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BAYESIAN MODELING LONGITUDINAL DYADIC DATA WITH NONIGNORABLE DROPOUT, WITH APPLICATION TO A BREAST CANCER STUDY

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Dyadic data are common in the social and behavioral sciences, in which members of dyads are correlated due to the interdependence structure within dyads. The analysis of longitudinal dyadic data becomes complex when nonignorable dropouts occur. We propose a fully Bayesian selection-model-based approach to analyze longitudinal dyadic data with nonignorable dropouts. We model repeated measures on subjects by a transition model and account for within-dyad correlations by random effects. In the model, we allow subject's outcome to depend on his/her own characteristics and measure history, as well as those of the other member in the dyad. We further account for the nonignorable missing data mechanism using a selection model in which the probability of dropout depends on the missing outcome. We propose a Gibbs sampler algorithm to fit the model. Simulation studies show that the proposed method effectively addresses the problem of nonignorable dropouts. We illustrate our methodology using a longitudinal breast cancer study.

1. Introduction. Dyadic data are common in psychosocial and behavioral studies [Kenny, Kashy and Cook (2006)]. Many social phenomena, such as dating and marital relationships, are interpersonal by definition, and, as a result, related observations do not refer to a single person but rather to both persons involved in the dyadic relationship. Members of dyads often influence each other's cognitions, emotions and behaviors, which leads to interdependence in a relationship. For example, a husband's (or wife's) drinking behavior may lead to lowered marital satisfaction for the wife (or husband). A consequence of interdependence is that observations of the two individuals are correlated. For example, the marital satisfaction scores of husbands and wives tend to be positively correlated. One of the primary objectives of relationship research is to understand the interdependence of individuals within dyads and how the attributes and behaviors of one dyad member impact the outcome of the other dyad member.

In many studies, dyadic outcomes are measured over time, resulting in longitudinal dyadic data. Repeatedly measuring dyads brings in two complications. First, in addition to the within-dyad correlation, repeated measures on each subject are

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also correlated, that is, within-subject correlation. When analyzing longitudinal dyadic data, it is important to account for these two types of correlations simultaneously; otherwise, the analysis results may be invalid. The second complication is that longitudinal dyadic data are prone to the missing data problem caused by dropout, whereby subjects are lost to follow-up and their responses are not observed thereafter. In psychosocial dyadic studies, the dropouts are often nonignorable or informative in the sense that the dropout depends on missing values. In the presence of the nonignorable dropouts, conventional statistical methods may be invalid and lead to severely biased estimates [Little and Rubin (2002)].

There is extensive literature on statistical modeling of nonignorable dropouts in longitudinal studies. Based on different factorizations of the likelihood of the outcome process and the dropout process, Little (1995) identified two broad classes of likelihood-based nonignorable models: selection models [Wu and Carroll (1988); Diggle and Kenward (1994); Follman and Wu (1995); Glynn, Laird and Rubin (1986)] and pattern mixture models [Wu and Bailey (1989); Little (1993, 1994); Hogan and Laird (1997); Roy (2003); Hogan, Lin and Herman (2004)]. Other likelihood-based approaches that do not directly belong to this classification have also been proposed in the literature, for example, the mixed-effects hybrid model by Yuan and Little (2009) and a class of nonignorable models by Tsonaka et al. (2010). Another general approach for dealing with nonignorable dropouts is based on estimation equations and includes Robins, Rotnitzky and Zhao (1995), Rotnitzky, Robins and Scharfstein (1998), Scharfstein, Rotnitzky and Robins (1999) and Farewell (2010). Recent reviews of methods handling nonignorable dropouts in longitudinal data can be found in Verbeke and Molenberghs (2000), Molenberghs and Kenward (2007), Little (2009), Ibrahim and Molenberghs (2009) and Daniels and Hogan (2008). In spite of the rich body of literature noted above, to the best of our knowledge, the nonignorable dropout problem has not been addressed in the context of longitudinal dyadic data. The interdependence structure within dyads brings new challenges to this missing data problem. For example, within dyads, one member's outcome often depends on his/her covariates, as well as the other member's outcome and covariates. Thus, the dropout of the other member in the dyad causes not only a missing (outcome) data problem for that member, but also a missing (covariate) data problem for the member who remains in the study.

We propose a fully Bayesian approach to deal with longitudinal dyadic data with nonignorable dropouts based on a selection model. Specifically, we model each subject's longitudinal measurement process using a transition model, which includes both the patient's and spouse's characteristics as covariates in order to capture the interdependence between patients and their spouses. We account for the within-dyad correlation by introducing dyad-specific random effects into the transition model. To accommodate the nonignorable dropouts, we take the selection model approach by directly modeling the relationship between the dropout process and missing outcomes using a discrete time survival model.

The remainder of the article is organized as follows. In Section 2 we describe our motivating data collected from a longitudinal dyadic breast cancer study. In Section 3 we propose a Bayesian selection-model-based approach for longitudinal dyad data with informative nonresponse, and provide estimation procedures using a Gibbs sampler in Section 4. In Section 5 we present simulation studies to evaluate the performance of the proposed method. In Section 6 we illustrate our method by analyzing a breast cancer data set and we provide conclusions in Section 7.

2. A motivating example. Our research is motivated by a single-arm dyadic study focusing on physiological and psychosocial aspects of pain among patients with breast cancer and their spouses [Badr et al. (2010)]. For individuals with breast cancer, spouses are most commonly reported as being the primary sources of support [Kilpatrick et al. (1998)], and spousal support is associated with lower emotional distress and depressive symptoms in these patients [Roberts et al. (1994)]. One specific aim of the study is to characterize the depression experience due to metastatic breast cancer from both patients' and spouses' perspectives, and examine the dyadic interaction and interdependence of patients and spouses over time regarding their depression. The results will be used to guide the design of an efficient prevention program to decrease depression among patients. For example, conventional prevention programs typically apply interventions to patients directly. However, if we find that the patient's depression depends on both her own and spouse's previous depression history and chronic pain, when designing a prevention program to improve the depression management and pain relief, we may achieve better outcomes by targeting both patients and spouses simultaneously rather than targeting patients only. In this study, female patients who had initiated metastatic breast cancer treatment were approached by the project staff. Patients meeting the eligibility criteria (e.g., speak English, experience pain due to the breast cancer, having a male spouse or significant other, be able to carry on pre-disease performance, be able to provide informed consent) were asked to participate the study on a voluntary basis. The participation of the study would not affect their treatment in any way.

