# Pattern Mixture Models Incorporating Reasons for Dropout

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**Abstract**

For longitudinal data with dropouts, pattern mixture models (PMM) stratify the dataset by dropout patterns and model the repeated measures within each pattern. We propose a hierarchical PMM (HPMM) that incorporates not only dropout patterns but also various dropout reasons. Subjects are classified into random and nonrandom dropout groups and subsequently stratified according to dropout patterns within each group. The statistical inference is based on maximum likelihood. An ad-hoc method was also developed by estimating the potential dropout reasons for completers with a latent variable model and making inference with standard procedures for PMMs as if the group memberships were fully observed. Since classification of dropout reason is subjective, a simulation study was conducted to examine the potential bias of HPMM methods from group misclassification. These methods were also compared to the standard PMM, which disregarded differential dropout reasons, and a selection model that assumed ignorable dropouts.

**Key Words:** missing data, pattern mixture model, reasons for dropout

## 1. INTRODUCTION

Missing outcome data are prevalent in clinical trials with repeated measurements. Consequently, one of the most important considerations when selecting an analytic strategy is how it accounts for the missing data mechanism. If the data are missing completely at random (MCAR) or missing at random (MAR), available case analyses for repeated measures, such as a standard mixed model, can be used. However, if the data are missing not at random (MNAR), using a standard mixed model without accounting for the missingness may produce biased estimates.

### 1.1 Pattern Mixture Models

One analytical method that incorporates nonignorable missing values in repeated measures data is the pattern mixture model (PMM) (Little, 1995). This method factorizes the joint likelihood as:

$$[\mathbf{y}_i, R_i, \boldsymbol{\beta}_i|\mathbf{X}_i] = [\mathbf{y}_i|\mathbf{X}_i, \boldsymbol{\beta}_i, R_i][\boldsymbol{\beta}_i|\mathbf{X}_i, R_i][R_i|\mathbf{X}_i], \tag{1}$$

where $\mathbf{y}_i = \{y_{i1}, y_{i2}, \ldots, y_{iK}\}$ is a vector of repeated measures, $R_i$ is the dropout pattern such that $R_i = k$ if $\{y_{i1}, \ldots, y_{ik}\}$ are observed and $\{y_{ik+1}, \ldots, y_{iK}\}$ are missing, $\boldsymbol{\beta}_i$ represents the random intercept and slope effects, and $\mathbf{X}_i$ represents the baseline covariates. For an individual $i$, $[\mathbf{y}_i|\mathbf{X}_i, \boldsymbol{\beta}_i, R_i]$ models the repeated measures, $[\boldsymbol{\beta}_i|\mathbf{X}_i, R_i]$ models the between-subject variation, and $[R_i|\mathbf{X}_i]$ models the distribution of the dropout pattern.

A typical pattern mixture model that can handle nonignorable dropouts is the random-effects-dependent dropout pattern mixture model, which assumes that the outcome $\mathbf{y}_i$ only depends on the dropout pattern $R_i$ through the random effects $\boldsymbol{\beta}_i$. Thus, the joint likelihood is simplified from (1) as (Little, 1995):

$$[\mathbf{y}_i, R_i, \boldsymbol{\beta}_i|\mathbf{X}_i] = [\mathbf{y}_i|\mathbf{X}_i, \boldsymbol{\beta}_i][\boldsymbol{\beta}_i|\mathbf{X}_i, R_i][R_i|\mathbf{X}_i]. \tag{2}$$

