development and these relationships warrant further consideration in longitudinal studies (e.g., Dishion & McMahon, 1998). As such, parenting behaviors, such as parental monitoring, included as a mediator in a causal chain impacting timing to onset of alcohol use, could plausibly have differential impacts on onset of alcohol use across development. Extending investigation of the model to

consider time-varying covariates could enhance our understanding of dynamic risk and protective factors that can change in impact across time.

Statement of Purpose

The overarching purpose of this dissertation is to understand how the addition of a mediator with a time variant effect impacts parameter estimation and fit of the DTSM model estimated in a mixture modeling framework (Fairchild et al., 2015; Fairchild et al., 2018; Masyn, 2014; Muthen & Masyn, 2005). This investigation will be done within the context of an applied example to simultaneously inform applied considerations in timing to onset of youth alcohol use, as well as to evaluate statistical performance of the model in a related single-cell, simulation study and an expanded Monte Carlo simulation study. Specifically, I will conduct an applied investigation which utilizes a DTSM model with a time variant mediator to understand how interparental support predicts timing to onset of youth alcohol use indirectly through parental monitoring (i.e., Study One). Parental monitoring will be free to have differential effects across time to better understand how this parenting behavior is differentially predictive over adolescent development. I will subsequently use information gathered from the applied example to inform parameter estimates in a single-cell simulation study (i.e., Study Two). With results of this single cell-simulation study as the foundation, I will conduct an expanded Monte Carlo study that varies sample size, number of waves of data, pattern of the time variant effect and model (mis)specification, with the ultimate intention to provide recommendations for the field about use of this model by examining bias in parameter estimation, power, type one error, confidence interval coverage and performance of fit statistics (i.e., Study Three).

With respect to the three studies, I hypothesize:

1) *In Study One, greater interparental support will predict greater parental monitoring in the applied example. In turn, greater parental monitoring will be associated with a lower hazard odds of onset to alcohol use in the younger adolescent years, but will be non-significant at older ages. It is predicted that there will be a varying effect of parental monitoring over the course of adolescent development. In addition, it is hypothesized that greater interparental support will be directly associated with later onset of alcohol use.*
2) *In Study Two, results will suggest acceptable levels of relative bias in parameter estimates as well as acceptable type one error, power, and confidence interval coverage, given the large sample size and many waves of data in the applied example in Study One from which population parameters for the study will be derived.*
3) *In Study Three, in which a variety of conditions are studied, it is anticipated that outcomes of interest will be impacted by sample size, number of waves of data, pattern of the time variant effect and model (mis)specification. More specifically, it is anticipated that bias in parameter estimation will increase with decreasing sample size and model misspecification. Power will increase with increasing sample size. And model fit statistics will perform best when there is the greatest discrepancy between the population model and the misspecified model and sample size is large.*

CHAPTER TWO

REVIEW OF THE LITERATURE

Mediation Analysis

Exploring the relationship between a predictor (X) and outcome (Y) can inform important hypotheses about whether a bivariate relationship exists between X and Y. However, once this relationship is supported, it may also be of interest to introduce a third variable to further understand how or why the relationship between X and Y occurs. Mediation analysis introduces a third variable to the model and, in its simplest form, explains how a mediator or mechanism of interest (M) indirectly conveys the effect of a predictor (X) on an outcome (Y). Here the effect of X on Y is decomposed into the direct effect and the indirect effect. The direct effect is the influence of X on Y, controlling for the mediator and the indirect effect is the effect of X on Y through M (for a comprehensive review of statistical mediation analysis see MacKinnon, 2008).

The Single Mediator Model. The single mediator model simply describes how a single mediating variable (M) conducts the effect of a predictor (X) onto an outcome (Y). The model is represented conceptually in Figure 2.1 and defined by the following equations:

$$M = i_{01} + aX + \varepsilon_1 \quad (1)$$

$$Y = i_{02} + c'X + bM + \varepsilon_2 \quad (2)$$

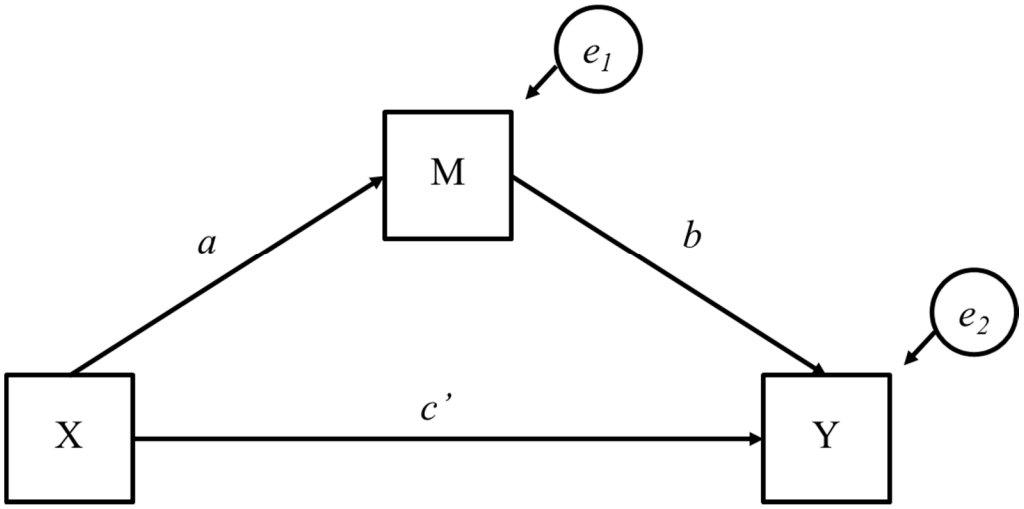

Figure 2.1 Single Mediator Model.

In Equation 1, the *a* coefficient is the regression coefficient relating X to M. In Equation 2, *c'* represents the direct effect of X on Y, that is, the partial regression coefficient relating X to Y while controlling for M. The *b* coefficient relates M to Y while controlling for X. [1]

Use of Mediation Analysis in Psychology. Mediation analysis can inform questions related to developmental pathways and understanding the etiology of risk behaviors as well as in evaluation of prevention and intervention programs (for review see Chapter two in MacKinnon, 2008). Mediation models are beneficial in two research contexts: "mediation by design" and "mediation for explanation" (Fairchild & Mackinnon, 2014; MacKinnon, 2008). In mediation by design, mediation is used to design interventions or prevention programs; mediation variables are identified a priori, and researchers then examine whether an intervention created change on the targeted mechanism of action and whether the changes in the mediator were associated with changes in the ultimate outcome (Fairchild & MacKinnon, 2014; MacKinnon et al., 2007). The insight garnered from "mediation by design" analyses are a crucial part of program evaluation and can be used to improve and streamline subsequent interventions by focusing on the most effective components as well as help to identify which intervention components are most critical in changing outcomes (MacKinnon et al., 2007; MacKinnon, 2008).

[1] While this is the simplest form of the mediation model, the model can be extended to include additional complexities such as multiple mediators, serial mediators, or multilevel data (for possible extensions of the model see MacKinnon, 2008). In addition, the model can be extended to include survival outcomes which are detailed later in this review (i.e., DTSM; Fairchild et al., 2015; 2018).

Alternatively, in "mediation for explanation" analyses, mediation analysis is used to answer research questions in investigations for which there is a known relationship between a predictor and outcome; the researcher wants to understand if there is an intermediate variable in the causal sequence between X and Y that could help elucidate their relationship (Fairchild & MacKinnon, 2014; MacKinnon, 2008). For example, given the economic burden and negative health, behavioral and social outcomes associated with early onset alcohol use, there is a need to understand the developmental risk and protective factors, as well as effective prevention and intervention efforts so that these negative outcomes can be ameliorated for high-risk youth. Application of mediation analysis to timely and critical research questions related to adolescent alcohol use in both mediation by design and mediation for explanation scenarios would inform both the developmental and prevention/intervention literatures.

Approaches for estimating the mediated effect. There have been several methods suggested for quantifying the mediated effect. In landmark publications, Judd and Kenny (1981) and Baron and Kenny (1986) presented the causal steps approach; a series of conclusions that must be met to provide evidence for a mediated effect. To briefly outline them, first, the predictor must influence the outcome. If there is no overall effect of X on Y, the authors suggest that it follows that there can be no indirect effect. However, it should be noted that more recent research has noted the fallibility of this requirement and is now often relaxed (MacKinnon & Fairchild, 2009; Shrout & Bolger, 2002). Even so, in relation to the equations presented above, when used, this step is tested with an additional, initial regression equation in which the outcome (i.e., *Y*) is regressed only on the predictor (i.e., *X*):

$$Y = \beta_0 + cX + \varepsilon \quad (3)$$

The second proposed causal step by Kenny and colleagues was that the predictor must predict the mediator and subsequently, the mediator must predict the outcome, when controlling for the predictor. This conclusion establishes the "causal chain" or the indirect effect of X on Y through M. The final conclusion per Judd and Kenny (1981) was that the predictor no longer significantly predicts the outcome when controlling for the mediator. While this final step is needed to support a hypothesis of a *fully* mediated effect, Baron and Kenny (1986) later suggested that it is not needed to support *partial* mediation.

In a brief literature review of two high impact journals in psychology, Fritz and MacKinnon (2007) found that researchers utilized the causal steps method to test for the presence of mediation five times more than other approaches. In a similar review of the literature in school psychology, Fairchild and McQuillin (2010) found that approximately 31% of studies published that tested for a mediated effect utilized the causal steps method. However, while the causal steps approach to mediation is still commonly used, there are several notable limitations. The first limitation is that the causal steps approach requires a significant relationship between the predictor and the outcome. While this seems intuitive, there can be instances where X does not significantly predict Y, yet there is a significant indirect effect. For example, this may occur in "inconsistent mediation models" in which a suppression effect is present and the direct effect and indirect effect are in the opposite directions, potentially nullifying the overall effect (Davis, 1985; MacKinnon, Fairchild & Fritz, 2007; MacKinnon, Krull, & Lockwood, 2001). The assumption that there needs to be a relationship between the predictor and the outcome is one of the identifying features of this approach that separates it from more recent

approaches for testing mediation (MacKinnon et al., 2001; 2007). In addition, while Baron and Kenny (1986) and Judd and Kenny (1981) outline a series of logical steps that insinuate a mediational chain, it lacks a statistical test of the indirect effect; it neither yields a point estimate of the mediated effect nor a standard error (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). In addition, as compared to more contemporary methods to test for mediated effects, the causal steps method is underpowered (Fritz & MacKinnon, 2007; MacKinnon et al., 2002; MacKinnon, Lockwood, & Williams, 2004). Indeed, these methods are underpowered in detecting small indirect effects, even in sample sizes of 1,000 (MacKinnon et al., 2002); a sample of 20,886 is needed to detect a small mediated effect when there is complete mediation (i.e., c'=0; Fritz & MacKinnon, 2007). When c' is equal to zero in the population, adequate power (i.e., $\beta = .80$; Cohen, 1992) is obtained for a medium sized indirect effect when sample sizes are approximately 500 or more and for large effects when sample sizes approximate 100 participants (MacKinnon et al., 2002). These findings are problematic in psychological research given that many effect sizes are small and it has been estimated that approximately half of studies testing for a mediated effect use a sample size of less than 200 (Fritz & MacKinnon, 2007; Rosnow & Rosenthal, 2003).

A variation on the causal steps method is the test of joint significance. This test suggests the presence of a mediation effect when both the *a* path and the *b* path are significant (Kenny, Kashy, & Bolger, 1998; MacKinnon et al., 2002). This technique has greater power to detect effects as compared to the causal steps method, but also lacks a parameter estimate of the mediated effect. This method is adequately powered (i.e., $\beta = .80$) to detect a small effect when the sample size is approximately 500 or more,

adequately powered to detect a medium effect when sample sizes are approximately equal to or greater than 100 and powered to detect a large effect in small sample sizes (e.g., ~ 50; MacKinnon et al., 2002). Despite these improvements in power, this approach does not yield information on the point estimate or standard error of the mediated effect (i.e., *ab*; MacKinnon et al., 2002). This and other limitations of the causal steps method mentioned above spurred the establishment of other contemporary tests for mediation.

Contemporary approaches to quantifying a mediated effect focus on either the difference in coefficients (i.e., $c - c'$) or the product of the coefficients (i.e., $a*b$; see MacKinnon, Warsi & Dwyer, 1995; MacKinnon, 2008). In the difference of coefficients approach, the focus is on comparing the relationship between X and Y before and after controlling for M, where $c - c'$ defines the mediated effect and is estimated by two equations (i.e., Equation 2 and 3 above). The *c* parameter is estimated as the overall effect of X on Y, without consideration of M. (i.e., see Equation 3). The *c'* parameter is the direct effect of X on Y when controlling for M (i.e., see Equation 2). The difference in these coefficient yields the point estimate of the mediated effect. If the *c'* coefficient is equal to 0 then the effect of X on Y is completely mediated (Judd & Kenny, 1981; MacKinnon et al., 1995).

Alternatively, in the product of the coefficients approach to quantifying the mediated effect, the product of the *a* and *b* parameters, discussed in relation to Equation 1 and 2 above, conveys the indirect effect of X on Y through M. The *a* parameter reflects the impact of X on M and the *b* parameter represents the impact of M on Y. Together, *ab* represents the point estimate of impact that a one unit change in X has on Y indirectly through M (MacKinnon, 2008; MacKinnon et al., 1995). The logic of this approach

derives from path analysis and path tracing rules to estimate indirect effects (Wright, 1934).

In many situations, both the product of coefficients and difference of the coefficients approaches will yield equivalent estimates (MacKinnon et al., 1995). For example, when the dependent variable is continuous and ordinary least squares estimation is utilized, the product of coefficients and difference of the coefficients approaches are algebraically equivalent (MacKinnon & Dwyer, 1993; MacKinnon, et al., 1995). However, this is not the case when the outcome is dichotomous (MacKinnon et al., 2007). Research suggests that the product of the coefficients method is more flexible and amenable to models that are more complex than the single mediator model with a continuous outcome (MacKinnon, et al., 2007; MacKinnon et al., 1995). For example, in a multiple mediator model, the difference in coefficients approach does not allow for examination of individual mediated effects. Only one estimate of the overall mediated effect is estimated (i.e., $c - c'$). Therefore, the researcher cannot compare strength of different individual mediated effects. With these limitations in mind, the remainder of the discussion will focus on the product of the coefficients approach.

Testing the significance of the mediated effect (i.e., ab). A general approach to testing the significance of the indirect effect is to divide the *ab* parameter by a standard error and compare the resulting test statistic to a standard normal distribution. While many estimates of the standard error for *ab* have been derived, the most commonly used normal theory estimator was derived by Sobel (1982, 1986) using the multivariate delta method based on a first order Taylor series approximation:

$$\hat{\sigma}_{ab}^2 = \hat{a}^2\hat{\sigma}_b^2 + \hat{b}^2\hat{\sigma}_a^2 \quad (4)$$

Though standard error estimates based on the multivariate delta method are close to their true value in many conditions and have very low type one error rates (MacKinnon et al., 2002), this technique assumes that the distribution of *ab* is normally distributed and that the derived test statistic (i.e., ab/s_{ab}) can be compared to a standard normal distribution for testing statistical significance. However, the distribution of the product of two normally distributed parameters is not normally distributed (Aroian, 1947). Rather, the resultant sampling distribution of *ab* is often kurtotic and asymmetric (MacKinnon, Lockwood, & Hoffman, 1998). As such use of a normal theory estimator will be underpowered in small sample sizes (MacKinnon et al., 1998). To support this, Monte Carlo simulation studies suggest that in order to detect a small effect, a sample size of 1000 is needed to be adequately powered when using the Sobel (1982, 1986) standard error (i.e., $\beta \geq .8$; Cohen, 1992). This is problematic considering that many effects in the social sciences are small (Rosnow & Rosenthal, 2003). However, when considering medium and large effects, this method is adequately powered except in the case of a moderate effect and small sample size (i.e., $n = 50$ or less). Given that *ab* is not normally distributed and this has led to problems with an inability to detect effects when they are present, other estimation techniques have been recommended that better account for these issues.