Depression in patients and spouse was measured at three time points (baseline, 3 months and 6 months) using the Center for Epidemiologic Studies Depression Scale (CESD) questionnaires. However, a substantial number of dropouts occurred. Baseline CESD measurements were collected from 191 couples; however, at 3 months, 101 couples (105 patients and 107 spouses) completed questionnaires, and at 6 months, 73 couples (76 patients and 79 spouses) completed questionnaires. The missingness of the CESD measurements is likely related to the current depression levels of the patients or spouses, thus an nonignorable missing data mechanism is assumed for this study. Consequently, it is important to

account for the nonignorable dropouts in this data analysis; otherwise, the results may be biased, as we will show in Section 6.

3. Models. Consider a longitudinal dyadic study designed to collect J repeated measurements of a response Y and a vector of covariates $\mathbf{X}$ for each of n dyads. Let Y_{kij}, $\mathbf{X}_{kij}$ and $\mathbf{H}_{kij} = (y_{ki,j-1}, \ldots, y_{ki1})^T$ denote the outcome, $p \times 1$ covariate vector and outcome history, respectively, for the member k of dyad i at the jth measurement time with $k = 1, 2$; $i = 1, \ldots, n$; $j = 1, \ldots, J$. We assume that $\mathbf{X}$ is fully observed (e.g., is external or fixed by study design), but Y is subject to missingness due to dropout. The random variable D_{ki}, taking values from 2 to $J + 1$, indicates the time the member k of the ith dyad drops out, where $D_{ki} = J + 1$ if the subject completes the study, and $D_{ki} = j$ if the subject drops out between the $(j - 1)$th and jth measurement time, that is, $\{y_{ki1}, \ldots, y_{ki,j-1}\}$ are observed and $\{y_{kij}, \ldots, y_{kiJ}\}$ are missing. We assume at least 1 observation for each subject, as subjects without any observations have no information and are often excluded from the analysis.

When modeling longitudinal dyadic data, we need to consider two types of correlations: the within-subject correlation due to repeated measures on a subject, and the within-dyad correlation due to the dyadic structure. We account for the first type of correlation by a transition model, and the second type of correlation by dyad-specific random effects b_i, as follows:

$$
\begin{aligned}
Y_{1ij}|b_i &= b_i + \alpha_1 + \mathbf{H}_{1ij}^T\boldsymbol{\beta}_1 + \mathbf{H}_{2ij}^T\boldsymbol{\gamma}_1 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\beta}}_1 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\gamma}}_1 + e_{1ij},\\
Y_{2ij}|b_i &= b_i + \alpha_2 + \mathbf{H}_{2ij}^T\boldsymbol{\beta}_2 + \mathbf{H}_{1ij}^T\boldsymbol{\gamma}_2 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\beta}}_2 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\gamma}}_2 + e_{2ij},\\
b_i &\sim N(0, \tau_b^2).
\end{aligned} \tag{3.1}
$$

Regression parameters in this random-effects transition model have intuitive interpretations similar to those of the actor–partner interdependence model, a conceptual framework proposed by Cook and Kenny (2005) to study dyadic relationships in the social sciences and behavior research fields. Specifically, $\tilde{\boldsymbol{\beta}}_1$ and $\boldsymbol{\beta}_1$ represent the "actor" effects of the patient, which indicate how the covariates and the outcome history of the patient (i.e., $\mathbf{X}_{1ij}$ and $\mathbf{H}_{1ij}$) affect her own current outcome, whereas $\tilde{\boldsymbol{\gamma}}_1$ and $\boldsymbol{\gamma}_1$ represent the "partner" effects for the patient, which indicate how the covariates and the outcome history of the spouse (i.e., $\mathbf{X}_{2ij}$ and $\mathbf{H}_{2ij}$) affect the outcome of the patient. Similarly, $\tilde{\boldsymbol{\beta}}_2$ and $\boldsymbol{\beta}_2$ characterize the actor effects and $\tilde{\boldsymbol{\gamma}}_2$ and $\boldsymbol{\gamma}_2$ characterize the partner effects for the spouse of the patient. Estimates of the actor and partner effects provide important information about the interdependence within dyads. We assume that residuals e_{1ij} and e_{2ij} are independent and follow normal distributions $N(0, \sigma_1^2)$ and $N(0, \sigma_2^2)$, respectively; and e_{1ij} and e_{2ij} are independent of random effects b_i's. The parameters α_1 and α_2 are intercepts for the patients and spouses, respectively.

In many situations, the conditional distribution of Y_{kij} given $\mathbf{H}_{kij}$ and $\mathbf{X}_{kij}$ depends only on the q prior outcomes $y_{ki,j-1}, \ldots, y_{ki,j-q}$ and $\mathbf{X}_{kij}$. If this is the case, we obtain the so-called qth-order transition model, a type of transition model that is most useful in practice [Diggle et al. (2002)]. The choice of the model order q depends on subject matters. In many applications, it is often reasonable to set $q = 1$ when the current outcome depends on only the last observed previous outcome, leading to commonly used Markov models. The likelihood ratio test can be used to assess whether a specific value of q is appropriate [Kalbfleisch and Lawless (1985)]. Auto-correlation analysis of the outcome history also can provide useful information to determine the value of q [Gottman (1981); Kendall and Ord (1990)].

Define $\mathbf{Y}_{ki} = (Y_{ki1}, \ldots, Y_{kid_{ki}})$ and $\mathbf{X}_{ki} = (\mathbf{X}_{ki1}, \ldots, \mathbf{X}_{kid_{ki}})$ for $k = 1, 2$. Given $\{\mathbf{X}_{1i}, \mathbf{X}_{2i}\}$ and the random effect b_i, the joint log likelihood of $(\mathbf{Y}_{1i}, \mathbf{Y}_{2i})$ for the ith dyad under the qth-order (random-effects) transition model is given by