Little (1995) considered a special case of this model for repeated measures data on subjects in $J$ treatment groups:

$$[\mathbf{y}_i|\boldsymbol{\beta}_i] \sim N_K\left(\begin{bmatrix} 1 & t_{i1} \\ \vdots & \vdots \\ 1 & t_{iK} \end{bmatrix} \begin{bmatrix} \beta_{i0} \\ \beta_{i1} \end{bmatrix}, \sigma_e^2\mathbf{I}\right),$$

$$[\boldsymbol{\beta}_i|x_i = j, R_i = k] \sim N_2(\boldsymbol{\beta}_j^{(k)}, \boldsymbol{\Gamma}), \quad j = 1, \ldots, J,$$

and

$$[R_i|x_i = j] \sim Multinomial(\pi_{j1}, \ldots, \pi_{jK}),$$

where $\boldsymbol{\beta}_i = [\beta_{i0}, \beta_{i1}]^T$ represents a random intercept and slope, $x_i$ indicates the treatment group, $\pi_{jk}$ represents the proportion of the population with dropout pattern $R_i = k$ given treatment $x_i = j$, and $\boldsymbol{\beta}_j^{(k)} = (\beta_{j0}^{(k)}, \beta_{j1}^{(k)})^T$ is the

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expected intercept and slope for subjects in treatment group $j$ with dropout pattern $k$. The expected value of the parameter of interest, $\boldsymbol{\beta}_i$, is estimated by averaging over the dropout pattern as follows:

$$E(\boldsymbol{\beta}_i|x_i = j) = \sum_{k=1}^{K} \pi_{jk}\boldsymbol{\beta}_j^{(k)}. \tag{3}$$

## 2. HIERARCHICAL PATTERN MIXTURE MODELS

### 2.1 HPMM Likelihood

All dropouts are considered to be nonrandom in standard PMMs such as those discussed in Section 1.1. However, in many clinical trials dropouts occur for a variety of random and nonrandom reasons, and ignoring these differential dropout reasons may lead to biased estimates. To account for the fact that some individuals may be classified as having random dropout and others classified as having nonrandom dropout, we propose a hierarchical pattern mixture model (HPMM) that incorporates the dropout reason classification, denoted by $G$, into the random-effects-dependent dropout pattern mixture model (2).

As in a standard PMM, an individual who drops out after time $k$ is assigned dropout pattern $R_i = k$. However, unlike the standard PMM, if their dropout is nonrandom they are classified as $G_i = 1$ and if their dropout is random they are classified as $G_i = 0$. A completer ($R_i = K$) is assumed to have an unobserved potential dropout reason classification $G_i$. To illustrate the hierarchical pattern mixture model, Figure 1 shows an example of this data structure with four repeated measurements and three unique dropout patterns. For the general case, the joint likelihood for the HPMM is:

$$[\mathbf{y}_i, \boldsymbol{\beta}_i, R_i, G_i|\mathbf{X}_i] = [\mathbf{y}_i|\boldsymbol{\beta}_i, \mathbf{X}_i][\boldsymbol{\beta}_i|R_i, G_i, \mathbf{X}_i][R_i|G_i, \mathbf{X}_i][G_i|\mathbf{X}_i]. \tag{4}$$

We focus on a special case of this model, where the fixed treatment effect $\alpha$ is of primary interest:

$$[\mathbf{y}_i|\boldsymbol{\beta}_i, \mathbf{X}_i] \sim N_K\left(\begin{bmatrix} x_i & 1 & t_{i1} \\ \vdots & \vdots & \vdots \\ x_i & 1 & t_{iK} \end{bmatrix} \begin{bmatrix} \alpha \\ \beta_{i0} \\ \beta_{i1} \end{bmatrix}, \sigma_e^2\mathbf{I}\right),$$

$$[\boldsymbol{\beta}_i|R_i = k, G_i = g, x_i = j] \sim N_2(\boldsymbol{\beta}_{jk}^{(g)}, \boldsymbol{\Gamma}^{(g)}), \quad k = 1, 2 \ldots, K, \quad j = 0, 1,$$

$$[R_i|G_i = g, x_i = j] \sim Multinomial(\pi_{j1}^{(g)}, \ldots, \pi_{jK}^{(g)}),$$