Distribution of the products methods of testing for mediation take into account the non-normal sampling distribution of *ab*. In the asymmetric distribution of the product test, critical values are obtained from the *ab* distribution and asymmetric confidence intervals are created to test for the presence of mediation. The distribution of the products methods stemmed from the work of Meeker, Cornwell, and Aroian (1981) whom created

tables of critical values for the distribution of the product of two normal variables. These tables described critical values for the indirect effect at different values of α, β, σ_α, σ_β. MacKinnon et al. (2004) & MacKinnon et al. (2002) conceptualized a method to test for mediation using asymmetric confidence intervals derived from an expansion of Meeker et al. (1981) distribution of the product tables. These confidence intervals, that are asymmetric to reflect the true nature of the distribution of *ab*, can be constructed based on the following equations:

$$UCL = \hat{\alpha}\hat{\beta} + Meeker\ Upper * \hat{\sigma}_{\hat{\alpha}\hat{\beta}} \quad (5)$$

$$LCL = \hat{\alpha}\hat{\beta} + Meeker\ Lower * \hat{\sigma}_{\hat{\alpha}\hat{\beta}} \quad (6)$$

Unlike confidence intervals based on a standard, normal distribution, calculation of the upper and lower confidence limits yield two different values given asymmetry in the distribution of *ab*. The upper limit of the confidence interval is created by multiplying the derived critical value associated with the distribution of the product of two random variables (Meeker et al., 1981) by the standard error of *ab* and adding it to the *ab* parameter estimate. The lower limit is calculated in the same manner but the lower level critical value is used.

Alternative approaches to estimating asymmetric confidence intervals include resampling approaches, which build an empirical sampling distribution of *ab* to test the parameter for significance at desired levels of alpha (Efron & Tibsharani, 1994). Resampling approaches use the original dataset to create new datasets using sampling with replacement and then identify the corresponding percentiles of the sampling distribution associated with a desired level of alpha; parameter estimates, including *ab*, are then calculated in each of these datasets to create an empirical distribution of the

parameter estimate (Efron & Tibsharani, 1994; Shrout & Bolger, 2002). There are several resampling methods that can be used to produce these empirical distributions of *ab* including, but not limited to the non-parametric percentile, bias-corrected, and accelerated bias-corrected bootstrapping methods (Efron & Tibsharani, 1994). Results of several simulation studies suggest that the bias-corrected bootstrapped asymmetric confidence limits yield the best balance between adequate power to detect the presence of an indirect effect and Type one error rates (Fritz & MacKinnon, 2007; MacKinnon et al., 2004; Shrout & Bolger, 2002). The bias-corrected bootstrap method takes into account the asymmetric distribution of the *ab* parameter distribution, as well as invokes a correction factor when the mean value of *ab* in the empirical sampling distribution is not equivalent to the sample estimate of *ab* (Efron & Tibshirani, 1994). However, while the bias corrected bootstrap has the greatest power, it can also have the highest Type 1 error rate (Fritz & MacKinnon, 2007; MacKinnon et al., 2004). Given that research in the social sciences is often clouded by small sample sizes, small effect sizes and the resulting reduced power to detect mediated effects, the bias-corrected bootstrap method will be used to test for mediation in both the simulations and applied example in this research.

Assumptions of the Single Mediator Model. Many of the assumptions in mediation analysis are akin to those in general linear modeling (see MacKinnon, 2008 for a complete review of assumptions). First, correct functional form is assumed. More specifically, in a single mediator model where all variables are continuous, it is assumed relations between variables are linear. For example, a one unit increase in X is associated with a linear increase in M. While nonlinear relationships between variables can be specified, it is assumed that whatever model is specified is the correct functional form.

Additionally, it is assumed that there are no interactions among variables. That is to say, that there is a homogeneous effect of M on Y across levels of X as well as a homogenous effect of X on Y across levels of M. It is also assumed that variables are normally distributed, no variables are omitted from the model and variables are measured correctly without error. Finally, there are several assumptions about residuals. It is assumed that predictors do not correlate with residuals and that error terms across the two equations (i.e., Equations 1 and 2 when examining *ab*) do not correlate. And finally, mediation analysis requires homogeneity of variance across levels of the predictors as well as normally distributed residuals.

Causality in Mediation Analysis. In addition to the assumptions outlined above, there are several additional assumptions that must be considered in relation to causal inference (see Chapter 13 in MacKinnon, 2008). To make causal inferences in mediation analysis, one needs to consider temporal precedence of variables in the model. To be causal, X should precede M, which should in turn precede Y. In addition, it is assumed that the timing of measurement captures the unfolding of the causal relationships. For example, one needs to consider if a change in M results in an instantaneous change in Y or whether the causal effect is delayed. In addition, unless the predictor (i.e., X) and the mediator (i.e., M) are both randomized, true causal inference is not tenable in the mediation model without additional statistical considerations. Researchers often want to make causal claims based on their research using mediation models and recent statistical approaches have been developed to address limitations in this domain, as well as have provided machinery to conduct sensitivity analyses to omitted confounders (e.g., VanderWeele, 2015). For example, in an application similar to the research proposed,

VanderWeele (2011) describes that in a mediation model with a rare proportional hazards outcome, the *ab* estimate is equivalent to causal inference approaches for estimating the indirect effect. While causal inference in mediation analysis is a well-studied and still burgeoning area of inquiry, it will not be addressed in the current research. However, causal inference in DTSM models represents an important domain for extension of this research in the future.

Survival Analysis

Survival analysis is a statistical model in which the outcome of interest is the timing of a particular event occurrence (Miller, 2011). In these models, time can be represented continuously or discretely. In either case, these analyses help answer questions about whether or not an event occurs and if so, when. It also allows researchers to garner information about the probability of survival (i.e., not experiencing an event of interest) and how survival rates can be impacted by covariates of interest (Cox, 1972). Survival analysis has origins in the study of human life and is steeped in terminology related to life and death (Cox, 1972). Indeed, the term 'survival analysis' is a result of the initial application of these analyses in medical research endeavors where the outcome of interest was death/survival. However, over time, similar methods concerned with event time analysis arose in different substantive areas (Allison, 1984). This methodology has been used in a wide breadth of applications over many decades, and has been more recently utilized in the social sciences (Allison, 1984; Singer & Willett, 1991) to understand phenomena such as the etiology of risky behavior, school failure and removal, as well as to evaluate prevention and intervention studies (e.g., (Clarke et al., 2001; Li et al., 2011; Plank, DeLuca, & Estacion, 2008).

In survival analysis, the survivor function represents the probability that a person survives longer than time *t.* In continuous time survival analysis, this equation is[2]:

$$S(t) = P(T > t) \tag{7}$$

The survivor function is a monotonically decreasing function, where the probability of surviving is one at baseline and falls toward zero as time reaches infinity. Thus, all survivor functions have a similar shape, a negatively accelerating extinction curve. This phenomena was noted by Hunt, Barnett, and Branch (1971) after examining 84 studies related to relapse rates in addiction treatment and asserting that "all the curves were remarkably similar" (p. 455). The authors portended the utility of survivor functions by indicating that they "hoped to use the differences in slope between individual curves as a differential criterion to evaluate various treatment techniques" (p. 455).

Though the survival function provides a strong basis for understanding survival models, estimation of a hazard function is arguably more crucial for conducting the analyses. In contrast to a focus on surviving, or not failing, the hazard function represents the instantaneous potential per unit time for failure to occur, given that the subject has survived up to time *t* (Miller, 2011). In continuous time survival models, the hazard function is represented by the following equation:

$$h(t) = \lim_{\Delta t \to 0} \frac{P(t \leq T < t + \Delta t | T \geq t)}{\Delta t} \tag{8}$$

The numerator is the conditional probability that an individual's survival time (i.e., *T*) falls in the interval between the time point of interest (i.e., *t*) and a designated time interval (i.e., Δ*t*), given that survival time is greater than or equal to the time point of

[2] Much like ordinary least squares versus logistic regression, different equations are needed for continuous versus discrete time survival analysis.

interest. The numerator thus yields a probability per unit of time of survival, or the conditional failure rate. The hazard function is always nonnegative and has no upper bound. The hazard function is often the outcome variable in survival models given that it is an instantaneous measure of potential and can be used to identify an appropriate model form (e.g., exponential, Weibull, lognormal; Miller, 2011).

Considerations for censored data in survival models. One critical feature of survival data that differentiates it from other types of data is censoring (Leung, Elashoff, & Afifi, 1997). Censoring occurs when some information about a study participant's time to event is unknown; in this way censoring can be viewed as a special type of missing data mechanism. Individuals can have right, left, or interval censored data (see Table 2.1). Survival times are considered to be right censored when a participant does not experience the event of interest during the study period. This may occur when an individual participates for the duration of the study but does not experience the event of interest, or when a participant withdraws from a research study or is "lost to follow-up". In these cases, it is known that survival time exceeds a certain point (i.e., beyond the period the individual was observed) but the exact timing of the event is unknown. Despite censoring, these cases yield critical information about event non-occurrence during the period that the individual was observed and they are included in the likelihood function for the data. Alternatively, left censoring occurs when an individual experiences the event of interest prior to the study beginning. For example, as is indicated in Table 2.1, the left censored individual experiences the event (e.g., first occurrences of alcohol use, divorce, or unemployment) before the study's first wave of data collection. However, the issue of left censored data may be completely obfuscated in a study if exclusion criteria is

Table 2.1

Censoring in Survival Analysis

Type of Censoring	Before Study	Time 1	Time 2	Time 3	Time 4	After Study
Right Censoring	0	0	0	0	0	1
Left Censoring	1	0	0	0	0	0
Interval Censoring	0	0	Missing	Missing	0	0

Note. 0 = No event, 1 = event occurred, Missing = Participant not observed.

outlined that specifies an individual cannot be included in the study if they have already experienced the event of interest. Finally, an individual can be interval censored. In this case, an individual provides data for some time points but not all and the exact timing of event occurrence is not known. For example, in Table 2.1, an individual in year one did not experience the event of interest, they were not observed in years two through three but indicated at time four that the event occurred prior to year four. It is therefore unknown whether the event occurred in year two or three but it is known that the event did indeed occur and occurred prior to year four.

Continuous versus discrete time survival analysis. Continuous time methods have dominated both the methodological and applied literature for survival models (Allison, 1984). However, discrete-time survival methods help overcome several challenges associated with continuous time methods and are often more appropriate in social science settings where discrete measurement is commonplace (Vermunt, 1997). First, discrete-time survival analysis is useful when outcomes are measured in a discrete fashion or actually occur in a discrete fashion (Allison, 1982; Singer & Willett, 1993; Willett & Singer, 1993). In many research applications, events are measured discretely (e.g., yearly) and when the time between measurement is large (e.g., months, years), it is likely more appropriate to model events in discrete time intervals (Allison, 1984). This can be useful in the social sciences, for example, when studying onset to drug use that is measured in weekly, monthly or yearly intervals. This methodology is also more flexible than continuous time methods and easily allows for the integration of time-varying covariates (Singer & Willett, 1993; Willett & Singer, 1993). Relatedly, the proportional hazards assumption, that requires the effect of a predictor to be constant over time, can be

easily relaxed in discrete time models to incorporate predictors that have time variant effects (Singer & Willett, 1993; Willett & Singer, 1993).

In discrete-time survival analysis, the discrete-time hazard is the outcome of interest and represents the conditional probability that a randomly selected individual will experience the event of interest in time period *j*, given that they did not experience it beforehand:

$$h_j = Pr[T = j \mid T \geq j] \tag{9}$$

The Cox model is a semiparametric approach to survival analysis in which there are no distributional assumptions related to the occurrence of events but there is an assumption made about a specific functional form between the predictors and the outcome of interest (Cox, 1972). While the model is often applied to continuous time survival outcomes, it can also be applied to discrete-time onset to event outcomes (Willett & Singer, 1993) so that the function can have logistic dependence on the observed time periods and predictors:

$$\ln[h(t_{ij})] = [\alpha_j D_{ij}] + \beta_1 pred_1 + \cdots \beta_x pred_x \tag{10}$$

Here the dummy coded variables (i.e., D_{ij}) represent a vector of the observed discrete time intervals while α_j is the time specific baseline log-hazard rate. And the β coefficients represent the association with predictors of interest. Thus, we can ascertain risk associated with each discrete time period as well as the impact of predictors on the log-hazard function.

Assumptions of the discrete time survival model. There are several assumptions associated with the discrete-time survival model that must be met to make inferences from the sample to the population (see Singer & Willett, 1993). First,

independent censoring is assumed and entails that missingness is not related to event occurrence. This suggests that individuals in the risk set are not systematically different from individuals that are censored and are representative of the population that is at risk for the event of interest. It is also assumed that there is a linear relationship between predictors and the logit hazard probability, however, polynomial terms or interactions may also be included in the model. Next, it is an inherent model assumption that there is no unobserved heterogeneity in the logit hazard. As can be seen in Equation 10, there is no error term included in the discrete-time survival model. Rather, it is assumed that the covariates included in the model account for variation in the logit hazard across individuals. Finally, use of this model assumes that the impact of a predictor on the logit hazard is constant across time periods (i.e., proportionality assumption). However, as purported by Singer and Willett (1991):

> "But we hasten to add that we have found, in studies of a wide variety of phenomena – including teachers' careers, child mortality, duration of breast feeding, time to undergraduate degree, time to doctorate, and age at first suicide ideation – that violations of the proportionality assumption are the rule, rather than the exception " (Singer & Willett, 1991, p. 279).

With this in mind, it is important to explore potential violations of this assumption as well as models that can accommodate nonproportionality. Should a violation arise, the model can easily be modified to account for this with the inclusion of an interaction of the covariate with time (Masyn, 2014; Willett & Singer, 1991; 1993). This is discussed in more detail below.

Discrete-time survival mediation models. Discrete time survival models can elucidate the impact of a predictor on the timing of event occurrence. However, it is often informative to move beyond these simplistic models to understand how or why a predictor influences timing to event outcomes by incorporating third variables. DTSM models (Fairchild et al., 2015) help researchers to elucidate the impact of predictors on the timing of occurrence of a particular event, such as the onset of drinking behaviors in youth. DTSM models integrate mediation analysis and discrete-time survival analysis to facilitate investigations that look at the influence of a predictor on the timing of an event directly as well as indirectly through a mediator. The simplest DTSM model can be represented with one continuous predictor, one continuous mediator and a survival outcome, and is defined by two equations:

$$M = b_0 + aX + \varepsilon_1 \tag{11}$$

$$Y = ln\left(\frac{h_{ij}|\, X_{ij}, M_{ij}}{1 - h_{ij}|\, X_{ij}, M_{ij}}\right) = \left[\alpha_j D_{ij}\right] + c'X_{ij} + bM_{ij} \tag{12}$$

Equation 11 reflects the impact of the predictor on the mediator. In Equation 12, the outcome is the log-hazard odds of event occurrence. The c' coefficient represents the effect of the predictor, X, on the log-hazard odds of event occurrence and the *b* coefficient represents the effect of the mediator on the log-hazard odds. The indirect effect is defined by the product of the *a* and *b* parameters while the direct effect is defined by *c'*.

To date, little methodological work has focused on estimating mediated effects in discrete-time models (i.e., versus continuous-time models) despite utility in research where data is not collected in a continuous-time manner or when outcome events do not occur in a continuous manner. Fairchild et al., (2018) conducted a simulation study of the

DTSM model to provide recommendations for the field about power, required sample size and accuracy of parameter estimation (NIDA - R01DA030349). While this guidance will promote utilization of this model in the field, the DTSM model has not been formally expanded to consider covariates that have varying effects over time. The impact of covariates with time variant effects is critical to understanding complex research questions, such as those related to the onset of alcohol use and the relationship with familial relationships and parenting behaviors. This research will build upon the Fairchild et al. (2018) work by extending the model to include a mediator with a time variant effect and examining the performance of the model in a Monte Carlo simulation study.

DTSM models with a mediator with a time-varying effect. While time invariant covariates remain at a constant value across time, such as demographic attributes like race/ethnicity and sex, time-varying covariates can be defined as any variable in the model that changes in value over the course of study. In longitudinal research, it is often the case that time-varying covariates are measured and hypothesized to impact outcomes. For example, in developmental, longitudinal research, many facets of an individual are developing and measured repeatedly over time, such as social, emotional and cognitive abilities. Moreover, both time-invariant and time-varying covariates can exert either a time variant or time-invariant effect on the outcome. A time variant effect is present when the effect of a predictor on an outcome differs in magnitude across measurement waves (i.e., time). For example, a time variant predictor, such as parenting behaviors at baseline, could have a small effect on onset of alcohol use in waves representing early adolescence and null effects in later waves representing late adolescence as youth become

more independent. Different discrete time survival models are required to represent these possibilities (see "Types of covariates" in Masyn, 2014; Singer & Willett, 1991; 1993).