$$\begin{aligned}
&\ell_i(\mathbf{Y}_{1i}, \mathbf{Y}_{2i} | \mathbf{X}_{1i}, \mathbf{X}_{2i}, b_i) \\
&\quad = \sum_{j=q+1}^{d_{1i}} \ell_{ij}(Y_{1ij} | \mathbf{X}_{1ij}, \mathbf{X}_{2ij}, \mathbf{H}_{1ij}, \mathbf{H}_{2ij}, b_i) + \ell_i(Y_{1i1}, \ldots, Y_{1iq} | \mathbf{X}_{1i}, \mathbf{X}_{2i}) \\
&\qquad + \sum_{j=q+1}^{d_{2i}} \ell_{ij}(Y_{2ij} | \mathbf{X}_{1ij}, \mathbf{X}_{2ij}, \mathbf{H}_{1ij}, \mathbf{H}_{2ij}, b_i) + \ell_i(Y_{2i1}, \ldots, Y_{2iq} | \mathbf{X}_{1i}, \mathbf{X}_{2i}),
\end{aligned}$$

where $\ell_{ij}(Y_{kij} | \mathbf{X}_{1ij}, \mathbf{X}_{2ij}, \mathbf{H}_{1ij}, \mathbf{H}_{2ij}, b_i)$ is the likelihood corresponding to model (3.1), and $\ell_i(Y_{ki1}, \ldots, Y_{1iq} | \mathbf{X}_{1i}, \mathbf{X}_{2i})$ is assumed free of $\boldsymbol{\eta}_k = (\alpha_k, \boldsymbol{\beta}_k, \tilde{\boldsymbol{\beta}}_k, \boldsymbol{\gamma}_k, \tilde{\boldsymbol{\gamma}}_k)$, for $k = 1, 2$.

An important feature of model (3.1) that distinguishes it from the standard transition model is that the current value of the outcome Y depends on not only the subject's outcome history, but also the spouse's outcome history. Such a "partner" effect is of particular interest in dyadic studies because it reflects the interdependence between the patients and spouses. This interdependence within dyads also makes the missing data problem more challenging. Consider a dyad consisting of subjects A and B and that B drops out prematurely. Because the outcome history of B is used as a covariate in the transition model of A, when B drops out, we face not only the missing outcome (for B) but also missing covariates (for A). We address this dual missing data problem using the data augmentation approach, as described in Section 4.

To account for nonignorable dropouts, we employ the discrete time survival model [Agresti (2002)] to jointly model the missing data mechanism. Specifically, we assume that the distribution of D_{ki} depends on both the past history of the longitudinal process and the current outcome Y_{kij}, but not on future observations. Define the discrete hazard rate $\lambda_{kij}(\mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij}) = \Pr(D_{ki} = j | D_{ki} > j - 1, \mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij})$. It follows that the probability of dropout for the member

k in the ith dyad is given by

$$\Pr(D_{ki} = d|\mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij}) = \begin{cases} \prod_{j=2}^{d-1}\{1-\lambda_{kij}(\mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij})\}\lambda_{kid}(\mathbf{H}_{kid}, Y_{kid}, \mathbf{X}_{kid}), & \text{if } d \le J, \\ \prod_{j=2}^{J}\{1-\lambda_{kij}(\mathbf{H}_{kij}, Y_{kij}\mathbf{X}_{kij})\}, & \text{if } d = J+1. \end{cases}$$

We specify the discrete hazard rate $\lambda_{kij}(\mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij})$ using the logistic regression model:

$$\begin{aligned} \text{Logit}(\lambda_{1ij}(\mathbf{H}_{1ij}, Y_{1ij}, \mathbf{X}_{1ij})) &= c_i + \xi_1 + \mathbf{X}_{1ij}^T\boldsymbol{\psi}_1 + \mathbf{H}_{1ij}^T\boldsymbol{\delta}_1 + \phi_1 Y_{1ij}, \\ \text{Logit}(\lambda_{2ij}(\mathbf{H}_{2ij}, Y_{2ij}, \mathbf{X}_{2ij})) &= c_i + \xi_2 + \mathbf{X}_{2ij}^T\boldsymbol{\psi}_2 + \mathbf{H}_{2ij}^T\boldsymbol{\delta}_2 + \phi_2 Y_{2ij}, \\ c_i &\sim N(0, \tau_c^2), \end{aligned} \tag{3.2}$$

where c_i is the random effect accounting for the within-dyadic correlation, and $\xi_k, \boldsymbol{\psi}_k, \boldsymbol{\delta}_k$ and $\phi_k, k = 1, 2$, are unknown parameters. In this dropout model, we assume that, conditioning on the random effects, a subject's covariates, past history and current (unobserved) outcome, the dropout probability of this subject is independent of the characteristics and outcomes of the other member in the dyad. The spouse may indirectly affect the dropout rate of the patient through influencing the patient's depression status; however, when conditional on the patient's depression score, the dropout of the patient does not depend on her spouse's depression score.

In practice, we often expect that, given Y_{kij} and $Y_{ki,j-1}$, the conditional dependence of D_{ki} on $Y_{ki,j-2}, \ldots, Y_{ki,1}$ will be negligible because, temporally, the patient's (current) decision of dropout is mostly driven by his (or her) current and the most recent outcome statuses. Using the breast cancer study as an example, we do not expect that the early history of depression plays an important role for the patient's current decision of dropout; instead, the patient drops out typically because she is currently experiencing or most recently experienced high depression. The early history may influence the dropout but mainly through its effects on the current depression status. Once conditioning on the current and the most recent depression statuses, the influence from the early history is essentially negligible. Thus, we use a simpler form of the discrete hazard model

$$\text{Logit}(\lambda_{kij}(\mathbf{H}_{kij}, Y_{kij}, \mathbf{X}_{kij})) = c_i + \xi_k + \mathbf{X}_{kij}^T\boldsymbol{\psi}_k + \delta_k Y_{ki,j-1} + \phi_k Y_{kij}, \quad k = 1, 2.$$