and

$$[G_i|x_i = j] \sim Bernoulli(\gamma_j).$$

In this model, $\alpha$ reprents the parameter for the fixed treatment effect, $\boldsymbol{\beta}_i = [\beta_{i0}, \beta_{i1}]^T$ represents a random intercept and slope, $x_i$ is an indicator for treatment group, $\pi_{jk}^{(g)}$ represents the proportion of the population with dropout pattern $R_i = k$ given treatment $x_i = j$ and dropout reason classification $G_i = g$, and $\boldsymbol{\beta}_{jk}^{(g)} = (\beta_{j0}^{(g)}, \beta_{j1}^{(g)})^T$ is the expected intercept and slope for subjects in treatment group $x_i = j$ with dropout pattern $R_i = k$ and dropout reason classification $G_i = g$. The expected value of the parameter of interest, $\alpha$, is estimated as:

$$E(\alpha|x_i = j) = \gamma_j\alpha^{(1)} + (1 - \gamma_j)\alpha^{(0)}, \tag{5}$$

where $\gamma_j$ is the proportion of individuals with nonrandom dropout classification $G_i = 1$ given treatment $x_i = j$ and $\alpha^{(g)}$ is the treatment effect for dropout reason classification $G_i = g$.

### 2.2 Two Different Approaches for Estimation of the Treatment Effect

In order to obtain the overall treatment effect $\alpha$ we first need to estimate the individual treatment effects for the random and nonrandom dropout groups. To accurately estimate these treatment effects it is necessary to have some complete data within each dropout group, but unfortunately the potential dropout reason classification $G_i$ for each completer is unobserved. We propose two methods of estimation that accomodate this challenge: an ad-hoc method based on a trajectory analysis and the maximum likelihood method.

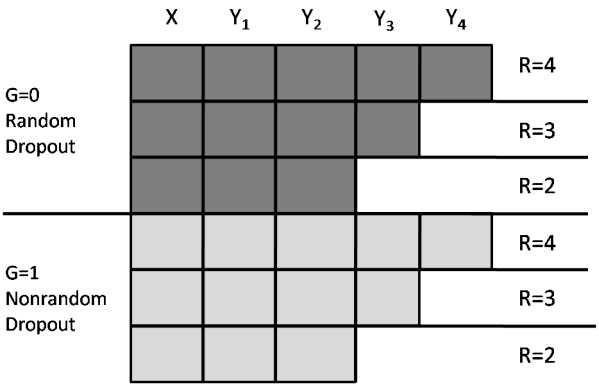


**Figure 1**: Illustration of Hierarchical Pattern Mixture Model Data Structure.

### *2.2.1 Inference-Based Trajectory Analysis*

To include the data from the completers in our model, we utilize a trajectory analysis such as PROC TRAJ in SAS (Jones et al., 2001). A trajectory model is created based on the observations with complete follow-up data and is subsequently used to classify the completers as belonging to either the random or nonrandom dropout group. After classifying the completers based on the trajectory analysis we use all the data to fit a mixed model. Hedeker et al. (1997) presented a mixed model which included dropout pattern in order to obtain PMM estimates. We utilize this concept to create a model which will allow us to obtain HPMM estimates. Essentially, it is a mixed model which includes the treatment effect and the interaction of treatment by dropout reason group, adjusting for time, dropout pattern, and other covariates of interest as follows:

$$y_{it} = \beta_{i0} + \alpha_1 x_i + \alpha_2 G_i + \beta_{i1} Time_i + \alpha_3 R_i + \alpha_4 G_i R_i + \alpha_5 G_i x_i + \alpha_6 R_i Time_i. \tag{6}$$

We also separately estimate $\hat{\gamma}_j$, the proportion of individuals with nonrandom dropout given treatment $x_i = j$. Finally, we obtain the overall treatment effect estimate for $\alpha$ using:

$$E(\alpha | x_i = j) = \hat{\gamma}_j(\hat{\alpha}_1 + \hat{\alpha}_5) + (1 - \hat{\gamma}_j)\hat{\alpha}_1,$$

where $\hat{\alpha}_1$ and $\hat{\alpha_5}$ are the model estimates from (6).