Time-varying covariates can be included in the discrete-time survival model to allow events at time t_i to be explained by covariates measured at that moment (Masyn, 2014; Willett & Singer, 1991; 1993). These effects are interpreted similarly to fixed covariates if they have a time invariant effect. When this is the case, the inclusion of the time-varying variable does not violate the proportional hazard assumption, the assumption that the effect conveyed on the log-hazard by the covariate does not change over time periods. As mentioned above, in social science research this may be a rigid assumption, especially when considering the impact of predictors over the course of child and adolescent development (Willett & Singer, 1993). However, the model can be expanded to allow covariates to have a time variant effect by including a statistical interaction of the covariate with time. To adjust Equation 12 to allow a time variant effect of the mediator:

$$Y = ln\left(\frac{h_{ij}|\, X_{ij},\, M_{ij}}{1 - \; h_{ij}|\, X_{ij},\;\; M_{ij}}\right) = \left[\alpha_j D_{ij}\right] + c'X_{ij} + \beta_1 M_1 + \beta_2 (M_1 \times D_1)$$

$$\ldots \beta_x\left(M_1 \times D_j\right) \qquad (13)$$

Here, all terms retain their previous meaning, however, one time-invariant mediator with a time variant effect (M_1), predicts the log-hazard function differentially over time periods, which is indicated in the equation by the statistical interaction terms (i.e., ($\beta_x\left(M_1 \times D_j\right)$). Equation 11 remains as earlier defined. In this dissertation work, I will evaluate how inclusion of a time invariant, continuous mediator with a time variant effect influences estimation in DTSM models.

This model has particular public health relevance to answering questions related to alcohol use and abuse including understanding the trajectories associated with the onset of early youth alcohol use as well as evaluating dual-approach prevention and intervention programs. By incorporating both mediation and discrete-time survival analysis as well as a mediator with a time variant effect, the model allows for the examination of direct and indirect effects of a predictor on the timing of the occurrence of alcohol use while also considering the impact of the mediator may vary over time. In research on developmental trajectories, this model could help researchers understand how developmental pathways operate in concert with parenting behaviors to impact timing to onset of youth alcohol use. The information garnered could then inform how targets of treatment for youth alcohol use may change over the course of development. In turn, the model could be used in program evaluation of dual-focused prevention/intervention strategies by examining the impact of the intervention on time to onset of alcohol use through hypothesized mechanisms of action while simultaneously considering mechanisms of action that may have a varying effect over time.

DTSM models in a structural equation modeling framework. Mediation analysis and discrete time survival analysis can both be conducted in a structural equation modeling framework (e.g., Cole & Maxwell, 2003; Masyn, 2014; Muthén & Masyn, 2005). Accordingly, models integrating both mediation analysis and discrete time survival analysis can be conducted in a structural equation modeling framework. Modeling in the structural equation modeling framework affords several benefits (Fairchild et al., 2015; Masyn, 2014; Muthen & Masyn, 2005). Most statistical models assume that variables in the model are measured without error, however, this is unlikely

to be true. In structural equation modeling, the researcher can model latent constructs by incorporating measurement models to partition true variance and error variance. Partitioning out measurement error in mediation analysis can help to guard against Type I and Type II errors (Cole & Maxwell, 2003). Further, modeling discrete time survival outcomes in a structural equation modeling framework easily allows for the inclusion for time invariant or time variant effects (Fairchild et al., 2015; Masyn, 2014).

Fairchild et al., (2015) demonstrate how the DTSM model with time invariant effects of the covariates can be estimated in the SEM framework (see path model in Figure 2.2). The model is denoted by the following equations:

$$M = b_0 + aX + \varepsilon_1 \tag{14}$$

$$\eta = ln\left(\frac{\Pr(e_j=1|\, X_{ij}, M_{ij})}{1-\Pr(e_j=1|\, X_{ij}, M_{ij})}\right) = \tau_j + c'X_{ij} + bM_{ij} \tag{15}$$

Equation 14 can be interpreted identically to Equation 11. In Equation 15, η is the ultimate outcome of interest, however, and defines a continuous latent variable representing the latent propensity for onset of the event. Moreover, e_j is a time-specific, binary outcome indicator that denotes whether or not the event of interest occurred. Similarly, τ_j is a time-specific threshold value, with the negative value equal to the time-specific intercept denoted in Equation 12. As noted by Fairchild et al., (2015), when using maximum likelihood estimation, the logistic regression approach to discrete time survival analysis and this latent variable modeling approach are equivalent:

> "[T]he log odds of the marginal hazard probabilities in the logistic regression-based approach are equivalent to the log odds of the event indicator probabilities in the SEM-based approach, such that maximum likelihood estimates of the event indicator probabilities in Equation [15]

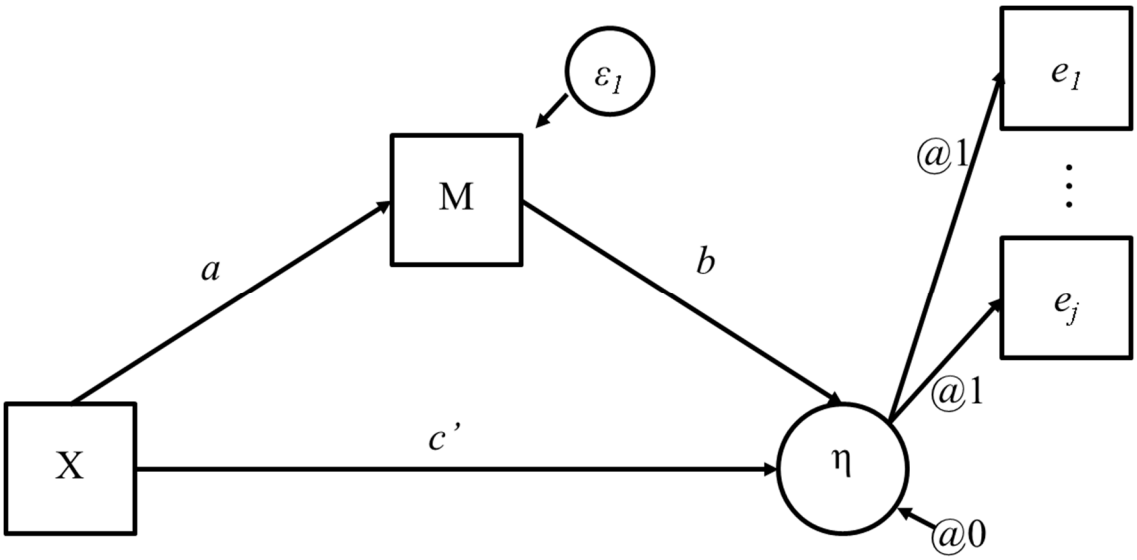

Figure 2.2 DTSM Model in a SEM Framework.

will equal maximum likelihood estimates of the marginal hazard probabilities in Equation [12]" (Fairchild et al., 2015, p. 7).

Further, as presented in Masyn (2014), there are several parameterizations of the discrete time survival model in a structural equation modeling framework that are equivalent models when using full information maximum likelihood and when considering time to onset of only single (i.e., non-recurring) events. Another equivalent model would be estimating the model presented in Equations 14 and 15 as a single class mixture model. Estimation in a mixture modeling framework can allow for further extensions, such as nonparametric modeling of frailties (i.e., unobserved heterogeneity) in the timing to event onset outcome and incorporation of growth mixture modeling (Muthen & Masyn, 2005). Muthen & Masyn (2005) introduce discrete time survival analysis estimated in a mixture modeling framework (Muthen & Muthen, 2001; Muthen & Shedden, 1999). In this approach, the expectation-maximization (*EM*) algorithm (Dempster, Laird & Rubin, 1976) is used to obtain maximum likelihood estimates in a general latent variable modeling framework (Muthen, 2004; Muthen & Shedden, 1999). Muthen & Masyn (2005) present estimation of multiple classes to understand "long term survivors" and to incorporate growth mixture modeling. While these extensions are out of the scope of the present research, given these benefits, in the present research the DTSM model will be modeled in a mixture modeling framework to allow future extensions of the model.

Specifically, the discrete time survival mediation model with a time variant effect will be modeled as a single class mixture model. The model under study is depicted in

Figure 2.3 and largely remains the same as presented above in Equations 14, 15, and Figure 2.2, however to there are two important differences. First, the diagram denotes that the model is estimated as a single class mixture model (i.e., K = 1). In addition, with the integration of a mediator with a time variant effect into the model, there will be multiple mediated effects, one for each binary onset indicator (i.e., e_j) included in the model. The indirect effect at each time interval will be reflected by the *a* path parameter multiplied by the *b* path for each time interval. Alternatively, there will be only one direct effect, as the impact of X on Y while controlling for M is being modeled in a traditional proportional hazard approach with a time invariant effect.

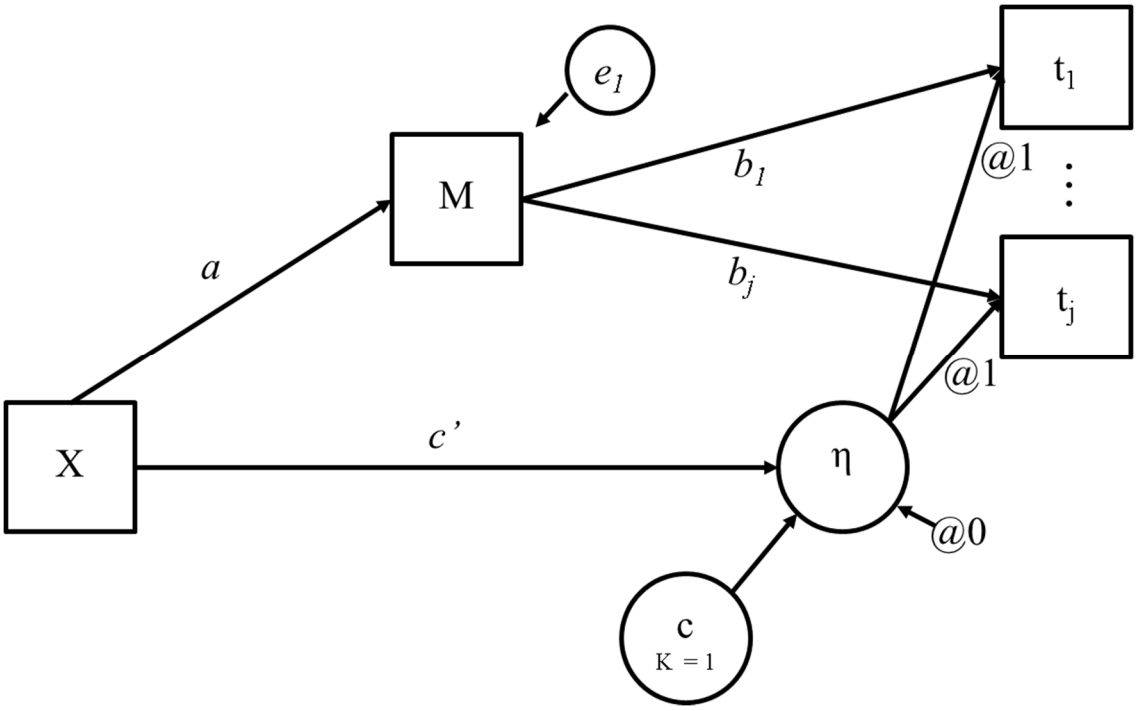

Figure 2.3 DTSM Model with a Time Variant Effect Estimated in a Mixture Modeling Framework.

CHAPTER THREE

STUDY ONE: APPLIED EXAMPLE

Method

Data and participants. The data for the DTSM model application (i.e., Study One) derives from a subsample collected through the NLSY97, a national, longitudinal study of approximately 9,000 youth. These data are part of the National Longitudinal Surveys program funded primarily by the Bureau of Labor Statistics to understand issues related to the youth labor force such as education, training, government program participation, among other topics. The broader project was supplemented by funds from the National Institute of Child Health and Human Development, the Department of Education, the Office of Juvenile Justice and Delinquency Prevention, the Department of Defense and the Department of Labor to fund special, additional sets of questions related to each funder's interests. Currently, 16 waves of data have been collected with 79.5% of the original sample retained at the most recent interview. Data for this study were a subsample of youth that had two residential parents and were selected for completion of the parental monitoring measure.

In wave one of data collection, an adult in each home completed the NLSY97 screening measure. If a potentially eligible youth lived in the home, any NLSY97-eligible youth(s) and one of the youth's parents were interviewed using a computer-assisted personal interview instrument, administered by an interviewer with a laptop computer.

Software guided interviewers through the electronic questionnaire on a laptop, selecting the next question based on a participant's answers. During sensitive portions, when an interview occurred in person, the participant entered responses directly into the laptop. For subsequent waves of data collection, the interviews were also conducted using a computer-assisted personal interview instrument or by telephone.

Measures. Measures of constructs representing the predictor, mediator and time to event outcome are as follows:

Interparental support. The inter-parental support (IS) measure was the predictor (i.e., X). This measure assessed the residential father's support of the residential mother as reported by the youth at wave one of the study. The six-item rating scale was rated on a five point likert scale ranging from "never" to "always". The items used were adapted from a measure used in another study (i.e., IOWA Youth and Family Project; Conger & Elder, 1994). Items are as follows: "Does he scream at her when he is angry?"; "Is he fair and willing to compromise when they disagree?"; "Does he express affection or love for her?"; "Does he insult or criticize her or her ideas?"; "Does he encourage or help her with things that are important to her?"; "Does he blame her for his problems?" (Conger & Elder, 1994; Moore et al., 1999). The items "Does he scream at her when he is angry?", "Does he insult or criticize her or her ideas?" and "Does he blame her for his problems?" were reverse coded before scoring so that higher scores on the IS measure would reflect higher levels of IS, as rated by the youth.

Psychometric assessment of this measure was conducted by Moore et al. (1999) using wave one data. The data were scored by creating a sum of the six items, resulting in possible scores falling between 0 and 24, with higher scores indicating more parental

support. The mean score for the 3,189 youth involved in the study was 19.00 (SD = 4.28). Cronbach's alpha indicated adequate levels of internal consistency (α = .81; Cronbach, 1951). In addition, this measured demonstrated predictive validity, with greater support being associated with lower levels of substance use, delinquency and emotional and behavioral difficulties. In the subsample to be utilized for these analyses, internal consistency decreased unremarkably from α = .81 to α = .79; this indicates adequate levels of internal consistency in the current subsample (Cronbach, 1951).

Parental monitoring. The parental monitoring (PM) measure was used as the mediator variable. NLSY procedures suggest that this measure was completed by a selected subsample of youth that were between 12 and 14 years old at wave one of data collection. This measure assessed youth-reported monitoring by the mother at wave two of the study. The four-item rating scale was rated on five point likert scale ranging from "knows nothing" to "knows everything". The items were meant to be representative of items commonly used in the literature (Hetherington, Cox, & Cox, 1982; Maccoby & Mnookin, 1992). Items are as follows: "How much does she know about your close friends, that is, who they are"; "How much does he/she know about your close friends' parents, that is, who they are?"; "How much does she know about who you are with when you are not at home?"; "How much does she know about who your teachers are and what you are doing in school?" (Hetherington et al., 1982; Maccoby & Mnookin, 1992). The data were scored such that higher scores reflect greater monitoring by the mother, as reported by the youth.

Psychometric assessment of this measure was conducted by Moore et al. (1999) using wave one data. The data were scored by creating a sum of the four items, resulting

in possible scores falling between 0 and 16. The mean score for the 5,240 youth was 10.24 (SD = 3.30). Cronbach's alpha indicated adequate levels of internal consistency (α = .71; Cronbach, 1951). In addition, this measure demonstrated predictive validity, with greater parental monitoring being significantly associated with higher report of parental limit-setting, greater parental strictness, decreased substance use and delinquency as well as decreased emotional and behavioral difficulties. In the subsample to be utilized for these analyses, internal consistency increased unremarkably from α = .71 to α = .73; this indicates adequate levels of internal consistency in the current subsample (Cronbach, 1951).