4. Estimation. Under the Bayesian paradigm, we assign the following vague priors to the unknown parameters and fit the proposed model using a Gibbs sampler:

$$\begin{aligned}
\alpha_k, \boldsymbol{\beta}_k, \tilde{\boldsymbol{\beta}}_k, \boldsymbol{\gamma}_k, \tilde{\boldsymbol{\gamma}}_k, \xi_k, \boldsymbol{\psi}_k, \delta_k \text{ and } \phi_k &\sim \text{constant}, \qquad k = 1, 2;\\
\sigma_k^2 &\sim IG(a, b), \qquad k = 1, 2;\\
\tau_b^2 &\sim IG(a, b);\\
\tau_c^2 &\sim IG(a, b);
\end{aligned}$$

where $IG(a, b)$ denote an inverse gamma distribution with a shape parameter a and a scale parameter b. We set a and b at smaller values, such as 0.1, so that the data dominate the prior information. Let $\mathbf{y}_{\text{obs}}$ and $\mathbf{y}_{\text{mis}}$ denote the observed and missing part of the data, respectively. Considering the kth iteration of the Gibbs sampler, the first step of the iteration is "data augmentation" [Tanner and Wong (1987)], in which the missing data $\mathbf{y}_{\text{mis}}$ are generated from their full conditional distributions. Without loss of generality, suppose for the ith dyad, member 2 drops out of the study no later than member 1, that is, $d_{1i} \geq d_{2i}$, and let $d_i = \max(d_{1i}, d_{2i})$. Assuming a first-order ($q = 1$) transition model (or Markov model) and letting $\boldsymbol{\theta}$ denote a generic symbol that represents the values of all other model parameters, the data augmentation consists of the following 3 steps:

(1) For $j = d_{2i}, \ldots, d_i - 1$, draw y_{2ij} from the conditional distribution

$$\begin{aligned}
y_{2ij}|\mathbf{y}_{\text{obs}}, \boldsymbol{\theta} \propto N\Bigg(&\frac{\sigma_2^{-2}\mu_1^* + \beta_2\sigma_2^{-2}\mu_2^* + \gamma_1\sigma_1^{-2}\mu_3^*}{\sigma_2^{-2} + \beta_2^2\sigma_2^{-2} + \gamma_1^2\sigma_1^{-2}}, \frac{1}{\sigma_2^{-2} + \beta_2^2\sigma_2^{-2} + \gamma_1^2\sigma_1^{-2}}\Bigg)\\
&\times \lambda_{2id_{2i}}(\mathbf{H}_{2id_{2i}}, y_{2id_{2i}}, \mathbf{X}_{2id_{2i}})^{I(j=d_{2i})},
\end{aligned}$$

where

$$\begin{aligned}
\mu_1^* &= b_i + \beta_2 y_{2i,j-1} + \gamma_2 y_{1i,j-1} + \alpha_2 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\beta}}_2 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\gamma}}_2,\\
\mu_2^* &= y_{2i,j+1} - b_i - \gamma_2 y_{1ij} - \alpha_2 - \mathbf{X}_{2i,j+1}^T\tilde{\boldsymbol{\beta}}_2 - \mathbf{X}_{1i,j+1}^T\tilde{\boldsymbol{\gamma}}_2,\\
\mu_3^* &= y_{1i,j+1} - b_i - \beta_1 y_{1ij} - \alpha_1 - \mathbf{X}_{1i,j+1}^T\tilde{\boldsymbol{\beta}}_1 - \mathbf{X}_{2i,j+1}^T\tilde{\boldsymbol{\gamma}}_1.
\end{aligned}$$

(2) Draw y_{2i,d_i} from the conditional distribution

$$y_{2i,d_i}|\mathbf{y}_{\text{obs}}, \boldsymbol{\theta} \sim N(b_i + y_{2i,d_i-1}\beta_2 + y_{1i,d_i-1}\gamma_2 + \alpha_2 + \mathbf{X}_{2id_i}^T\tilde{\boldsymbol{\beta}}_2 + \mathbf{X}_{1id_i}^T\tilde{\boldsymbol{\gamma}}_2, \sigma_2^2).$$

(3) Draw y_{1i,d_i} from the conditional distribution

$$\begin{aligned}
y_{1i,d_i}|\mathbf{y}_{\text{obs}}, \boldsymbol{\theta} \propto &N(b_i + y_{1i,d_i-1}\beta_1 + y_{2i,d_i-1}\gamma_1 + \alpha_1 + \mathbf{X}_{1id_i}^T\tilde{\boldsymbol{\beta}}_1 + \mathbf{X}_{2id_i}^T\tilde{\boldsymbol{\gamma}}_1, \sigma_1^2)\\
&\times\lambda_{1id_{1i}}(\mathbf{H}_{1id_i}, y_{1id_i}, \mathbf{X}_{1id_i}).
\end{aligned}$$

Now, with the augmented complete data $\mathbf{y} = \{\mathbf{y}_{\text{obs}}, \mathbf{y}_{\text{mis}}\}$, the parameters are drawn alternatively as follows:

(4) For $i = 1, \ldots, n$, draw random effects b_i from the conditional distribution

$$b_i|\mathbf{y}, \boldsymbol{\theta} = N\Bigg(\frac{\sum_{j=2}^{d_i}(y_{1ij} - \mu_{1ij})\sigma_2^2\tau_b^2 + \sum_{j=2}^{d_i}(y_{2ij} - \mu_{2ij})\sigma_1^2\tau_b^2}{(d_i - 1)\sigma_1^2\tau_b^2 + (d_i - 1)\sigma_2^2\tau_b^2 + \sigma_1^2\sigma_2^2}, \frac{\sigma_1^2\sigma_2^2\tau_b^2}{(d_i - 1)\sigma_1^2\tau_b^2 + (d_i - 1)\sigma_2^2\tau_b^2 + \sigma_1^2\sigma_2^2}\Bigg),$$

where

$$\mu_{1ij} = y_{1i,j-1}\beta_1 + y_{2i,j-1}\gamma_1 + \alpha_1 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\beta}}_1 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\gamma}}_1,$$
$$\mu_{2ij} = y_{2i,j-1}\beta_2 + y_{1i,j-1}\gamma_2 + \alpha_2 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\beta}}_2 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\gamma}}_2.$$

(5) Draw σ_k^2 from the conditional distribution

$$\sigma_k^2|\mathbf{y}, \boldsymbol{\theta} = IG\Bigg(a + \frac{\sum_{i=1}^{n}(d_i - 1)}{2}, b + \frac{\sum_{i=1}^{n}\sum_{j=2}^{d_i}(y_{kij} - u_{kij})^2}{2}\Bigg),$$

where

$$u_{1ij} = b_i + y_{1i,j-1}\beta_1 + y_{2i,j-1}\gamma_1 + \alpha_1 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\beta}}_1 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\gamma}}_1,$$
$$u_{2ij} = b_i + y_{2i,j-1}\beta_2 + y_{1i,j-1}\gamma_2 + \alpha_2 + \mathbf{X}_{2ij}^T\tilde{\boldsymbol{\beta}}_2 + \mathbf{X}_{1ij}^T\tilde{\boldsymbol{\gamma}}_2.$$