### *2.2.2 Maximum Likelihood Estimation*

To directly estimate the treatment effect, we construct separate joint likelihoods for completers ($R_i = K$) and each combination of dropout reason classification $G_i = g$ and possible dropout pattern $R_i = k, k = 1, \ldots, K-1$. Each of these likelihoods is written in the form of the hierarchical pattern mixture model in (4). The missing outcome data and the random effects are then integrated out of each likelihood.

The set of completers is denoted $S$. Individuals in this set do not have an observed dropout reason. However, if they had dropped out, we assume they would have been assigned either $G_i = 1$ or $G_i = 0$. Therefore, the contribution to the likelihood function from subjects in $S$ is

$$\begin{aligned} L_S(\alpha, \phi) \quad = \quad & \prod_{i \in S} \int \Big[ f(y_{i1}, \ldots, y_{iK}, \boldsymbol{\beta}_i, R_i = K | G_i = 0, x_i, \alpha, \phi) pr(G_i = 0 | x_i) \\ & + f(y_{i1}, ..., y_{iK}, \boldsymbol{\beta}_i, R_i = K | G_i = 1, x_i, \alpha, \phi) pr(G_i = 1 | x_i) \Big] d\boldsymbol{\beta}_i, \end{aligned} \tag{7}$$

where $\phi$ represents nuisance parameters.

The individuals in dropout pattern $R_i = k$ have observed data $y_{obs} = \{y_{i1}, \ldots, y_{ik}\}$ and missing data $y_{mis} = \{y_{ik+1}, \ldots, y_{iK}\}$. The set of these individuals with $G_i = g$ are denoted $S_k^{(g)}$. The contribution to the likelihood from subjects in dropout pattern $R_i = k$ and dropout reason classification $G_i = g$ is:

$$L_{S_k^{(g)}}(\alpha, \phi) \quad = \quad \prod_{i \in S_k^{(g)}} \int \ldots \int \int f(y_{i1}, \ldots, y_{iK}, \boldsymbol{\beta}_i | R_i = k, x_i, G_i = g)\, dy_{iK} \ldots\, dy_{ik+1}\, d\boldsymbol{\beta}_i. \tag{8}$$

The full likelihood function is written as:

$$L_F(\alpha,\phi|y_{obs}) = \Big[\prod_{g=0}^{1}\prod_{k=1}^{K-1}\prod_{\{i:G_i=g,R_i=k\}} L(\alpha,\phi|y_{i,obs})\Big]\Big[\prod_{i\in S} L(\alpha,\phi|y_i)\Big] \quad (9)$$

$$= L_S(\alpha,\phi)\prod_{k=1}^{K-1}\Big[L_{S_k^{(0)}}(\alpha,\phi)L_{S_k^{(1)}}(\alpha,\phi)\Big]. \quad (10)$$

$L_F$ is maximized with respect to $\alpha$ and $\phi$, and equation (5) is used to obtain the overall estimate for the treatment effect $\alpha$.

### 2.3 Assigning Dropout Reason

The key to the HPMM is that individuals are grouped based on whether they dropped out randomly or nonrandomly. Typically, this "reason for dropout" assignment is based on information collected from a clinical trial termination form, which provides a list of potential reasons for an individual to drop out of the study. Although the termination form standardizes reasons for dropout within one study, it may vary greatly from one study to another based on the study design.

Even when utilized correctly, many termination forms from clinical trials are not adequate to determine whether dropout was random or nonrandom. Take, for example, the section of a termination form from a depression study in Table 1. This termination form lists six possible reasons for dropping out of the study. It may be clear that "Unacceptable Side Effects" and "Committed \ Attempted Suicide" are nonrandom reasons for dropout because it is very likely that they are related to the individuals' missing depression observation. Alternatively, it is most likely that someone who dropped out of a depression study because they "Became Pregnant" or because they "Moved from the Area" is dropping out for a random reason. However, it is unclear whether an individual who "found research too burdensome" or "lost contact" is dropping out randomly or nonrandomly based on the wording of the termination form. In these situations, the dropout reason is very subjective and may be easily misclassified by even the most competent data analyst.