Onset to alcohol use. These outcome data are a series of binary outcome indicators for each age that the youth participated in the study. These alcohol use onset indicators were created from questions regarding the age of a youth's first drink at wave one and questions asked at subsequent waves about the youth having their first drink after the date of the prior interview. The data were coded so that there was a variable for each year of age of the youth (e.g., onset at 18 years of age). Onset for this analysis was assessed up to 21 years of age, the legal drinking age in the United States. Each youth could only have one period indicated in which they onset use of alcohol. For each year before, in which a youth was considered at risk for initiating alcohol use, the variables were coded as zero. For each year after onset, the data was coded as missing so that the youth was no longer included in the risk set. Further, because of assumptions in this data around a Bernoulli stochastic process (Ozarow & Leung-Yan-Cheong, 1979), which suggests that periods of this survival data outside of observation are complicated and ergonic, deterministic coding was utilized to account for interval censored data (Ozarow

& Leung-Yan-Cheong, 1979). For interval censored individuals, we assigned the earliest possible event time. For example, if onset data was missing for age 13 and 14 but it was known that the youth began using alcohol at some undetermined point before the interview at age 15, then onset was coded at age 13. It is not believed that this will reduce variability in the outcome indicators as each individual could only have one period of onset overall (i.e., we do not allow multiple onset intervals). Right-censored individuals remained right-censored.

Analytic plan. A model building procedure was conducted to illustrate finding the best fitting model in a structural equation modeling framework and to examine testable assumptions. In this model building approach, the log-likelihood ratio test was utilized to test for significantly better fit between a series of nested models, beginning with a null model with no relationships modeled between the predictor, mediator, and the latent propensity for onset. Note that the use of the loglikelihood test is appropriate in this instance of mixture modeling because all models were single class solutions (Muthen, 2004; Muthen & Masyn, 2005). This would not be appropriate in situations in which models with different numbers of classes were compared (Muthen, 2004; Muthen & Masyn, 2005). The Akaike Information Criterion (AIC; Akaike, 1973), Bayesian Information Criterion (BIC; Schwarz, 1978) and the sample size adjusted BIC (aBIC; Sclove, 1987) were used to supplement the loglikelihood ratio test; smaller values of the AIC, BIC and aBIC indicated better fitting models (Akaike, 1973; Schwarz, 1978; Sclove 1987). The best fitting model based on these criteria was noted. However, regardless of fit, for demonstration purposes and for subsequent use of parameter estimates in Study

Two and Study Three, the focal model for this dissertation was interpreted (i.e., the DTSM model with a time variant effect of the mediator).

In this applied example using data from the NLSY97, the DTSM model with a time variant mediator was estimated in a mixture modeling framework (see Muthen & Masyn, 2005) to understand how IS impacts timing to onset of youth alcohol use directly and indirectly through PM. Analyses were run in Mplus (see code for running the applied example in Appendix A [i.e., DTSM model with time variant effects in the NLSY97 sample]; Muthén & Muthén, 1998-2015) using the EM algorithm to obtain maximum likelihood estimates in a general latent variable modeling framework (Muthen, 2004; Muthen & Shedden, 1999). To investigate mediation, PM was regressed on IS to produce an *a* path estimate. The onset-to-event outcome indicators (i.e., onset of youth alcohol use from age 14 to 21) were regressed on the mediator, PM, to yield each of the *b* path estimates (i.e., $b_{14} - b_{21}$). And the onset-to-event outcome latent variable was regressed on IS to yield the *c'* parameter estimate. The *a* and *b* parameter estimates were multiplied to determine the significance of the indirect effects by examining bias-corrected bootstrapped confidence intervals, in line with currently recommended techniques in the literature (MacKinnon et al., 2004; Preacher & Hayes, 2008).

Results

Descriptive statistics. The final sample for analyses consisted of 1,026 youth that had completed the IS and PM measures and did not have left censored outcome data. Youth were primarily male (i.e., 52.6%), Caucasian (63.3%), and non-Hispanic (78.2%), with ages at wave one of data collection falling between 12 and 16 years of age (M = 13.13, SD = .94).

Youth-reported levels of mother monitoring (i.e., PM) ranged from .00 - 4.00 with a mean of 2.69 (*SD* = .76). This suggests that on average, across the four PM items, a youth reported their mother fell between "knows some things" and "knows most things". These scores approximated a normal distribution, with a skewness of -.76 (*SE* = .076) and kurtosis of .60 (*SE* = .15). Youth-reported father support of the mother (i.e., IS) ranged from .50 – 4.00 with a mean of 3.30 (*SD* = .66). This suggests that on average, across the six IS items, a youth reported their father "usually" to "always" engaged in supportive behaviors. Only 23% of the sample reported a total IS score lower than 3.00 (i.e., father was "usually" supportive of the mother), suggesting that youth perception of IS was predominately positive. The IS total score was non-normally distributed, with skewness of -1.28 (*SE* = 0.08) and kurtosis of 1.66 (*SE* = 0.15). However, bootstrapped standard errors were utilized for analyses which are nonparametric estimates of the standard error (Efron, 1981; Efron & Tibshirani, 1993).

Finally, youth were between the age of 14 and 18 at wave three of data collection, with a mean age of 15.74 (*SD* = .85). Accordingly, the sequence of outcome variables represent onset of alcohol use from age 14 to 21, the legal age of alcohol use in the United States. Youth were not included in these analyses if they began drinking before wave three (i.e., left censored). A table describing the number of youth at-risk and those that began drinking (i.e., onset) in a given period from age 14 to age 21 is presented in Table 3.1, as well as the respective hazard probability (i.e., *h(j)*).

DTSM model building. A model building approach was utilized to determine which model best fit the data and then to assess the tenability of the testable assumptions

Table 3.1

Timing of onset of youth alcohol use

	Age 14	Age 15	Age 16	Age 17	Age 18	Age 19	Age 20	Age 21
At-risk	31.00	445.00	676.00	754.00	561.00	422.00	322.00	219.00
Onset	5.00	99.00	149.00	197.00	137.00	96.00	98.00	48.00
h(j)	.16	.22	.22	.26	.24	.23	.30	.22

associated with a DTSM model with a mediator that has a time variant effect. Fit information (i.e., Loglikelihood ratio test, AIC, BIC, aBIC) can be found in Table 2.2.

The first model that was fit was a null model in which the means and variances of FI and PM were estimated. In addition, the latent construct representing onset, with mean and variance constrained to zero, was estimated with each of the onset variables loading equally (i.e., loadings of alcohol-use onset variables at ages 14-21 were constrained to load equally at 1.00). This model was utilized as the baseline model with a log-likelihood = - 4089.757, AIC = 8203.514, BIC = 8262.715 and aBIC = 8224.601.

The alternative model built upon the previous model by regressing the timing to onset of adolescent alcohol use latent construct on the independent variables, IS and PM. Note that there was no indirect effect of IS on onset modeled here, only the direct effects of IS and PM on the time to onset latent construct. This model appeared to fit worse than the null model given a negligible change in the loglikelihood value as well as larger AIC, BIC and aBIC values.

The next model that was fit was the DTSM model with a time *invariant* effect of the mediator, PM, on the latent propensity for onset outcome. That is, IS predicted the time to onset latent construct directly and indirectly through PM. The loglikelihood ratio test indicated that this DTSM model fit significantly better than the null model, χ^2 (3) = 28.05 , $p < .05$. This was further supported by AIC, BIC and aBIC values that were smaller than those obtained for the null model.

Subsequently the DTSM model with time invariant effects was compared to the DTSM model with a time variant effect of the mediator. It did not appear that the model

Table 3.2

Model building: Model fit indicators

Model	Free parameters	Log-likelihood	Akaike (AIC)	Bayesian (BIC)	Adj. BIC (aBIC)
Null	12	-4089.757	8203.514	8262.715	8224.601
Alternative	14	-4089.739	8207.477	8276.545	8232.080
DTSM	15	-4075.733	8181.466	8255.468	8207.826
Add M time variant	22	-4070.328	8184.655	8293.191	8223.316
Add frailties	23	-4070.592	8187.183	8300.652	8227.602
Add X variant	29	-4067.924	8193.847	8336.916	8244.809
Add X&M Moderator	23	-4069.881	8185.763	8299.232	8226.181

with a time variant effect of PM on the time to event indicators fit significantly better than the DTSM model with time invariant effects, $\chi 2\ (7) = 10.81$, $p > .05$.

This was corroborated by AIC, BIC and aBIC values that were larger than those obtained when estimating the DTSM model with a time invariant effect of the mediator. Given these findings, in a real data application, the DTSM model without a time variant effect of the mediator would likely be retained as the final model and assumptions would be checked accordingly. However, given that the goal of obtaining parameter estimates was to inform population parameters for a Monte Carlo study focused on estimation of the DTSM model with mediator they conveyed a time variant effect on the outcome, the DTSM model with a time variant mediator was treated as the best fitting model here.

Since the model with a time variant effect of M and time invariant effect of X was retained, the remainder of the model building procedure was utilized to demonstrate the examination of the testable assumptions associated with a DTSM model with a time variant effect of the mediator. First, a frailty term was added to the model to test the assumption related to the presence of unobserved heterogeneity in the logit hazard. A smaller loglikelihood value and larger AIC and BIC values for this model suggested that this model assumption was reasonable. Next, I tested the assumption related to whether there was a time invariant effect of IS on the timing to onset of youth alcohol use by estimating a model where there was a time variant effect of both PM and IS on timing to onset of youth alcohol use and comparing fit of that model to the DTSM model with a time variant effect of PM and time invariant effect of IS. The model that was expanded to include the time variant effect of IS did not fit significantly better, $\chi^2\ (7) = 4.81$, $p > .05$, and also produced AIC, BIC and aBIC values that were larger than the more

parsimonious model. This suggests that the assumption related to no time variant effect of IS on the outcome was defensible. Finally, I tested the assumption that there was no significant interaction between the predictor (i.e., IS) and mediator (i.e., PM) by fitting a model that incorporated this interaction term. This model did not fit significantly better χ^2 (1) = .894, $p > .05$ and returned larger AIC and BIC values that the more parsimonious model, suggesting that this assumption was justifiable.

I also assessed the tenability of the assumption related to linearity of the predictors on the timing to event outcome using the Box-Tidwell (1962) transformation test. When examining the linearity of the relationship between IS and the latent construct representing the discrete-time to event outcome, there was no statistically significant impact of the interaction between IS and it's natural log. Similarly there was no statistically significant impact of PM and the interaction with it's natural log on the outcomes. This suggested that these assumptions were sound.

Results of the DTSM model with a time variant effect. Statistically significant paths of the DTSM model with a time variant effect are presented in Figure 3.1. As depicted, there was no statistically significant impact of the predictor, IS on the time to event latent construct, c' = -.001 (.062), p = .992. This suggests that there is no direct impact of IS on the latent propensity for youth alcohol use (i.e., log odds in an observed variable model). Alternatively, there was a significant impact of IS on PM, a = .187 (.039), $p < .01$. A one-unit scale change in IS was associated with a .187 unit change in PM. While there were no significant effects of PM on the log odds of event occurrence at age 14 and ages 16 - 21, there was a significant impact of PM on the log odds of youth alcohol use at age 15, b_{15} = - .318 (.156), p = .042. At age 15, increased PM was

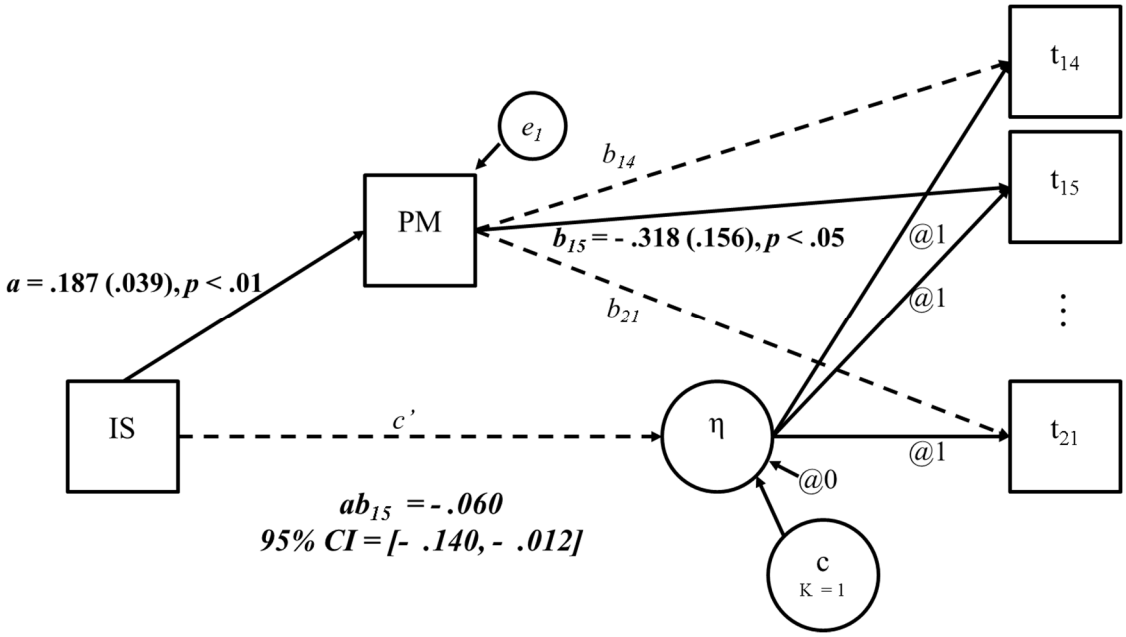

Figure 3.1

Applied Example: DTSM Model with a Time Variant Effect of the Mediator

Note: Solid lines denote statistically significant paths.

associated with a decrease in the log odds of youth alcohol use. The overall indirect effect of IS on the log odds of event occurrence at age 15 was estimated to be statistically significant when examining a 95% bias-corrected, bootstrapped confidence interval, ab_{15} = - .060, CI = [- .140, - .012].

Applied Example Discussion

Results from these applied analyses suggested that the DTSM model with a time invariant impact of PM on the log odds of event occurrence fit the data best. However, given the focus of this dissertation, the DTSM model with a time variant mediator was retained as the final model for demonstration purposes as well as for parameter estimates for the following Monte Carlo studies. Model building and checking of assumptions suggested that the model assumptions were tenable. Results of the final, retained model suggested that there was no direct effect of IS on the latent propensity for event occurrence. However, there was a significant indirect effect of IS on the log odds of youth alcohol onset through PM at age 15.

While this model was primarily estimated to supply parameter estimates for the subsequent Monte Carlo studies, it may also inform the applied youth alcohol use literature. Briefly, these findings align with the applied literature in this area in several ways. First, positive family environments have long been linked to healthy youth development, including the prevention of alcohol use (Anderson & Henry, 1994; Repetti, Taylor, & Seeman, 2002). Healthy family relationships and positive parenting behaviors, such as monitoring, have been implicated as important for delaying onset of youth alcohol use (Van Ryzin, Fosco, & Dishion, 2012). As expected, both IS and PM played a role in delaying time to onset of youth alcohol use. Some researchers suggest that this

impact of these predictors may vary over the course of child development (e.g.,Dishion & McMahon, 1998). This also aligned with the findings from this study given that IS and PM were only influential predictors of onset at age 15. This suggests that these important family functioning and parenting behaviors may be particularly important in earlier adolescence. It is anticipated that if there were not issues of data sparseness at age 14 (see Table 3.1), that the effect may have been observed at that age as well.

However, there are notable limitations with the current research and findings should be interpreted with caution. First, analyses were conducted with a small subset of youth in the NLSY97 study that completed the IS and PM measures (i.e., youth with two residential parents and in the selected subsample for collection of the PM measure). While the broader NLSY sample was collected to be nationally representative, it is not anticipated that the subsample used for these analyses will mirror national characteristics. For example, for inclusion, youth in this sample were required to have two residential parents. In addition, given that the goal of this applied example was to garner parameter estimates for the subsequent simulation studies, the model was simplified and no covariates were included (e.g., gender, peer influences, etc.). Many other factors are anticipated to play a role in this complex, longitudinal process (e.g., see Donovan, 2004). And as noted above, there were issues of data sparseness (i.e., see Table 3.1), particularly at age 14 and findings related to these onset indicator variables should be interpreted with caution.