(6) Draw τ_b^2 from the conditional distribution

$$\tau_b^2|\mathbf{y}, \boldsymbol{\theta} = IG\Bigg(a + \frac{n}{2}, b + \frac{\sum_{i=1}^{n} b_i^2}{2}\Bigg).$$

(7) Draw $\boldsymbol{\eta}_1 = (\alpha_1, \beta_1, \gamma_1, \tilde{\boldsymbol{\beta}}_1, \tilde{\boldsymbol{\gamma}}_1)$ from the normal distribution

$$\boldsymbol{\eta}_1|\mathbf{y}, \boldsymbol{\theta} = N\big((\mathbf{Z}_1^T\mathbf{Z}_1)^{-1}\mathbf{Z}_1^T(\mathbf{y}_1 - b_i), (\mathbf{Z}_1^T\mathbf{Z}_1)^{-1}\sigma_1^2\big),$$

where $\mathbf{y}_1 = (y_{11,2}, \ldots, y_{11,d_1}, \ldots, y_{1i,2}, \ldots, y_{1i,d_i}, \ldots, y_{1n,2}, \ldots, y_{1n,d_n})^T$ and

$$\mathbf{Z}_1 = \begin{pmatrix} 1 & \cdots & 1 & \cdots & 1 & \cdots & 1 & \cdots \\ y_{11,1} & \cdots & y_{11,d_i-1} & \cdots & y_{1i,1} & \cdots & y_{1i,d_i-1} & \cdots \\ y_{21,1} & \cdots & y_{21,d_i-1} & \cdots & y_{2i,1} & \cdots & y_{2i,d_i-1} & \cdots \\ \mathbf{X}_{11,2} & \cdots & \mathbf{X}_{11,d_1} & \cdots & \mathbf{X}_{1i,2} & \cdots & \mathbf{X}_{1i,d_i} & \cdots \\ \mathbf{X}_{21,2} & \cdots & \mathbf{X}_{21,d_1} & \cdots & \mathbf{X}_{2i,2} & \cdots & \mathbf{X}_{2i,d_i} & \cdots \end{pmatrix}^T.$$

(8) Similarly, draw $\boldsymbol{\eta}_2 = (\alpha_2, \beta_2, \gamma_2, \tilde{\boldsymbol{\beta}}_2, \tilde{\boldsymbol{\gamma}}_2)$ from the conditional distribution

$$\boldsymbol{\eta}_2|\mathbf{y}, \boldsymbol{\theta} = N\big((\mathbf{Z}_2^T\mathbf{Z}_2)^{-1}\mathbf{Z}_2^T(\mathbf{y}_2 - b_i), (\mathbf{Z}_2^T\mathbf{Z}_2)^{-1}\sigma_2^2\big),$$

where $\mathbf{Z}_2$ and $\mathbf{y}_2$ are defined in a similar way to $\mathbf{Z}_1$ and $\mathbf{y}_1$.

(9) Draw $\boldsymbol{\varpi}_1 = (\xi_1, \boldsymbol{\psi}_1, \delta_1, \phi_1)$ and $\boldsymbol{\varpi}_2 = (\xi_2, \boldsymbol{\psi}_2, \delta_2, \phi_2)$ from the conditional distributions

$$\boldsymbol{\varpi}_1|\mathbf{y}, \boldsymbol{\theta} \propto \prod_{i=1}^{n} \prod_{j=2}^{d_{1i}-1} (1-\lambda_{1ij})\lambda_{1id_{1i}},$$

$$\boldsymbol{\varpi}_2|\mathbf{y}, \boldsymbol{\theta} \propto \prod_{i=1}^{n} \prod_{j=2}^{d_{2i}-1} (1-\lambda_{2ij})\lambda_{2id_{2i}}.$$

(10) Draw random effects c_i from the conditional distribution

$$c_i|\mathbf{y}, \boldsymbol{\theta} \propto N(0, \tau_c^2) \prod_{j=2}^{d_{1i}-1} (1-\lambda_{1ij})\lambda_{1id_{1i}} \prod_{j=2}^{d_{2i}-1} (1-\lambda_{2ij})\lambda_{2id_{2i}}.$$

(11) Draw τ_c^2 from the conditional distribution

$$\tau_c^2|\mathbf{y}, \boldsymbol{\theta} = IG\left(a + \frac{n}{2}, b + \frac{\sum_{i=1}^{n} c_i^2}{2}\right).$$

5. Simulation studies. We conducted two simulation studies (A and B). Simulation A consists of 500 data sets, each with 200 dyads and three repeated measures. For the ith dyad, we generated the first measurements, Y_{1i1} and Y_{2i1}, from normal distributions $N(5, 1)$ and $N(7, 1)$, respectively, and generated the second and third measurements based on the following random-effects transition model:

$$\begin{aligned}
Y_{1ij}|b_i &\sim N(b_i + \beta_1 Y_{1i,j-1} + \gamma_1 Y_{2i,j-1} + \tilde{\beta}_1 X_1 + \tilde{\gamma}_1 X_2, 1), \qquad j = 2, 3,\\
Y_{2ij}|b_i &\sim N(b_i + \beta_2 Y_{2i,j-1} + \gamma_2 Y_{1i,j-1} + \tilde{\beta}_2 X_2 + \tilde{\gamma}_2 X_1, 1), \qquad j = 2, 3,\\
b_i &\sim N(0, 1),
\end{aligned}$$

where $\beta_1 = \gamma_1 = 0.5$, $\beta_2 = \gamma_2 = 0.6$, $\tilde{\beta}_1 = \tilde{\gamma}_1 = \tilde{\beta}_2 = \tilde{\gamma}_2 = 1$, and covariates X_1 and X_2 were generated independently from $N(0, 1)$. We assumed that the baseline (first) measurements Y_{1i1} and Y_{2i1} were observed for all subjects, and the hazard of dropout at the second and third measurement times depended on the current and last observed values of Y, that is,

$$\begin{aligned}
\operatorname{logit}(\lambda_{1ij}|c_i) &= c_i - Y_{1ij} - 0.5Y_{1i,j-1} - 6, \qquad j = 2, 3,\\
\operatorname{logit}(\lambda_{2ij}|c_i) &= c_i - Y_{2ij} - 0.5Y_{2i,j-1} - 6, \qquad j = 2, 3,\\
c_i &\sim N(0, 1).
\end{aligned}$$