Although some group misclassification may come from the wording of the termination form, it is often the case that individuals, by no fault of their own, are unable to verbalize adequately why they have decided to drop out of a study. In addition, many individuals may drop out of a study for a variety of reasons, not all of which they wish to discuss. This is a right of any study participant. However, in these situations, there is inherent error in assigning dropout reason, even with the most well-designed termination form.

**Table 1**: Termination Form Example

| Dropout Reasons | Classification of Dropout Group |
|---|---|
| 1. Unacceptable Side Effects | Non-Random |
| 2. Committed \ Attempted Suicide | Non-Random |
| 3. Moved From the Area | Random |
| 4. Became Pregnant | Random |
| 5. Found Research too Burdensome | ? |
| 6. Lost Contact | ? |

## 3. SIMULATION STUDY

Due to the subjective nature of classifying dropout reasons, we conducted a simulation study to determine how well the HPMM trajectory and MLE models perform under different percentages of misclassified reason-for-dropout. We compared these methods to the standard pattern mixture model and a selection model assuming random dropout.

### 3.1 Data Generation

We simulated 300 datasets of $N = 300$ observations each. Data were simulated in the context of a repeated mesaures clinical trial with four follow-up time points. Some individuals remained in the study for all four time points ($R_i = 4$),

whereas others dropped out of the study for random and nonrandom reasons between times $t_2$ and $t_3$ ($R_i = 2$) or between times $t_3$ and $t_4$ ($R_i = 3$), as shown in Figure 1. We simulated each $x_i$, $G_i$, and $R_i$ as shown in Table 2.

The random effects $\boldsymbol{\beta}_i$ were simulated as:

$$[\boldsymbol{\beta}_i | R_i = k, G_i = g] \sim N_2(\mathbf{B}_k^{(g)}, \boldsymbol{\Gamma}^{(g)}),$$

where

$$\mathbf{B}_k^{(0)} = \begin{pmatrix} b_{00} + b_{01} \\ b_{10} + b_{11} \end{pmatrix},$$

$$\mathbf{B}_k^{(1)} = \begin{pmatrix} b_{00} + b_{01}\eta_k \\ b_{10} + b_{11}\eta_k \end{pmatrix},$$

and

$$\boldsymbol{\Gamma}^{(g)} = \begin{bmatrix} \sigma_0^{(g)} & \rho^{(g)}\sqrt{\sigma_0^{(g)}\sigma_1^{(g)}} \\ \rho^{(g)}\sqrt{\sigma_0^{(g)}\sigma_1^{(g)}} & \sigma_1^{(g)} \end{bmatrix}.$$

We selected the parameter values: $(\eta_2, \eta_3, \eta_4) = (3, 2, 1)$, $(b_{00}^{(0)}, b_{01}^{(0)}, b_{10}^{(0)}, b_{11}^{(0)}) = (15, 0, 1, 0)$, $(b_{00}^{(1)}, b_{01}^{(1)}, b_{10}^{(1)}, b_{11}^{(1)}) = (25, .7, .6, .8)$, $(\sigma_0^{(1)}, \sigma_1^{(1)}, \rho^{(1)}) = (2, .2, .002)$, and $(\sigma_0^{(0)}, \sigma_1^{(0)}, \rho^{(0)}) = (1, .1, .004)$.

The repeated mesaures outcome was simulated as

$$[\mathbf{y}_i | \boldsymbol{\beta}_i, x_i, \mathbf{Z}] \sim N_4(x_i\alpha^{(g)} + \mathbf{Z}\boldsymbol{\beta}_i, \boldsymbol{\Sigma}^{(g)})$$

where $\alpha^{(0)} = -2$ and $\alpha^{(1)} = -.5$ were the treatment effects for the random and nonrandom dropout groups, $\mathbf{Z}$ was the design matrix for the random slope and intercept, and

$$\boldsymbol{\Sigma}^{(g)} = \sigma_e^2\mathbf{I}_4 + \mathbf{Z}\boldsymbol{\Gamma}^{(g)}\mathbf{Z}^T,$$

with $\sigma_e^2$=2. The true treatment effect $\alpha$ was calculated to be $.3\alpha^{(1)} + (1 - .3)\alpha^{(0)} = -1.55$.