So that the remaining simulations are rooted in conditions that reflect real-world research, parameters from this applied example serve as the foundation for the subsequent simulation studies. All aspects of the applied model were retained for the next

simulation study including the sample size and parameter estimates. However, the number of data waves was reduced by two waves. Specifically, onset at ages 14 and ages 21 were not modeled in the subsequent studies. The number of valid cases in these cells, especially age 14, was notably sparse. Though this data sparseness warrants further consideration, it is outside of the scope of the current work. Therefore, further simulation studies utilized estimates for onset measured at six time points. Moreover, it is believed that fewer waves of data may be more representative of what is feasible for collection in the context of many applied research projects.

CHAPTER FOUR

STUDY TWO: SINGLE – CELL SIMULATION STUDY

Method

In Monte Carlo simulation studies, data are generated as specified by the researcher so that population values of parameters are known (Muthén & Muthén, 2002). When population parameters are generated and known, it allows for examination of quantitative properties such as bias in parameter estimation and standard error, statistical power, and type one error rates (Muthén & Muthén, 2002). Using parameter estimates obtained from the NLSY application, a Monte Carlo simulation study was conducted of the DTSM model that incorporated a mediator with a time variant effect to assess bias in parameter estimation, power, type one error and coverage of the bias-corrected, bootstrapped confidence intervals. Given no previous work provides a strong foundation for effect sizes of parameters in the model under review, we will consider the ability of the model to recapture estimates from the applied analysis in Study One, which will serve as the population.

Population model. This project was conducted in Mplus and R software packages (Muthén & Muthén, 1998-2015; R Core Team, 2017). Data generation and model estimation were run in Mplus, through MplusAutomation in R, given the software's flexibility and utility in modeling (see code for Study Two in Appendix B; Hallquist & Wiley, 2018; Muthén & Muthén, 1998-2015; RCore Team, 2017). One

thousand datasets were generated in line with the parameter estimates, sample size (i.e., 1026) and number of data waves from the abbreviated NLSY applied example (i.e., a total of eight waves without onset at age 14 and 21; see Figure 4.1).

The exogenous predictor (i.e., X) was generated as a continuous variable with a mean and variance determined by the applied example (i.e., $\mu = 0$, $\sigma^2 = .438$). All endogenous variables in the model were generated according to Equations 14 and 15. More specifically, M was specified from the linear regression of M on X, with an intercept equal to zero and disturbance term equal to .554. The timing to occurrence of an event outcome data were generated in line with applied example parameter estimates in the context of a disproportional hazard odds model. Data for each time point were generated using the threshold values obtained in the abbreviated applied example (i.e., see Table 4.1). These data were coded such that after the first instance of onset, the subsequent outcome time points were coded as missing. Given that investigation of multi-spell survival models that accommodate investigation of repeated events is outside of the scope of this project (Willett & Singer, 1995), this coding was necessary for estimation of this model so that after the first occurrence, the case was removed from the risk set.

Model estimation. The DTSM model with a time variant mediator was estimated in a mixture modeling framework as a single class mixture model (see Muthen & Masyn, 2005). Analyses were run in Mplus (Muthén & Muthén, 1998-2015) through MplusAutomation in R (Hallquist & Wiley, 2018; RCore Team, 2017) using the EM algorithm to obtain maximum likelihood estimates in a general latent variable modeling framework (Muthen, 2004; Muthen & Shedden, 1999).

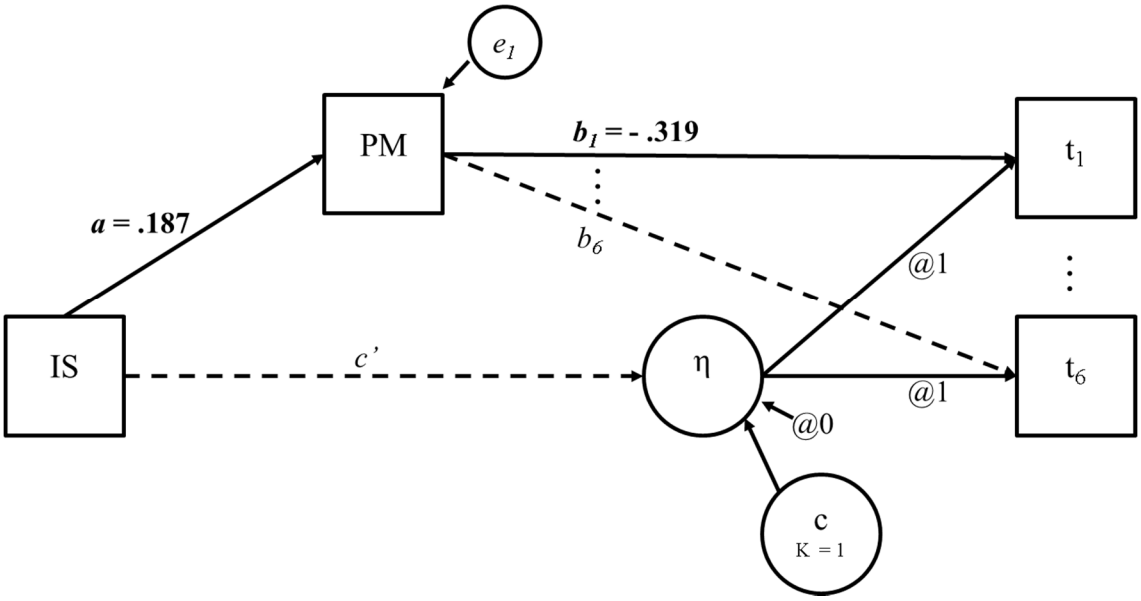

Figure 4.1

Population Model for Study Two

Note. Dashed lines indicate non-significant paths (i.e., these paths were equal to zero in the population model)

Table 4.1

Event Indicator Thresholds and Baseline Hazard Rates

Event indicator	Threshold (τ)	*h(j)*
1	1.26	.22
2	1.26	.22
3	1.04	.26
4	1.13	.24
5	1.23	.23
6	0.82	.30

In each sampled data set, the DTSM model with a mediator with a time variant effect was estimated using the logit link for the time-to-event outcome data. As discussed in the review of the literature, the bias-corrected bootstrap has the greatest power to detect the mediated effect (MacKinnon et al., 2004). In this resampling method of testing for the significance of the mediated effect, the empirically built distribution accounts for the asymmetry in the sampling distribution of *ab* and builds the empirical distribution around the true population parameter (Efron & Tibshirani, 1994). I utilized 1,000 bootstrap draws to construct the bias-corrected confidence intervals in each replicated sample.

Simulation outcomes. To understand how this model recaptures parameter estimates of the indirect effect, I evaluated relative bias in parameter estimation as well as several other statistical properties related to the significant and non-significant mediated effects including power, type one error and confidence interval coverage.

Bias in parameter estimation. Due to sampling from the overall population, the parameter estimates in each sample varied around the specified population parameters. To understand this variability, I examined percentage relative bias of the nonzero *ab* parameter estimate (i.e., on time to event indicator one in Figure 4.1). Relative bias can be defined as the average deviance of a given sample estimate from the population parameter estimate, relative to the population parameter value and is denoted by the following equation:

$$RB\left(\hat{\theta}\right) = \sum_{j=1}^{n_r}\left(\frac{\widehat{\theta_{ij}}-\theta_i}{\theta_i}\right) / n_r \qquad (16)$$

Here θ_{ij} is the parameter estimate in the sample, θ_i represents the population parameter and n_r reflects the number of replications. This estimate can then be multiplied by 100% to yield an estimate of the percentage relative bias. Lower values of bias are

preferred. A boundary of percentage relative bias less than 5% has been suggested as an indicator of an unbiased parameter estimate (Hoogland & Boomsma, 1998). The values obtained were compared to this criterion.

Power. Power was explored to detect the mediated effect that was nonzero in the population model (i.e., indirect effect on time to event indicator one in Figure 4.1). Empirical power was calculated as the number of times that the parameter estimate of interest was statistically significant across the 1,000 replication samples, utilizing a 95% bias-corrected, bootstrapped confidence interval for hypothesis testing. Often, a value of .80 power is sought (Cohen, 1992); the power estimate for the significant mediated effect in the population model was compared to this criterion.

Type one error. To further understand the accuracy of hypothesis testing with the 95% bias-corrected, bootstrapped confidence interval, I examined type one error associated with mediated effect parameter estimates that were equal to zero in the population model (i.e., mediated effects on time to event indicators two-six in Figure 4.1). In this context, a type one error occurs when the null hypothesis is rejected but the null is true. Type one errors are represented when a significant mediated effect is detected in a replication from which the population effect is null. The type one error rate was calculated as the number of times this occurs, divided by the number of replications. These rates were compared to the nominal value of .05, conventionally used as the α-level in the applied literature. More specifically, rejection rates between 2% and 8% were deemed acceptable (Shi, DiStefano, McDaniel & Jiang, 2018).

Confidence interval coverage. In this vein, I also examined confidence interval coverage to understand how often the nonzero mediated effect population value was

contained within the 95% bias-corrected, bootstrapped confidence interval (i.e., indirect effect on time to event indicator one in Figure 4.1). It was anticipated that the population value would be contained within the interval in approximately 95% of the replications; the obtained value was compared to this expected value to understand accuracy of the 95% bias-corrected, bootstrapped confidence interval. Moreover, it has been suggested that a confidence interval with coverage values of less than 90% is too wide and problematic (Collins, Schafer & Kam, 2001; Enders, 2001). As stated by Collins, Shafer and Kam (2001):

> Accurate coverage translates directly to an accurate Type I error rate. If the coverage of a nominal 95% interval is actually 90%, then the actual Type I error rate for a testing procedure with a .05-level criterion is twice as high as it ought to be. (p. 340).

Results

All replications converged and were thus retained for examination of the following outcomes.

Percentage relative bias. Percentage relative bias was calculated for the single, significant mediated effect (i.e., ab_1 in Figure 4.1). Average percentage relative bias across the 1,000 replications was 1.848% (see Figure 4.2). The condition average fell well below a stringent criterion of ± 5.00%, indicating that the parameter estimate was generally unbiased under the conditions specified (Hoogland & Boomsma, 1998). However, while the mean percentage relative bias suggested that on average, an estimate of the mediated effect would be unbiased under these conditions, it was noted that there

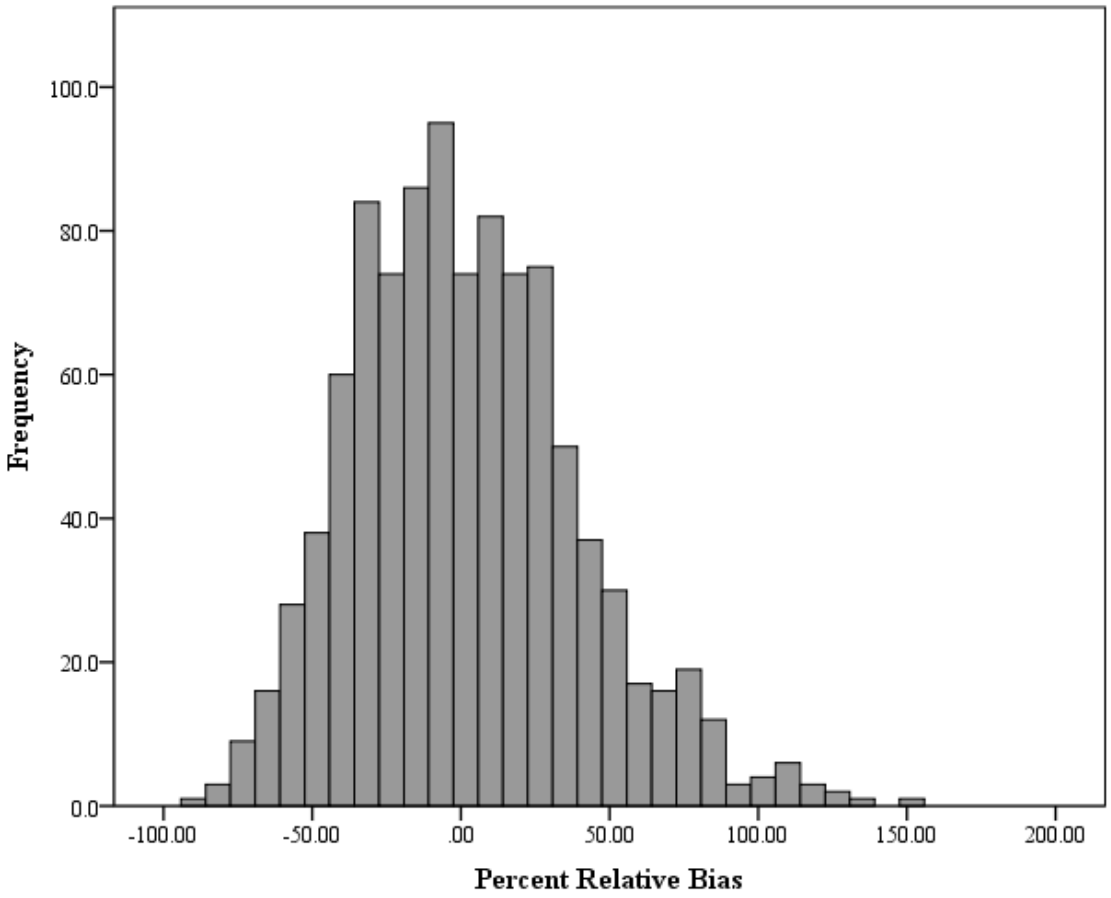

Figure 4.2

Distribution of Percentage Relative Bias across Replications

was a wide range of relative bias across the 1,000 replications within the condition (i.e., Range: -90.00% to 150%).

Power. Power was examined for the single, nonzero indirect effect (i.e., ab_1 in Figure 4.1). Of the 1,000 replications, 908 presented with a significant mediated effect using a 95% bias-corrected, bootstrapped confidence interval to test for statistical significance (i.e., power = .908). Compared to a desirable level of power (i.e., .80; Cohen, 1992), under the conditions modeled here, there was adequate power to detect the mediated effect.

Type one error. Type one error was examined for the five, non-significant mediated effects (i.e., $ab_2 - ab_6$ in Figure 4.1). Type one error rates ranged from .068 - .056 and are presented in Table 4.2. All rates fell within the acceptable range (i.e., 2% - 8%), suggesting that Type one error rates were in line with their expected nominal values (i.e., $\alpha = .05$).

Coverage. The population parameter for the significant mediated effect (i.e., $ab_1 = -.060$) was represented in 952 of 1,000 95% bias-corrected, bootstrapped confidence intervals. Confidence interval coverage in 95.2% of replications falls directly in line with an expected value of representation in 95% of replications and is well above the suggested 90% criterion (Collins, Schafer & Kam, 2001; Enders, 2001). This suggests adequate confidence interval coverage under these population conditions.

Single-Cell Monte Carlo Discussion

Closely mirroring the applied example, a simulation study was conducted to study percent relative bias, power, type 1 error, and confidence interval coverage associated with estimating mediated effects in the discrete time survival mixture framework. Results

Table 4.2

Type One Error for $ab_2 - ab_6$

	ab_2	ab_3	ab_4	ab_5	ab_6
Type one error	.068	.061	.063	.060	.056

suggested that under conditions of large model size (i.e., n = 1,026) eight waves of data, and one mediated effect (ab_1 = -.060), outcomes of interest were found to be ideal. For the significant mediated effect, power was above the desired .80 value, indicating that there was more than adequate power to detect the mediated effect. Confidence interval coverage was 95.2% which was directly in line with the expected 95% value. This indicates that the coverage rate is accurate and that type one error is controlled. Similarly, when examining the type one error rates of the non-significant indirect effects, all type one error rates were within acceptable limits. This suggests under the population conditions in the single-cell simulation study, type one error was controlled.

Finally, the average percent relative bias was generally small indicating that the mediated effect parameter estimate was not biased on average under the specified population conditions. However, there was a wide standard deviation associated with this mean estimate of percentage relative bias. While a researcher may not expect biased parameter estimates on average, the reality is that bias varied widely from replication to replication in the study.

Altogether, results were favorable. This was anticipated given the ideal conditions that were modeled in this single cell Monte Carlo study (e.g., large sample size, many waves of data). Given these results, the Monte Carlo study was expanded to include conditions that were less ideal for model estimation and more realistic in applied social sciences research. Conditions modeled are detailed extensively below.