Under this dropout model, on average, 24% (12% of member 1 and 13% of member 2) of the dyads dropped out at the second time point and 45% (26% of member 1 and 30% of member 2) dropped out at the third measurement time. We applied the proposed method to the simulated data sets. We used 1,000 itera-

TABLE 1
Bias, standard error (SE) and coverage rate of 95% credible intervals under different methods for simulation A

	Complete-case analysis			Available-case analysis			Proposed method		
Parameter	**Bias**	**SE**	**Coverage**	**Bias**	**SE**	**Coverage**	**Bias**	**SE**	**Coverage**
β_1	−0.03	0.06	0.93	−0.01	0.05	0.94	−0.01	0.05	0.95
γ_1	−0.06	0.05	0.81	−0.03	0.04	0.88	0.07	0.04	0.96
$\tilde{\beta}_1$	−0.16	0.12	0.72	−0.10	0.10	0.81	0.05	0.08	0.94
$\tilde{\gamma}_1$	−0.17	0.12	0.75	−0.10	0.10	0.78	0.02	0.09	0.97
β_2	−0.06	0.06	0.89	−0.06	0.05	0.84	0.08	0.05	0.97
γ_2	−0.04	0.05	0.87	−0.00	0.04	0.95	−0.04	0.06	0.96
$\tilde{\beta}_2$	−0.17	0.12	0.73	−0.10	0.10	0.84	−0.01	0.12	0.95
$\tilde{\gamma}_2$	−0.17	0.12	0.72	−0.10	0.10	0.81	0.01	0.09	0.97

tions to burn in and made inference based on 10,000 posterior draws. For comparison purposes, we also conducted complete-case and available-case analyses. The complete-case analysis was based on the data from dyads who completed the follow-up, and the available-case analysis was based on all observed data (without considering the missing data mechanism).

Table 1 shows the bias, standard error (SE) and coverage rate of the 95% credible interval (CI) under different approaches. We can see that the proposed method substantially outperformed the complete-case and available-case analyses. Our method yielded estimates with smaller bias and coverage rates close to the 95% nominal level. In contrast, the complete-case and available-case analyses often led to larger bias and poor coverage rates. For example, the bias of the estimate of $\tilde{\beta}_1$ under the complete-case and available-case analyses were -0.16 and -0.10, respectively, substantially larger than that under the proposed method (i.e., 0.05); the coverage rate using the proposed method was about 94%, whereas those using the complete-case and available-case analyses were under 82%.

The second simulation study (Simulation B) was designed to evaluate the performance of the proposed method when the nonignorable missing data mechanism is misspecified, for example, data actually are missing at random (MAR). We generated the first measurements, Y_{1i1} and Y_{2i1}, from normal distribution $N(3, 1)$ independently, and generated the second and third measurements based on the same transition model as in Simulation A. We assumed the hazard of dropout at the second and third measurement times depended on the previous (observed) value of Y quadratically, but not on the current (missing) value of Y, that is,

$$\begin{aligned} \operatorname{logit}(\lambda_{1ij}|c_i) &= c_i + Y_{1i,j-1}^2 - 15, \qquad j = 2, 3, \\ \operatorname{logit}(\lambda_{2ij}|c_i) &= c_i + Y_{2i,j-1}^2 - 15, \qquad j = 2, 3, \\ c_i &\sim N(0, 1). \end{aligned} \tag{5.1}$$

Under this MAR dropout model, on average, 37% (21% of member 1 and 21% of member 2) of the dyads dropped out at the second time point and 27% (24% of member 1 and 33% of member 2) dropped out at the third measurement time. To fit the simulated data, we considered two nonignorable models with different specifications of the dropout (or selection) model. The first nonignorable model assumed a flexible dropout model

$$\text{logit}(\lambda_{kij}|b_i) = c_i + \xi_k + \delta_k Y_{ki,j-1}^2 + \phi_k Y_{ki,j},$$

which included the true dropout process (5.1) as a specific case with $\phi_k = 0$; and the second nonignorable model took a misspecified dropout model of the form

$$\text{logit}(\lambda_{kij}|b_i) = c_i + \xi_k + \delta_k Y_{ki,j-1} + \phi_k Y_{ki,j}.$$

Table 2 shows the bias, standard error and coverage rate of the 95% CI under different approaches. When the missing data were MAR, the complete-case analysis was invalid and led to biased estimates and poor coverage rates because the complete cases are not random samples from the original population. In contrast, the available-case analysis yielded unbiased estimates and coverage rates close to the 95% nominal level. For the nonignorable models, the one with the flexible dropout model yielded unbiased estimates and reasonable coverage rates, whereas the model with the misspecified dropout model led to biased estimates (e.g., $\hat{\beta}_1$ and $\hat{\beta}_2$) and poor coverage rates. This result is not surprising because it is well known that selection models are sensitive to the misspecification of the dropout model [Little and Rubin (2002); Daniels and Hogan (2000)]. For nonignorable missing data, the difficulty is that we cannot judge whether a specific dropout model is misspecified or not based solely on observed data because the observed data contain no information about the (nonignorable) missing data mechanism. To address this difficulty, one possible approach is to specify a flexible dropout model to decrease the chance of model misspecification. Alternatively, maybe a better approach is to conduct sensitivity analysis to evaluate how the results vary when the dropout model varies. We will illustrate the latter approach in the next section.

6. Application. We applied our method to the longitudinal metastatic breast cancer data. We used the first-order random-effects transition model for the longitudinal measurement process. In the model, we included 5 covariates: chronic pain measured by the Multidimensional Pain Inventory (MPI) and previous CESD scores from both the patients and spouses, and the patient's stage of cancer. In the discrete-time dropout model, we included the subject's current and previous CESD scores, MPI measurements and the patient's stage of cancer as covariates. Age was excluded from the models because its estimate was very close to 0 and not significant. We used 5,000 iterations to burn in and made inference based on 5,000 posterior draws. We also conducted the complete-case and available-case analyses for the purpose of comparison.