**Table 2**: Data Simulation

| Variable | Notation | Distribution |
|---|---|---|
| Treatment Indicator | $[x_i]$ | Bernoulli(.5) |
| Dropout Reason | $[G_i \mid x_i]$ | Bernoulli$\big(.3\mathrm{I}(x_i = 1) + .5\mathrm{I}(x_i = 0)\big)$ |
| Dropout Time | $[R_i \mid G_i = 0]$ | Multinomial$(4/8, 3/8, 1/8)$ |
| Dropout Time | $[R_i \mid G_i = 1]$ | Multinomial$(3/8, 3/8, 2/8)$ |

### 3.2 Trajectory Method

The trajectory model was created using only the completers' data with the following SAS code:

```
PROC TRAJ DATA=COMPLETERS OUT=OF OUTPLOT=OP OUTSTAT=OS;
    VAR Y1 Y2 Y3 Y4;
    INDEP TIME1 TIME2 TIME3 TIME4;
    MODEL CNORM;
    MIN 0;
    MAX 45;
    NGROUPS 2;
    ORDER 2 2;
RUN;
%TRAJPLOT(OP,OS,"Y", "TIME");
```

The groups created by the trajectory were separated mainly by the difference in intercept between the random and nonrandom dropout groups. Therefore, based on our assumptions regarding how random and nonrandom dropout would affect the outcome, we selected the trajectory group with the higher intercept to be nonrandom dropout and the trajectory group with the lower intercept to be random dropout. After classifying the completers based on this trajectory model, we created the following mixed model with random intercept and slope:

$$y_{it} = \beta_{0i} + \alpha_1 x_i + \alpha_2 G_i + \beta_{1i} Time_i + \alpha_3 R_i + \alpha_4 G_i R_i + \alpha_5 G_i x_i + \alpha_6 R_i Time_i,$$

and used the following SAS code based on Hedeker, et al.(1997) to generate treatment effect estimates for the random and nonrandom dropout groups:

```
PROC MIXED DATA= ;
    MODEL Y=X G Time R G*R G*X R*Time;
    RANDOM INTERCEPT Time \ TYPE=AR(1);
RUN;
```

We also estimated the frequency of observations with $G_i = 1$ given $x_i = 1$ to obtain $\hat{\gamma}_1$. Finally, we estimated the overall treatment effect $\alpha$ as follows:

$$E(\alpha|x_i = 1) = \hat{\gamma}_1(\hat{\alpha}_1 + \hat{\alpha}_5) + (1 - \hat{\gamma}_1)\hat{\alpha}_1.$$

### 3.3 MLE Method

We constructed the joint likelihoods as follows:

$$\begin{aligned} L_S &= \prod_{i\in S}\Big[(1-\gamma_j)\pi_{jK}^{(0)}(2\pi)^{-K/2}|\mathbf{\Sigma}^{(0)}|^{-1/2}e^{\{-\frac{1}{2}(\mathbf{y}_i-x_i\alpha^{(0)})^T\mathbf{\Sigma}^{(0)\,-1}(\mathbf{y}_i-x_i\alpha^{(0)})\}} \\ &\qquad + \gamma_j\pi_{jK}^{(1)}(2\pi)^{-K/2}|\mathbf{\Sigma}^{(1)}|^{-1/2}e^{\{-\frac{1}{2}(\mathbf{y}_i-x_i\alpha^{(1)})^T\mathbf{\Sigma}^{(1)\,-1}(\mathbf{y}_i-x_i\alpha^{(1)})\}}\Big] \end{aligned}$$

$$L_{S_k^{(0)}} = \prod_{i\in S_k^{(0)}}\left[(1-\gamma_j)\pi_{jk}^{(0)}(2\pi)^{-k/2}|\mathbf{\Sigma}_k^{(0)}|^{-1/2}e^{\{-\frac{1}{2}(\mathbf{y}_i-x_i\alpha^{(0)})^T\mathbf{\Sigma}_k^{(0)\,-1}(\mathbf{y}_i-x_i\alpha^{(0)})\}}\right]$$