CHAPTER FIVE

STUDY THREE: EXPANDED MONTE CARLO STUDY

Method

Based on the favorable results of the single cell Monte Carlo study, the simulation study was expanded to reflect conditions that may be more typical in applied social sciences research. For example, the population model in the single cell study entailed many waves of data (i.e., eight) and a large sample size (i.e., n = 1,026). These are ideal conditions that may not often be realistic in applied research settings. In the expanded Monte Carlo study, conditions were manipulated to understand how variations in sample size, number of waves of data, pattern of the mediated effects and model (mis)specification impacted estimation of the DTSM model with a mediator with a time variant effect.

Simulation conditions. The factors manipulated in each condition were sample size, number of waves of data, pattern of the mediated effects and model (mis)specification. Levels of the factors were as follows:

Sample size. The sample size in the single cell simulation was 1,026 to mirror the sample size in the applied example. Smaller samples sizes were modeled in the expanded study to understand how sample size impacted estimation of the DTSM model with a time variant effect in a mixture modeling framework. More specifically the sample sizes modeled included 250, 500 and 1,000, with the smaller sample sizes (i.e., 250 and 500)

falling more in line with sample sizes that may be observed in applied social sciences research.

Waves of data. The single cell simulation study consisted of eight waves of data. That is, the predictor was measured at time one, the mediator at time two, and the timing to onset indicators were measured from waves three to eight (i.e., six separate timing to onset indicators). To understand how the number of waves of data impact estimation in the DTSM model with a time variant effect of the mediator, a condition with six waves of data was also included in the expanded Monte Carlo study. When there were six waves of data, the predictor was assessed at wave one, the mediator at wave two and the time to event indicators from wave three to six (i.e., four separate timing to onset indicators). Thus, there were two levels of this condition (i.e., six or eight waves)

Pattern of time variant effect. There was only one nonzero mediated effect in the population model for the single cell Monte Carlo study. To understand how the number of nonzero time variant effects impacted estimation, this factor was varied. In some conditions only one mediated effect was nonzero, akin to the applied example and single cell Monte Carlo study (i.e., see Figure 4.1). At the other level of this factor, half of the mediated effects were nonzero, with the same population parameter estimate for each nonzero mediated effect (i.e., ab = -.060). It is important to note, when there were eight waves of data, with six time to event outcomes, there were three nonzero mediated effects in the 'half significant' condition. Alternatively, when there were only six waves of data, with four time to event indicators, there were two nonzero mediated effects in the 'half significant' condition.

Model (mis)specification. Finally, to understand how model specification impacted model estimation, model specification was varied. In the correctly specified condition, the model from which the data were generated was fit to the data (i.e., the DTSM model with a mediator with a time variant effect). In the misspecified conditions, a nested model with a time invariant effect of the mediator was fit to the data (i.e., DTSM model), ignoring the time variant mediated effects in the population model. Exploring model misspecification is of particular importance in mixture modeling given that previous research insinuates that misspecification may bias estimates and cloud interpretation of fit statistics (e.g., see Enders & Tofighi, 2008; Gray, 1994; Tofighi, & Enders, 2008)

These conditions resulted in a fully crossed design consisting of three sample sizes (i.e., n = 250, 500, 1,000) x two waves of data (i.e., 6 or 8) x two patterns of time variant effects (i.e., one nonzero mediated effect, half nonzero mediated effects) x two levels of specification (i.e., correctly specified, misspecified), ultimately yielding 24 unique parameter combinations and 12,000 data sets to investigate (i.e., the correctly specified and misspecified models were estimated in each data set).

Model Estimation. Two different models were estimated in this Monte Carlo study. In correctly specified conditions, the DTSM model with a time *variant* effect of the mediator was estimated in a mixture modeling framework as a single class mixture model (see Muthen & Masyn, 2005). Similarly, in misspecified conditions, the DTSM model with a time *invariant* effect of the mediator was estimated in a mixture modeling framework as a single class mixture model (see Muthen & Masyn, 2005). All analyses were run in Mplus (Muthén & Muthén, 1998-2015) through MplusAutomation in R

(Hallquist & Wiley, 2018; RCore Team, 2017) using the EM algorithm (Dempster, Laird & Rubin, 1976) to obtain maximum likelihood estimates in a general latent variable modeling framework (Muthen, 2004; Muthen & Shedden, 1999). In each sampled data set the DTSM model with a mediator with a time *variant* effect and with a mediator with a time *invariant* effect was modeled using the logit link for the time-to-event outcome data. As discussed in the review of the literature, the bias-corrected bootstrap has the greatest power to detect the mediated effect (MacKinnon et al., 2004). In this resampling method of testing the significance of the mediated effect, the empirically built distribution accounts for the asymmetry in the sampling distribution of *ab* and builds the empirical distribution around the true population parameter (Efron & Tibshirani, 1994). I utilized 1,000 bootstrap draws to construct the bias-corrected confidence intervals in each replicated sample.

Simulation Outcomes. Several of the outcomes of interest in the applied example are synonymous with the outcomes investigated above, including percentage bias in parameter estimation of the nonzero indirect effect(s), confidence interval coverage, power, and type one error. In addition, in the expanded study, performance of the loglikelihood ratio test, AIC, BIC and aBIC to discern the correct population model was examined.

Bias in parameter estimation. To understand variability in estimates of nonzero mediated effects, I examined percentage relative bias of nonzero *ab* parameter estimates. Relative bias can be defined as the average deviance of a given sample estimate from the population parameter estimate, relative to the population parameter value and is denoted by the following equation:

$$RB\left(\hat{\theta}\right) = \sum_{j=1}^{n_r}\left(\frac{\widehat{\theta_{ij}}-\theta_i}{\theta_i}\right) / n_r \quad (16)$$

Here θ_{ij} is the parameter estimate in the sample, θ_i represents the population parameter and n_r reflects the number of replications. This estimate can then be multiplied by 100% to yield an estimate of the percentage relative bias. Lower values of bias are preferred. A boundary of percentage relative bias less than 5% was used as the criterion for an unbiased parameter estimate (Hoogland & Boomsma, 1998). The values obtained were compared to this criteria for both correctly and misspecified conditions. Under both conditions, empirical estimates were compared to a population mediated effect of -.060.

Power. Power to detect a mediated effect that was nonzero in the respective population model was also explored across all conditions. Empirical power for each condition was calculated as the number of times that the mediated effect parameter estimate was statistically significant across the 1,000 replication samples; Bias-corrected, bootstrapped confidence intervals (95%) were utilized for hypothesis testing. Often, a value of .80 power is sought (Cohen, 1992); the power estimate for each nonzero mediated effect in the population model was compared to this criterion.

Type one error. To further understand the accuracy of hypothesis testing with the 95% bias-corrected, bootstrapped confidence intervals, I examined type one error associated with mediated effect parameter estimates that were zero in the respective population model in correctly specified conditions[3]. Type one errors were represented when a significant mediated effect was detected in a replication from which the

[3] Note that there was only one mediated effect estimated in misspecified conditions. The number of times this effect was statistically significant was explored; there was no opportunity to explore type one error in misspecified conditions.

population effect was null. The type one error rate was calculated as the number of times this occurs, divided by the number of replications. These rates were compared to the nominal value of .05, conventionally used as the α- level in the applied literature. More specifically, rejection rates between 2% and 8% were deemed acceptable (Shi, DiStefano, McDaniel & Jiang, 2018).

Confidence interval coverage. Confidence interval coverage was also examined in correctly specified conditions to understand how often the mediated effect population value was contained within the 95% bias-corrected, bootstrapped confidence interval[4]. It was anticipated that the population value will be contained within the interval in approximately 95% of the replications; the obtained value was compared to this expected value to understand accuracy of the 95% bias-corrected, bootstrapped confidence interval. Moreover, it has been suggested that a confidence interval with coverage values of less than 90% is too wide and problematic (Collins, Schafer & Kam, 2001; Enders, 2001); confidence interval coverage greater than 90% was deemed acceptable.

Model fit. Both the correctly specified and misspecified models that are being observed here are conceptualized and estimated as single class mixture models. Given that these models have the same number of classes, the loglikelihood ratio test can be used to determine the better fitting model (Muthen & Masyn, 2005). When comparison involves models that have differing numbers of classes, the BIC is recommended for usage (Muthen & Masyn, 2005). While model comparisons in this simulation study do

[4] Confidence interval coverage was not examined in misspecified conditions. While it was of interest to understand how frequently the mediated effect was significant across misspecified conditions, it was not anticipated that looking at confidence interval coverage with a population parameter of *ab* = -.060 would be particularly meaningful.

not involve models with differing numbers of classes, the BIC as well as aBIC and AIC were studied as possible additional indicators of model fit. In this study, to understand if the nested loglikelihood ratio test, AIC, BIC and aBIC were likely to detect a misspecified model, model fit statistics were compared between correctly (i.e., a DTSM model with a time variant effect of the mediator) and incorrectly specified models (i.e., a DTSM model with a time invariant effect of the mediator). More specifically, the percentage of times that the nested loglikelihood ratio test indicated that the DTSM model with a time variant effect was significantly better fitting was calculated. Higher percentage rates indicate greater rates of indicating the correctly specified model. In addition, the rates at which the AIC, BIC and aBIC denote that the DTSM model with a time variant effect was a better fitting model were calculated (i.e., the AIC/BIC/aBIC is smaller for the DTSM model with a time variant effect than the DTSM model with a time invariant effect).

Results

All model replications converged across cells in the simulation study.

Percentage relative bias. Percentage relative bias for nonzero mediated effects is presented below in Table 5.1. In correctly specified conditions, all but two values were below the 5% relative bias criterion, suggesting that mediated effects were predominately unbiased (Hoogland & Boomsma, 1998). In the conditions in which the model was correctly specified, there were eight waves of data, and sample size was small (i.e., 250), percentage relative bias reached 6.35% when half of the mediated effects were nonzero and 5.06% when only one of the mediated effects was nonzero. Percentage relative bias generally increased in magnitude with decreasing sample size. The exception was for the

Table 5.1

Percentage Relative Bias in Nonzero Mediated Effects

			Correctly Specified			*Misspecified*
Pattern	Waves	N	ab_1	ab_2	ab_3	ab_1
1	8	1000	1.25	--	--	***-70.15***
		500	1.53	--	--	***-69.61***
		250	**5.06**	--	--	***-67.89***
1	6	1000	-0.07	--	--	***-63.43***
		500	0.38	--	--	***-63.53***
		250	0.56	--	--	***-62.99***
2	8	1000	1.17	0.60	-4.53	***-30.57***
		500	1.46	1.00	-3.81	***-29.97***
		250	4.89	**6.35**	-2.33	***-27.64***
2	6	1000	-0.12	-0.19	--	***-36.15***
		500	0.39	-0.53	--	***-36.19***
		250	0.60	0.34	--	***-35.00***

specific mediated effect, ab_3, which decreased in magnitude with decreasing sample size. In addition, while the pattern of the mediated effect did not seem to impact the level of relative bias, the magnitude of bias was attenuated with fewer waves of data. That is, percentage relative bias was smaller when there were six waves of data as compared to eight waves of data.

While mediated effects were predominately overestimated in correctly specified conditions, effects were underestimated, and to a larger degree, in misspecified conditions. In all conditions, the mediated effect was severely biased when the model was misspecified. Similar to correctly specified conditions, when there was only one nonzero mediated effect, bias was smaller in magnitude in conditions with six waves of data. However, when half of the mediated effects were nonzero, bias was smaller when there were eight waves of data. In contrast to correctly specified conditions, bias decreased in magnitude with decreasing sample size.

Coverage. Bias-corrected, bootstrapped confidence interval coverage was adequate across all studied conditions (see Table 5.2). Confidence interval coverage ranged from 92.9% – 96.4%, falling well above the suggested 90% criterion (Collins, Schafer & Kam, 2001; Enders, 2001).

Type one error. Akin to results related to confidence interval coverage, Type I error was well controlled across all studied conditions (see Table 5.3). Acceptable values were deemed to fall between 2% and 8% (Shi, DiStefano, McDaniel & Jiang, 2018), and across all correctly specified conditions, rates fell between .040 and .076.

Power. In correctly specified conditions, power to detect a nonzero mediated effect reached the .80 criterion (i.e., Cohen, 1992) only in conditions with large sample

Table 5.2

Coverage of Mediated Effect in Correctly Specified Models

Pattern	**Waves**	**N**	ab_1	ab_2	ab_3
1	8	1000	96.4	--	--
		500	95.9	--	--
		250	95.8	--	--
1	6	1000	94.2	--	--
		500	94.6	--	--
		250	95.2	--	--
2	8	1000	96.3	94.1	95.2
		500	95.7	94.3	95.4
		250	95.6	92.9	94.2
2	6	1000	94.0	95.5	--
		500	94.6	94.8	--
		250	95.4	93.7	--

Table 5.3

Type One Error of Mediated Effects in Correctly Specified Models

Pattern	**Waves**	**n**	ab_1	ab_2	ab_3	ab_4	ab_5	ab_6
1	8	1000	--	.076	.059	.064	.058	.062
		500	--	.075	.065	.073	.075	.073
		250	--	.058	.040	.063	.051	.058
1	6	1000	--	.073	.066	.069	--	--
		500	--	.061	.060	.072	--	--
		250	--	.048	.053	.070	--	--
2	8	1000	--	--	--	.070	.056	.061
		500	--	--	--	.074	.074	.072
		250	--	--	--	.057	.055	.044
2	6	1000	--	--	.071	.068	--	--
		500	--	--	.068	.067	--	--
		250	--	--	.052	.063	--	--

sizes (i.e., n = 1,000; see Table 5.4). Even when sample size was large, there were eight waves of data and half of the mediated effects were nonzero (i.e., $ab_{1\text{-}3}$ = -.060), power to detect ab_3 was low (i.e., power = .658). In general, power to detect nonzero mediated effects decreased with decreasing sample size. Power was conspicuously low when sample size was small (i.e., 250); this was especially so to detect ab_3 when sample size was small, there were eight waves of data and half of the mediated effects were nonzero (i.e., power = .195) as well as to detect ab_2 when sample size was small, there were six waves of data and half of the mediated effects were nonzero (i.e., power = .245). In conditions where there was more than one nonzero mediated effect, power decreased with increasing time points (i.e., power to detect ab_1 > power to detect ab_2). In addition, power to detect the mediated effect was greater when there were more data points (i.e., waves = 8).

In the misspecified model conditions in which a time invariant effect of the mediator was modeled on the time to event outcome, there were a handful of conditions in which power to detect a nonzero mediated effect exceeded the .80 criterion (Cohen, 1992). When half of the mediated effects were nonzero in the population model and sample size was large, power was high (i.e., > .93) to detect a nonzero mediated effect. Similarly, when there were eight waves of data, half of the mediated effects were nonzero in the population model and sample size was moderate, the time invariant mediated effect was significant in 810 of 1,000 replications. In all other misspecified conditions, power fell below .80, ranging from .140 - .658. Across these conditions, power decreased with decreasing sample size as well as increased when there was more than one nonzero mediated effect in the population model.

Table 5.4

Power to Detect Mediated Effects

			Correctly Specified			***Misspecified***
Pattern	**Waves**	**n**	ab_1	ab_2	ab_3	ab_1
1	8	1000	**.927**	--	--	.447
		500	.672	--	--	.258
		250	.366	--	--	.140
1	6	1000	**.906**	--	--	.516
		500	.641	--	--	.322
		250	.327	--	--	.158
2	8	1000	**.927**	**.821**	.658	**.984**
		500	.672	.567	.430	**.810**
		250	.362	.291	.195	.458
2	6	1000	**.903**	**.807**	--	**.935**
		500	.645	.547	--	.658
		250	.327	.245	--	.327

Model fit. The percentage of times that the loglikelihood ratio test indicated the correctly specified model was low across all studied conditions, ranging from .15 - .57 (see Table 5.5). This percentage was highest when the sample size was large; the number of waves of data and pattern of mediated effects did not appear to impact the percentage of times the loglikelihood ratio test indicated the correctly specified model.

The AIC appeared to perform better than the loglikelihood ratio test; the AIC indicated that the correctly specified model was better fitting more often than the loglikelihood ratio test. In general, the AIC appeared to perform better in terms of model selection when sample size was large and there were fewer waves of data (i.e., waves = six). The pattern of the mediated effect did not seem to play an important role in the performance of the AIC.