As shown in Table 3, the proposed method suggests significant "partner" effects for the patients. Specifically, the patient's depression increases with her

TABLE 2

Bias, standard error (SE) and coverage rate of 95% credible intervals under different methods for simulation B

	Complete-case analysis			Available-case analysis			Nonignorable model (flexible dropout model)			Nonignorable model (misspecifed dropout model)		
Parameter	**Bias**	**SE**	**Coverage**	**Bias**	**SE**	**Coverage**	**Bias**	**SE**	**Coverage**	**Bias**	**SE**	**Coverage**
β_1	−0.06	0.08	0.86	0.00	0.06	0.95	−0.01	0.06	0.95	0.14	0.06	0.78
γ_1	−0.09	0.08	0.82	0.00	0.05	0.96	0.07	0.05	0.97	−0.01	0.05	0.95
$\tilde{\beta}_1$	−0.11	0.14	0.84	0.00	0.10	0.95	0.04	0.08	0.96	0.03	0.08	0.94
$\tilde{\gamma}_1$	−0.13	0.14	0.84	0.00	0.10	0.96	0.02	0.09	0.97	0.02	0.09	0.98
β_2	−0.07	0.08	0.87	0.00	0.06	0.96	0.02	0.06	0.97	0.12	0.06	0.79
γ_2	−0.10	0.08	0.78	0.00	0.07	0.96	0.00	0.06	0.96	−0.08	0.06	0.93
$\tilde{\beta}_2$	−0.14	0.14	0.82	0.00	0.10	0.96	0.01	0.12	0.94	0.01	0.12	0.95
$\tilde{\gamma}_2$	−0.14	0.13	0.83	0.01	0.10	0.96	0.01	0.09	0.97	0.01	0.09	0.98

TABLE 3

Parameter estimates and 95% *credible intervals* (*shown in parentheses*) *for the patients' and spouses' measurement models based on the complete-case*, *available-case analyses and the proposed approach for the breast cancer data*

		Complete-case analysis	**Available-cases analysis**	**Proposed method**
Patients	Intercept	2.53 (−1.71, 6.77)	0.99 (−2.55, 4.52)	5.10 (3.31, 6.59)
	Patient CESD	0.43 (0.29, 0.58)	0.56 (0.44, 0.68)	0.87 (0.80, 0.93)
	Spouse CESD	0.07 (−0.06, 0.20)	0.06 (−0.06, 0.17)	0.14 (0.09, 0.19)
	Patient MPI	0.94 (0.22, 1.67)	0.82 (0.21, 1.43)	1.24 (0.83, 1.64)
	Spouse MPI	1.06 (0.29, 1.82)	0.90 (0.31, 1.48)	0.62 (0.40, 0.84)
	Cancer stage	0.39 (−0.81, 1.60)	0.59 (−0.43, 1.60)	0.10 (−0.47, 0.66)
Spouses	Intercept	3.68 (−0.55, 7.92)	2.00 (−1.63, 5.64)	8.16 (4.26, 11.9)
	Patient CESD	−0.05 (−0.19, 0.09)	0.01 (−0.11, 0.13)	0.68 (0.63, 0.74)
	Spouse CESD	0.77 (0.64, 0.90)	0.78 (0.66, 0.89)	0.76 (0.71, 0.81)
	Patient MPI	0.43 (−0.29, 1.15)	0.27 (−0.27, 0.81)	0.53 (0.33, 0.73)
	Spouse MPI	0.55 (−0.22, 1.31)	0.58 (−0.04, 1.20)	0.36 (−0.64, 1.15)
	Cancer stage	−0.42 (−1.63, 0.79)	−0.21 (−1.23, 0.80)	−0.50 (−0.92, 0.09)

spouse's MPI [estimate = 0.62 and 95% CI = (0.40, 0.84)] and previous CESD [estimate = 0.14 and 95% CI = (0.09, 0.19)]. In addition, there are also significant "actor" effects for the patients, that is, the patient's depression is positively correlated with her own MPI and previous CESD scores. For the spouses, we observed similar significant "partner" effects: the spouse's depression increases with the patient's MPI and previous CESD scores. However, the "actor" effects for the spouses are different from those for the patients. The spouse's depression correlates with his previous CESD scores but not the MPI level, whereas the patient's depression is related to both variables. Based on these results, we can see that the patients and spouses are highly interdependent and influence each other's depression status. Therefore, when designing a prevention program to reduce depression in patients, we may achieve better outcomes by targeting both patients and spouses simultaneously.

As for the dropout process, the results in Table 4 suggest that the missing data for the patients are nonignorable because the probability of dropout is significantly

TABLE 4

Parameter estimates and 95% *credible intervals* (*shown in parentheses*) *of the dropout model for the breast cancer data*

	Intercept	**Current CESD**	**Previous CESD**	**MPI**	**Cancer stage**
Patients	−0.8 (−8.3, 6.2)	−1.6 (−4.2, −0.3)	0.6 (−0.3, 1.6)	0.8 (−1.6, 3.8)	−0.4 (−0.9, 2.4)
Spouses	−15.6 (−25.6, −4.1)	0.8 (−0.2, 1.6)	−0.7 (−1.6, 0.5)	−0.2 (−2.1, 1.4)	2.9 (−1.7, 6.4)

associated with the patient's current (missing) CESD score. In contrast, the missing data for the spouse appears to be ignorable, as the probability of dropout does not depend on the spouse's current (missing) CESD score. For the variance components, the estimates of residuals variances for patients and spouses are $\hat{\sigma}_1^2 = 5.02$ [95% CI $= (2.98, 7.01)$] and $\hat{\sigma}_2^2 = 6.12$ [95% CI $= (4.03, 7.95)$], respectively. The estimates of the variances for the random effects b_i and c_i are $\hat{\tau}_b^2 = 9.95$ [95% CI $= (7.96, 11.92)$] and $\hat{\tau}_c^2 = 7.97$ [95% CI $= (5.99, 9.89)$], respectively, suggesting substantial variations across dyads.

Compared to the proposed approach, both the complete-case and available-case analyses fail to detect some "partner" effects. For example, for spouses, the complete-case and available-case analyses assert that the spouse's CESD is correlated with his own previous CESD scores only, whereas the proposed method suggested that the spouse's CESD is related not only to his own CESD but also to the patient's CESD and MPI level. In addition, for patients, the "partner" effect of the spouse's CESD is not significant under the complete-case and available-case analyses, but is significant under the proposed approach. These results suggest that ignoring the nonignorable dropouts could lead to a failure to detect important covariate effects.