$$L_{S_k^{(1)}} = \prod_{i\in S_k^{(1)}}\left[\gamma_j\pi_{jk}^{(1)}(2\pi)^{-k/2}|\mathbf{\Sigma}_k^{(1)}|^{-1/2}e^{\{-\frac{1}{2}(\mathbf{y}_i-x_i\alpha^{(1)})^T\mathbf{\Sigma}_k^{(1)\,-1}(\mathbf{y}_i-x_i\alpha^{(1)})\}}\right],$$

where $\mathbf{\Sigma}_k^{(g)} = \sigma_e^2\mathbf{I}_{k\times k} + \mathbf{Z}_{k\times 2}\mathbf{\Gamma}^{(g)}\mathbf{Z}_{2\times k}^T$. After each likelihood was created, we maximized the log of the full likelihood, $L_F(\alpha, \phi|y_{obs})$, with respect to all parameters using the "nlminb()" function in R. After maximization, we used the equation

$$E(\alpha|x_i = 1) = \hat{\gamma}_1\hat{\alpha}^{(1)} + (1 - \hat{\gamma}_1)\hat{\alpha}^{(0)}$$

to estimate the overall treatment effect $\alpha$.

### 3.4 Results

Simulation results are shown in Table 3. Without any misclassification, the HPMM Trajectory and HPMM MLE both had low biases and relatively small standard deviations. As the rate of misclassification increased, the biases and standard deviations of both methods also increased, however, the trajectory method had smaller bias than the MLE method for each level of misclassification. In this simulation study, both the MLE method and the trajectory method performed better than the standard pattern mixture model and the selection model assuming random dropout, even under 40% misclassification of dropout reason.

## 4. DISCUSSION

Through our simulation study, we showed that both the HPMM trajectory and HPMM MLE methods can produce treatment effect estimates with lower bias than alternative models such as the pattern mixture model or the selection model assuming random dropout. However, before more generalized conclusions can be drawn regarding the effectiveness of the HPMM method, extended simulation studies should be conducted. We generated data with a large difference between intercepts for the random and nonrandom dropout groups. In this scenerio, the trajectory model was shown to perform better than the MLE model with classification. However, it is possible that with a smaller difference between the intercepts, the MLE will perform better than the trajectory due to the nature of each of these methods. Another area to reserach before drawing further conclusions regarding the HPMM is the robustness of our method under different sample sizes. Our sample size was 300, however, the smaller-sample abilities of the method have not been assessed.

**Table 3**: Simulation Study Results

| Method | Percent Misclassification | \|Bias\| (Empirical SD) True $\alpha = -1.55$ |
|---|---|---|
| 1. HPMM with Trajectory | 0% | .01 (.26) |
| | 10% | .34 (.38) |
| | 25% | .72 (.47) |
| | 40% | .93 (.51) |
| 2. HPMM with MLE | 0% | .02 (.24) |
| | 10% | .46 (.39) |
| | 25% | 1.31 (.58) |
| | 40% | 1.69 (.67) |
| 3. Assume MAR | | 1.92 (.65) |
| 4. Standard PMM | | 1.75 (.60) |

One way we believe we can further increase the accuracy of the trajectory method is to utilize multiple imputation. Specifically, after creating the trajectory model, we plan to extract each individual's estimated probability of being in either the random or nonrandom reason-for-dropout group. We will repeatedly draw from these estimates to create new datasets with which to re-estimate the treatment effects. The overall treatment effect and standard error will be calculated, and power analyses will be performed to better understand the coverage rates.

Missing data are prevalent in clinical trials, particularly when a mental illness such as depression is the outcome of interest. When individuals drop out for a variety of both random and nonrandom reasons, the hierarchical pattern mixture model is a promising alternative to current methods such as the standard pattern mixture model because it allows for the strength of the dropout effect to differ based on whether individuals dropped out randomly or nonrandomly.

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