The BIC performed worst in terms of model selection (i.e., selecting the true population model as the better fitting model). The BIC indicated that the population model was the better fitting model in 0 – 50 replications per condition (i.e., out of 1,000 total replications per condition). The BIC performed better when there were fewer waves of data and when sample size was larger. Like findings related to the performance of the loglikelihood ratio test and AIC, the pattern of the mediated effects did not seem to impact the performance of the BIC.

Finally, the aBIC performed more favorably than the BIC but still not as well as the loglikelihood ratio test and AIC. The performance of the aBIC followed a similar pattern to the loglikelihood ratio test and AIC in that it's performance decreased with decreasing sample size. Additionally, the aBIC seemed to perform better when there were fewer waves of data (i.e., waves = 6). For example, when there was one, nonzero

Table 5.5

Model Fit

		8 Waves				*6 Waves*			
Pattern	n	*LRT*	*AIC*	*BIC*	*aBIC*	*LRT*	*AIC*	*BIC*	*aBIC*
1	1000	.56	.63	.00	.17	.56	.71	.04	.34
	500	.28	.34	.00	.11	.32	.47	.02	.24
	250	.17	.21	.00	.13	.18	.30	.01	.23
2	1000	.53	.59	.01	.16	.57	.72	.05	.34
	500	.26	.34	.00	.10	.31	.45	.02	.23
	250	.15	.21	.00	.13	.15	.28	.01	.20

mediated effect, and sample size was large (i.e., n = 1,000) the aBIC retained the population model in 17% of replications when there were eight waves of data and in 34% of replications when there were six waves of data. The pattern of the mediated effect did not appear to have a substantial impact on the performance of the aBIC.

Discussion of the Expanded Monte Carlo Study

The expanded Monte Carlo study was conducted to evaluate a mixture modeling framework for estimating a discrete time survival mediation model with a time variant effect of the mediator in conditions that were less ideal than those simulated in the single-cell Monte Carlo study presented in Study Two. Results suggest that across all correctly specified conditions, Type one error was well controlled and confidence interval coverage was adequate. Additionally, in correctly specified conditions, estimates of the indirect effect were predominately unbiased, with only two values exceeding the 5% cutoff. Therefore, on average across replications in correctly specified conditions studied, there is little concern regarding bias in mediated effects. In addition, in correctly specified conditions, power for the mediated effects exceeded the .80 cutoff when sample size was large (i.e., n = 1,000). However, even when sample size was large, power to detect the third mediated effect fell below the desired threshold (i.e., power for ab_3 = .658). This is expected, given that sample size for the discrete-time outcome indicators decreases with increasing waves of data collection. As described in the review of the literature and discussion of the coding scheme for the outcome data in Study One, once a subject experiences the event of interest, the subject's onset indicators at subsequent time points are coded as missing so that they are no longer included in the risk set. Therefore, it is understandable that power to detect the mediated effect decreases with increasing

time points. Although not studied here, it is likely that power would continue to decrease for mediated effects observed in later onset periods (e.g., on the onset indicator at waves 4-6). This warrants investigation in future research.

Fairchild and colleagues (2018) examined a general linear modeling approach to estimating the DTSM model under correctly specified conditions (i.e., with the logit link and estimating only time invariant effects). Under correctly specified conditions, results obtained here using a mixture modeling framework and with a time variant effect of the mediator generally align with this previous research. Given that Fairchild and colleagues (2018) only examined conditions in which the estimated model was correctly specified, only conditions in the current study that were correctly specified can be compared across overlapping outcomes (i.e., percentage relative bias, Type one error, and power to detect the mediated effect). Like results in the current study suggest, Fairchild et al., (2018) found that across all conditions studied the estimates of the mediated effect were unbiased (i.e., percentage relative bias < 1.5% across all studied conditions). In the current study, bias was of greater magnitude than the previous study but below a 5% criterion in all but two conditions. Fairchild et al., (2018) ascertained that none of the conditions studied influenced the magnitude of bias (i.e., number of waves of data, sample size, effect sizes of parameter estimates). However, in the current study it appears that bias generally increased in magnitude with decreasing sample size. In addition, while the pattern of the mediated effect did not seem to impact the level of relative bias, the magnitude of bias was attenuated with fewer waves of data. However, as suggested by Fairchild et al., (2018) it appears that, in general, there should be little alarm regarding bias in the mediated effect estimate when the model is correctly specified.

Similarly, like the work of Fairchild and colleagues (2018) exemplified, Type one error was well controlled across all correctly specified conditions studied. Also, akin to results of Fairchild et al., (2018) sample size impacted power to detect the mediated effect. However, in the previous study, sample size was implicated as impacting power through a series of interactions with parameter estimate effect sizes. For example, sample size interacted with the effect size of the *a* parameter estimate to impact power to detect the mediated effect. As sample size increased power also increased, but the gains were qualified by the magnitude of *a*, such that the change in power across sample size was most disparate when the effect size of *a* was small. It is anticipated that similar effects may have been observed in the current study, however, levels of the effect size of parameter estimates were not varied, so these effects could not have been observed in the current work. Rather, the mediated effect(s) were held constant (*ab* = -.060). In addition to sample size, in the present study, when conditions were correctly specified, power to detect the mediated effect was greater when there were more data points (i.e., waves = 8); an effect of waves of data on power was not denoted by Fairchild and colleagues (2018).

In general, results across both studies converge. Percentage relative bias was negligible, with slightly higher rates in the current study. Type one error was well controlled across both studies. And power to detect the mediated effect was similarly impacted by sample size across both studies, however, in the Fairchild et al., (2018) study the effect was moderated by effect sizes of parameter estimates, which were not manipulated in the current study. In addition, in the current study, number of waves of data impacted power to detect the mediated effect, with more waves of data associated with greater power.

The current research also extended the Fairchild et al., (2018) work by studying misspecified models. More specifically, data were generated to reflect a time variant effect of the mediator on the outcome indicators but a time invariant effect of the mediator was estimated. As a whole, results in misspecified conditions suggest that the model is sensitive to model misspecification, but that the relative fit indices are underpowered to reject a misspecified model in all conditions studied here. In misspecified conditions, percentage relative bias ranged from -27.64% to -70.15%, all grossly underestimating the nonzero time variant, mediated effect(s). This aligns with literature that suggests that misspecifications of finite mixture models can result in bias in estimation (Enders & Tofighi, 2008; Gray, 1994; McLachlan & Peel, 2000; Muthen, 2004). Bias was more pronounced in conditions with only one nonzero mediated effect in the population model, with percentage relative bias ranging from -62.99% to -70.15% in these conditions; estimates ranged from -27.64% to -36.15% when half of the mediated effects were nonzero in the population model. These findings align with power to detect the mediated effect in misspecified models. When there was only one significant mediated effect in the population model, the mediated effect modeled in the misspecified model was only significant in 14.0% to 51.6% of replications. Alternatively, when half of the population effects were significant but only one invariant effect was estimated in the misspecified model, 32.7% to 98.4% of indirect effects were statistically significant. Indeed, there was adequate power to detect a significant mediated effect in three of six conditions in which half of the mediated effects were nonzero in the population model. Together, this suggests that when there is only one significant mediated effect in the population model with a time variant effect of the mediator, but a single time invariant

effect of the mediator is estimated in a misspecified model, bias is likely to be high and the single, estimated mediated effect is unlikely to be nonzero, overall masking "how" or "why" a process unfolds at a particular time point.

This issue is further compounded by the fact that all of the relative fit indices observed in this study were underpowered across all studied conditions to detect a misspecified model. The focal model of this study, the DTSM with a time variant effect of the mediator, was conceptualized and estimated as a single class mixture model. The misspecified model was similarly conceptualized and estimated as a single class mixture model, but with a time invariant effect of the mediator. Given that these models have the same number of classes, the loglikelihood ratio test can be used to determine the better fitting model (Muthen & Masyn, 2005). Both the loglikelihood ratio test and AIC were consistently underpowered to reject the misspecified model, however, performed much better than the BIC and aBIC. Both the BIC and aBIC demonstrated very low power to reject the misspecified model, with the BIC performing worst. When comparison involves models that have differing numbers of classes, the BIC is recommended for comparing between models (Muthen & Masyn, 2005). In fact, it has been suggested in the finite mixture modeling literature that the BIC and aBIC have particular utility in class enumeration (Jedidi, Jagpal, & DeSarbo, 1997; Nylund, Asparouhov, & Muthén, 2007; Tofighi & Enders, 2006; Yang, 2006). While class enumeration was not the goal here, it was anticipated that the BIC and aBIC would informatively supplement the loglikelihood ratio test. However, it appears that when the number of classes is held constant, the loglikelihood ratio and AIC are most powered to reject the misspecified model, yet still not at desired levels (i.e., power = .80). Given the issues discussed above

regarding bias in the mediated effect and power to detect the mediated effect, being unable to detect a misspecified model is particularly problematic.

There are several limitations in the current study that should be addressed in future work in this area. First, performance of the model was only examined in 24 unique conditions. Future research should extend the currently studied conditions by examining additional levels of the factors studied here as well as other factors that were not considered in the current research. For example, it is anticipated that if significant indirect effects had been modeled at one of the latest event indicators, power to detect the indirect effect would be even lower. Similarly, as there were important effects noted in the work by Fairchild et al., (2018) involving effect sizes of various parameter estimates, this would warrant investigation in future research. Studying different patterns of the time variant mediated effects may also be important; varying the size of the mediated effects within a single population may produce interesting findings.

More subtly, in the Fairchild et al., (2018) research, the percentile bootstrapped confidence interval was utilized to assess the significance of the mediated effect in contrast to the bias-corrected bootstrapped confidence interval. Prior research indicates that the bias-corrected bootstrapped confidence interval has increased power over other approaches to detect a mediated effect, however, also demonstrates increased Type one error rates (Fritz & MacKinnon, 2007). However, it is worth nothing that in the conditions studied in the current work, the bias-corrected, bootstrapped confidence interval did not demonstrate inflated Type one error rates.

CHAPTER SIX

INTEGRATED DISCUSSION

The overarching goal of this work was to extend the existing research on DTSM models estimated in a structural equation modeling framework by incorporating a mediator with a time variant effect in a mixture modeling framework (Fairchild et al., 2015; Fairchild et al., 2018; Masyn, 2014; Muthen & Masyn, 2005). First, an applied example was utilized to demonstrate a model building approach to determine the best fitting model and to garner parameter estimates to be utilized in a Monte Carlo study (i.e., Study One). Next, a single cell simulation study was conducted using parameter estimates and data characteristics (i.e., sample size, number of waves of data) from the applied example to understand estimation of the DTSM model in a mixture modeling framework in conditions that were based in a real-world application but were also ideal (i.e., large sample size and many waves of data; Study Two). Finally, an extended Monte Carlo study was conducted to observe estimation of the model in less ideal conditions (i.e., sample size, number of waves of data, pattern of time variant effect of the mediator and [mis]specification) to determine how these factors impacted power, Type one error and confidence interval coverage of the mediated effect(s) as well as model fit.

Results of the applied example in Study One suggested that the DTSM model with a time invariant impact of PM on the log hazard odds of event occurrence fit the data best. However, given the focus of this research, the DTSM model with a time variant

mediator was retained as the final model for demonstration purposes as well as for parameter estimates for the subsequent Monte Carlo studies. Results of the final, retained model suggested that there was no direct effect of interparental support on the latent propensity for event occurrence. However, there was a single, significant indirect effect of IS on the log hazard odds of youth alcohol onset through parental monitoring at age 15.

It is interesting to consider the results of the model building procedure used in the NLSY97 data application after the explication of the results from the expanded Monte Carlo study (i.e., Study Three). Results of Study Three suggested that the loglikelihood ratio, AIC, BIC, and aBIC infrequently indicate that the correctly specified model is the best fitting model, even in ideal conditions similar to those observed in the NLSY97 application (e.g., large sample size). It may be that the fit indices were underpowered to detect that the DTSM model with a time invariant effect of the mediator was not the best fitting model. Interestingly, when the DTSM model with a time variant effect of the mediator was estimated, there was a single, significant mediated effect at age 15. If these findings are accurate, they may provide important insight to interventionists on timing of prevention and intervention efforts aimed at familial relations and parenting. These findings are masked by potentially underpowered fit indicators.

Parameter estimates and characteristics of the data from the applied example were used to conduct a single cell simulation. Results of the single-cell Monte Carlo in Study Two purported that under conditions similar to the applied example, power, type one error, confidence interval coverage and bias of the indirect effect were all within

acceptable limits. These favorable results served as the foundation for studying less ideal conditions in the expanded Monte Carlo study (i.e., Study Three).

Results of the expanded simulation in Study Three provided important information related to misspecification of DTSM models in a mixture modeling framework. In correctly specified conditions, type one error was well controlled and confidence interval coverage was adequate. Similarly, in correctly specified conditions, estimates of the indirect effect were predominately unbiased. Findings in misspecified conditions were quite disparate. The model appears to be quite sensitive to model misspecification, however, the relative fit indices appear to be unlikely to reject a misspecified model in all conditions studied here. Given the issues discussed above regarding relative bias in the mediated effect and power to detect the mediated effect, being unable to detect a misspecified model is particularly problematic. Future research should consider additional fit indices as well as additional investigation into the currently studied indices under additional conditions.

This work integrates and extends the extant literature in several ways. The current research expands the work by Fairchild and colleagues (2015; 2018) by extending the model to look at a mediator with a time variant effect. Traditionally, discrete time survival analysis assumes that the impact of a predictor on the logit hazard is constant across time periods (i.e., proportionality assumption; see Singer & Willett, 1993). However, it may be that "violations of the proportionality assumption are the rule, rather than the exception" (Singer & Willett, 1991, p. 279). Given this important observation, it is critical to consider the utilization of models that relax this assumption, such as the DTSM model with a time variant effect of the mediator. By incorporating both mediation

and discrete-time survival analysis as well as a mediator with a time variant effect, the model allows for the examination of direct and indirect effects of a predictor on the timing of the occurrence of an event while also considering that the impact of the mediator may vary over time. In research on developmental trajectories related to youth alcohol use, this model could help researchers understand how developmental pathways operate in concert with parenting behaviors to impact timing to onset of youth alcohol use differentially over time. The information garnered could then inform how targets of prevention or treatment for youth alcohol use may change over the course of development.

In addition to extending DTSM models to incorporate time variant effects of covariates, the current work integrates the work of Fairchild and colleagues (2015; 2018) and Muthen and Masyn (2005) by estimating the DTSM model in a finite mixture modeling framework. The current study estimates the model in its simplest mixture form as a single class mixture model (Muthen & Masyn, 2005). Estimating the model in the mixture modeling framework offers many attractive extension opportunities. In general, in structural equation modeling, latent constructs can be modeled by incorporating measurement models to partition true variance and error variance. Partitioning out measurement error in mediation analysis can help to guard against Type I and Type II errors (Cole & Maxwell, 2003). In particular, estimation in a mixture modeling framework can allow for further extensions, such as nonparametric modeling of frailties (i.e., unobserved heterogeneity) in the timing to event onset outcome and incorporation of other modeling techniques, such as growth mixture modeling (Muthen & Masyn, 2005). However, these gains come with notable limitations associated with mixture modeling,

such as sensitivity to model misspecification, that warrant careful consideration (Enders & Tofighi, 2008; Gray, 1994; McLachlan & Peel, 2000; Muthen, 2004).

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APPENDIX A

APPLIED EXAMPLE MPLUS CODE

```
TITLE: DTSM Model with a Time Variant Effect of the Mediator

- X: Father reported support of mother (FISM5)
- M: mother monitoring (MM3a, MM3b; duplicate variables)
- Y: onset of substance use 14 years on (de14-de21)

DATA:
FILE IS MIXTUREdata.csv;

VARIABLE:
NAMES ARE de14 de15 de16 de17 de18 de19
de20 de21 FISM5 MM3a MM3b;
USEVARIABLES ARE de14 de15 de16 de17 de18 de19
de20 de21 FISM5 MM3a MM3b;
CATEGORICAL = de14 de15 de16 de17 de18 de19
de20 de21;
MISSING ARE ALL (999);
CLASSES = class (1);

DEFINE:
CENTER FISM5 MM3a MM3b(GRANDMEAN);

ANALYSIS:
TYPE = MIXTURE;
ESTIMATOR = ML;
LINK = LOGIT;
ALGORITHM = EM INTEGRATION;
BOOTSTRAP = 1000;

MODEL:
%OVERALL%
 MM3a ON FISM5 (p1);
FISM5;
[FISM5];
[de14$1 de15$1 de16$1 de17$1 de18$1 de19$1 de20$1
de21$1];
```

```
ONSET BY de14@1 de15@1 de16@1 de17@1 de18@1 de19@1
de20@1 de21@1;
ONSET@0;
ONSET ON FISM5;
ONSET ON MM3b@0;
ONSET ON MM3a@0;
de14 de15 de16 de17 de18 de19 de20 de21 ON MM3b (p2 - p9);

MODEL CONSTRAINT:
NEW (ab1-ab8);
ab1 = p1 * p2;
ab2 = p1 * p3;
ab3 = p1 * p4;
ab4 = p1 * p5;
ab5 = p1 * p6;
ab6 = p1 * p7;
ab7 = p1 * p8;
ab8 = p1 * p9;

OUTPUT:
SAMPSTAT;
CINTERVAL(bcboot);
```

Programming Notes:

TITLE command:

Create a title for the analysis.

DATA command:

Indicate the data file.

VARIABLE command:

Name each variable in the dataset. Specify which variables will be used in the analyses. Specify the binary event outcome indicators for each time period by defining them as categorical. Identify the missing value code. Specify the estimation of a single class.

DEFINE command:

Center predictors.

ANALYSIS command:

Specify a mixture model with ML estimation, the logit link function and EM algorithm. Request 1000 bootstrap draws.

MODEL command:

Estimate the *a* path of the mediation model by regressing M on X and name the parameter. Estimate the mean and variance of X. Create a latent factor defined by the binary event indicators. Constrain all the factor loadings to be equal, estimate all thresholds and fix the variance of the latent factor to zero. Estimate the c' path of the mediation model by regressing the latent factor on X and name the parameter. Constrain the effect of the mediator (and it's duplicate) on the

latent construct at zero. Estimate the time variant effect of the mediator on each event indicator by regressing each binary outcome indicator on the mediator. Name each *b* parameter.

MODEL CONSTRAINT command:

Define each indirect effect by naming the indirect effect and calculate it using the respective estimated parameters.

OUTPUT command:

Request sample statistics and the bias-corrected, bootstrapped confidence intervals.

APPENDIX B

EXAMPLE SIMULATION R CODE

```
c=1

path=sprintf("C:\\DissSim\\c%d",c)
setwd(path)

batch<-paste0('C:\\Program Files\\Mplus','
           ',
           'Mplus  ', path,'\\Sim.inp', '  ', path,'\\Sim.out
           EXIT')

write.table(batch, "BATCH.bat", sep="",row.names=F,col.names = F,quote = F)

imp<-paste0('MONTECARLO:
          names = x m1 on1 on2 on3 on4 on5 on6;
          generate = on1-on6(1);
          categorical = on1-on6;
          nrep = 1000;
          seed = 051218;
          nobs = 1026;
          genclasses = c (1);
          classes = c (1);
          missing = on2-on6;
          repsave=all;
          save=rep*.DAT;

          ANALYSIS:
          TYPE = MIXTURE;
          ESTIMATOR = ML;
          LINK = LOGIT;
          ALGORITHM = EM INTEGRATION;

          MODEL POPULATION:

          %OVERALL%

          x@.438;
          [x@0];
```

```
        m1 ON x@.187;
        m1*.554;

        [
        on1$1*1.256
        on2$1*1.264
        on3$1*1.041
        on4$1*1.133
        on5$1*1.233
        on6$1*.826
        ];

        ONSET BY on1@1 on2@1 on3@1 on4@1 on5@1 on6@1;

        ONSET@0;

        ONSET ON x@0;
        ONSET ON m1@0;

        on1 ON m1@-.319;
        on2 ON m1@0;
        on3 ON m1@0;
        on4 ON m1@0;
        on5 ON m1@0;
        on6 ON m1@0;

        MODEL MISSING:

        %OVERALL%

        [on2-on6@-15];
        on2 ON on1@30;
        on3 ON on1-on2@30;
        on4 ON on1-on3@30;
        on5 ON on1-on4@30;
        on6 ON on1-on5@30;
        ')

write.table(imp, "Sim.inp", sep="",row.names=F,col.names = F,quote = F)
shell ("BATCH.bat")

batch<-paste0('C:\\Program Files\\Mplus','
          ',
          'Mplus  ', path,'\\ana.inp', '  ', path,'\\ana.out
          EXIT')
```

```
write.table(batch, "BATCH2.bat", sep="",row.names=F,col.names = F,quote = F)

NR=1000

ONonX=c(rep(NA,NR))
ONonXse=c(rep(NA,NR))
ONonXp=c(rep(NA,NR))

M1onX=c(rep(NA,NR))
M1onXse=c(rep(NA,NR))
M1onXp=c(rep(NA,NR))

On1onM2=c(rep(NA,NR))
On1onM2se=c(rep(NA,NR))
On1onM2p=c(rep(NA,NR))

On2onM2=c(rep(NA,NR))
On2onM2se=c(rep(NA,NR))
On2onM2p=c(rep(NA,NR))

On3onM2=c(rep(NA,NR))
On3onM2se=c(rep(NA,NR))
On3onM2p=c(rep(NA,NR))

On4onM2=c(rep(NA,NR))
On4onM2se=c(rep(NA,NR))
On4onM2p=c(rep(NA,NR))

On5onM2=c(rep(NA,NR))
On5onM2se=c(rep(NA,NR))
On5onM2p=c(rep(NA,NR))

On6onM2=c(rep(NA,NR))
On6onM2se=c(rep(NA,NR))
On6onM2p=c(rep(NA,NR))

XMEAN=c(rep(NA,NR))
XMEANse=c(rep(NA,NR))
XMEANp=c(rep(NA,NR))

XVAR=c(rep(NA,NR))
XVARse=c(rep(NA,NR))
XVARp=c(rep(NA,NR))
```

```
M1INT=c(rep(NA,NR))
M1INTse=c(rep(NA,NR))
M1INTp=c(rep(NA,NR))

M1RES=c(rep(NA,NR))
M1RESse=c(rep(NA,NR))
M1RESp=c(rep(NA,NR))

ON1TH=c(rep(NA,NR))
ON1THse=c(rep(NA,NR))
ON1THp=c(rep(NA,NR))

ON2TH=c(rep(NA,NR))
ON2THse=c(rep(NA,NR))
ON2THp=c(rep(NA,NR))

ON3TH=c(rep(NA,NR))
ON3THse=c(rep(NA,NR))
ON3THp=c(rep(NA,NR))

ON4TH=c(rep(NA,NR))
ON4THse=c(rep(NA,NR))
ON4THp=c(rep(NA,NR))

ON5TH=c(rep(NA,NR))
ON5THse=c(rep(NA,NR))
ON5THp=c(rep(NA,NR))

ON6TH=c(rep(NA,NR))
ON6THse=c(rep(NA,NR))
ON6THp=c(rep(NA,NR))

ab1=c(rep(NA,NR))
ab1L= c(rep(NA,NR))
ab1H= c(rep(NA,NR))

ab2=c(rep(NA,NR))
ab2L= c(rep(NA,NR))
ab2H= c(rep(NA,NR))

ab3=c(rep(NA,NR))
ab3L= c(rep(NA,NR))
ab3H= c(rep(NA,NR))

ab4=c(rep(NA,NR))
ab4L= c(rep(NA,NR))
```

```
ab4H= c(rep(NA,NR))

ab5=c(rep(NA,NR))
ab5L= c(rep(NA,NR))
ab5H= c(rep(NA,NR))

ab6=c(rep(NA,NR))
ab6L= c(rep(NA,NR))
ab6H= c(rep(NA,NR))

Rep= c(rep(NA,NR))
Condition= c(rep(NA,NR))

for(j in 1:1000){
  ana<-paste0('data: file is rep',j,'.dat;
              VARIABLE:
              NAMES ARE ON1
              ON2
              ON3
              ON4
              ON5
              ON6
              X
              M1
              C;

              USEVARIABLES ARE ON1
              ON2
              ON3
              ON4
              ON5
              ON6
              X
              M1
              M2;

              CATEGORICAL = ON1
              ON2
              ON3
              ON4
              ON5
              ON6;

              MISSING ARE ALL (999);

              CLASSES = class (1);
```

```
DEFINE:
M2 = M1;

ANALYSIS:
TYPE = MIXTURE;
ESTIMATOR = ML;
LINK = LOGIT;
ALGORITHM = EM INTEGRATION;
BOOTSTRAP = 1000;

MODEL:

%OVERALL%

M1 ON X (p1);

X;
[X];


[ON1$1 ON2$1 ON3$1 ON4$1 ON5$1 ON6$1];

ONSET BY ON1@1 ON2@1 ON3@1 ON4@1 ON5@1 ON6@1;

ONSET@0;

ONSET ON X;
ONSET ON M1@0;
ONSET ON M2@0;

ON1 ON2 ON3 ON4 ON5 ON6 ON M2 (p2 - p7);

MODEL CONSTRAINT:

NEW (ab1-ab6);
ab1 = p1 * p2;
ab2 = p1 * p3;
ab3 = p1 * p4;
ab4 = p1 * p5;
ab5 = p1 * p6;
ab6 = p1 * p7;

OUTPUT: SAMPSTAT; CINTERVAL(bcboot);
')
```

```
  write.table(ana, "ana.inp", sep="",row.names=F,col.names = F,quote = F)
  shell ("BATCH2.bat")

  library(MplusAutomation)
  ab_CIs<-extractModelParameters("C:\\DissSim\\c1\\ana.out", recursive =
FALSE)$ci.unstandardized

  ab1[j]=ab_CIs[nrow(ab_CIs)-5,6]
  ab1L[j]=ab_CIs[nrow(ab_CIs)-5,4]
  ab1H[j]=ab_CIs[nrow(ab_CIs)-5,8]

  ab2[j]=ab_CIs[nrow(ab_CIs)-4,6]
  ab2L[j]=ab_CIs[nrow(ab_CIs)-4,4]
  ab2H[j]=ab_CIs[nrow(ab_CIs)-4,8]

  ab3[j]=ab_CIs[nrow(ab_CIs)-3,6]
  ab3L[j]=ab_CIs[nrow(ab_CIs)-3,4]
  ab3H[j]=ab_CIs[nrow(ab_CIs)-3,8]

  ab4[j]=ab_CIs[nrow(ab_CIs)-2,6]
  ab4L[j]=ab_CIs[nrow(ab_CIs)-2,4]
  ab4H[j]=ab_CIs[nrow(ab_CIs)-2,8]

  ab5[j]=ab_CIs[nrow(ab_CIs)-1,6]
  ab5L[j]=ab_CIs[nrow(ab_CIs)-1,4]
  ab5H[j]=ab_CIs[nrow(ab_CIs)-1,8]

  ab6[j]=ab_CIs[nrow(ab_CIs),6]
  ab6L[j]=ab_CIs[nrow(ab_CIs),4]
  ab6H[j]=ab_CIs[nrow(ab_CIs),8]

  unstand<-extractModelParameters("C:\\DissSim\\c1\\ana.out", recursive =
FALSE)$unstandardized

  ONonX[j]=unstand[nrow(unstand)-27,3]
  ONonXse[j]=unstand[nrow(unstand)-27,4]
  ONonXp[j]=unstand[nrow(unstand)-27,6]

  M1onX[j]=unstand[nrow(unstand)-24,3]
  M1onXse[j]=unstand[nrow(unstand)-24,4]
  M1onXp[j]=unstand[nrow(unstand)-24,6]

  On1onM2[j]=unstand[nrow(unstand)-23,3]
  On1onM2se[j]=unstand[nrow(unstand)-23,4]
  On1onM2p[j]=unstand[nrow(unstand)-23,6]
```

```
On2onM2[j]=unstand[nrow(unstand)-22,3]
On2onM2se[j]=unstand[nrow(unstand)-22,4]
On2onM2p[j]=unstand[nrow(unstand)-22,6]

On3onM2[j]=unstand[nrow(unstand)-21,3]
On3onM2se[j]=unstand[nrow(unstand)-21,4]
On3onM2p[j]=unstand[nrow(unstand)-21,6]

On4onM2[j]=unstand[nrow(unstand)-20,3]
On4onM2se[j]=unstand[nrow(unstand)-20,4]
On4onM2p[j]=unstand[nrow(unstand)-20,6]

On5onM2[j]=unstand[nrow(unstand)-19,3]
On5onM2se[j]=unstand[nrow(unstand)-19,4]
On5onM2p[j]=unstand[nrow(unstand)-19,6]

On6onM2[j]=unstand[nrow(unstand)-18,3]
On6onM2se[j]=unstand[nrow(unstand)-18,4]
On6onM2p[j]=unstand[nrow(unstand)-18,6]

XMEAN[j]=unstand[nrow(unstand)-17,3]
XMEANse[j]=unstand[nrow(unstand)-17,4]
XMEANp[j]=unstand[nrow(unstand)-17,6]

XVAR[j]=unstand[nrow(unstand)-8,3]
XVARse[j]=unstand[nrow(unstand)-8,4]
XVARp[j]=unstand[nrow(unstand)-8,6]

M1INT[j]=unstand[nrow(unstand)-16,3]
M1INTse[j]=unstand[nrow(unstand)-16,4]
M1INTp[j]=unstand[nrow(unstand)-16,6]

M1RES[j]=unstand[nrow(unstand)-7,3]
M1RESse[j]=unstand[nrow(unstand)-7,4]
M1RESp[j]=unstand[nrow(unstand)-7,6]

ON1TH[j]=unstand[nrow(unstand)-14,3]
ON1THse[j]=unstand[nrow(unstand)-14,4]
ON1THp[j]=unstand[nrow(unstand)-14,6]

ON2TH[j]=unstand[nrow(unstand)-13,3]
ON2THse[j]=unstand[nrow(unstand)-13,4]
ON2THp[j]=unstand[nrow(unstand)-13,6]

ON3TH[j]=unstand[nrow(unstand)-12,3]
ON3THse[j]=unstand[nrow(unstand)-12,4]
```

```
  ON3THp[j]=unstand[nrow(unstand)-12,6]

  ON4TH[j]=unstand[nrow(unstand)-11,3]
  ON4THse[j]=unstand[nrow(unstand)-11,4]
  ON4THp[j]=unstand[nrow(unstand)-11,6]

  ON5TH[j]=unstand[nrow(unstand)-10,3]
  ON5THse[j]=unstand[nrow(unstand)-10,4]
  ON5THp[j]=unstand[nrow(unstand)-10,6]

  ON6TH[j]=unstand[nrow(unstand)-9,3]
  ON6THse[j]=unstand[nrow(unstand)-9,4]
  ON6THp[j]=unstand[nrow(unstand)-9,6]

  Rep[j]=j
  Condition[j]=1

}

result=data.frame(Condition, Rep, ab1, ab1L, ab1H,
                  ab2, ab2L, ab2H,
                  ab3, ab3L, ab3H,
                  ab4, ab4L, ab4H,
                  ab5, ab5L, ab5H,
                  ab6, ab6L, ab6H,
                  ONonX, ONonXse, ONonXp,
                  M1onX, M1onXse, M1onXp,
                  On1onM2, On1onM2se, On1onM2p,
                  On2onM2, On2onM2se, On2onM2p,
                  On3onM2, On3onM2se, On3onM2p,
                  On4onM2, On4onM2se, On4onM2p,
                  On5onM2, On5onM2se, On5onM2p,
                  On6onM2, On6onM2se, On6onM2p,
                  XMEAN, XMEANse, XMEANp,
                  XVAR, XVARse, XVARp,
                  M1INT, M1INTse, M1INTp,
                  M1RES, M1RESse, M1RESp,
                  ON1TH, ON1THse, ON1THp,
                  ON2TH, ON2THse, ON2THp,
                  ON3TH, ON3THse, ON3THp,
                  ON4TH, ON4THse, ON4THp,
                  ON5TH, ON5THse, ON5THp,
                  ON6TH, ON6THse, ON6THp)

write.table(result, "result.csv",col.names=TRUE,row.names=FALSE, sep = ",")
```