Nonidentifiability is a common problem when modeling nonignorable missing data. In our approach, the observed data contain very limited information on the parameters that link the missing outcome with the dropout process, that is, ϕ_1 and ϕ_2 in the dropout model. The identification of these parameters is heavily driven by the untestable model assumptions [Verbeke and Molenberghs (2000); Little and Rubin (2002)]. In this case, a sensible strategy is to perform a sensitivity analysis to examine how the inference changes with respect to the values of ϕ_1 and ϕ_2 [Daniels and Hogan (2000, 2008); Rotnitzky et al. (2001)]. We conducted a Bayesian sensitivity analysis by assuming informative normal prior distributions for ϕ_1 and ϕ_2 with a small variance of 0.01 and the mean fixed, successively, at various values. Figures 1 and 2 show the parameter estimates of the measurement models when the prior means of ϕ_1 and ϕ_2 vary from -3 to 3. In general, the estimates were quite stable, except that the estimate of cancer stage in the measurement model of patient (Figure 1) and the estimate of spouse's MPI in the measurement model of spouse (Figure 2) demonstrated some variations.

We conducted another sensitivity analysis on the prior distributions of σ_1^2, σ_2^2, τ_b^2 and τ_c^2. We considered various inverse gamma priors, $IG(a, b)$, by setting $a = b = 0.01$, 1 and 5. As shown in Table 5, the estimates of the measurement model parameters were stable under different prior distributions, suggesting the proposed method is not sensitive to the priors of these parameters.

7. Conclusion. We have developed a selection-model-based approach to analyze longitudinal dyadic data with nonignorable dropouts. We model the longitudinal outcome process using a transition model and account for the correlation

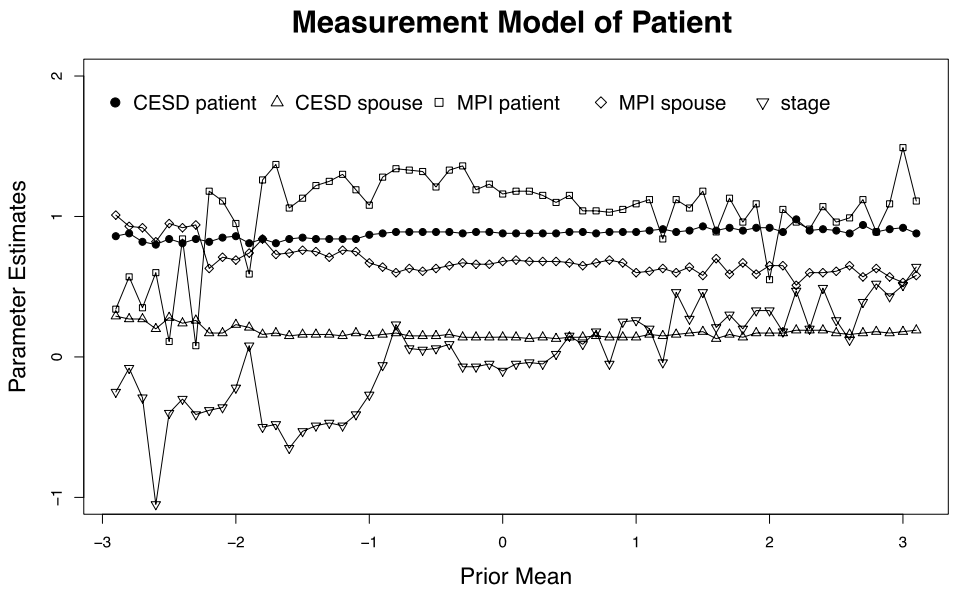

FIG. 1. *Sensitivity analysis of the proposed nonignorable model for the breast cancer data. The figure shows the parameter estimates of the patients' measurement model under informative normal priors for* ϕ_1 *and* ϕ_2 *with a mean varying from* -3 *to* 3 *and a fixed variance of* 0.01.

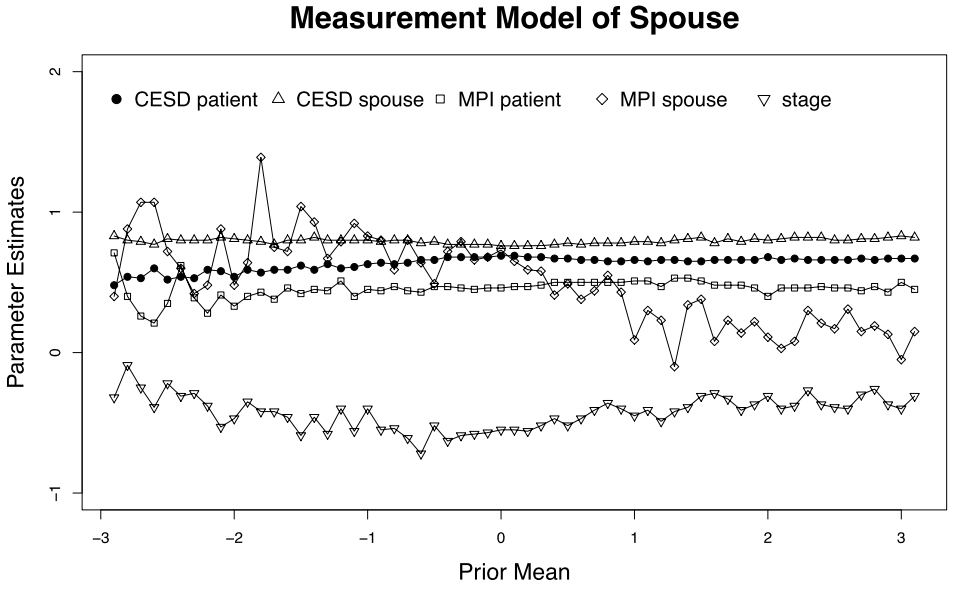

FIG. 2. *Sensitivity analysis of the proposed nonignorable model for the breast cancer data. The figure shows the parameter estimates of the spouses' measurement model under informative normal priors for* ϕ_1 *and* ϕ_2 *with a mean varying from* -3 *to* 3 *and a fixed variance of* 0.01.

TABLE 5

Parameter estimates and 95% *credible intervals* (*show in parentheses*) *for the patient's and spouse's measurement models by fixing a and b at* 0.01, 1 *and* 5 *for the inverse gamma prior* $IG(a, b)$ *on* σ_1^2, σ_2^2, τ_b^2 *and* τ_c^2

		$a = b = 0.01$	$a = b = 1$	$a = b = 5$
Patients	Intercept	4.72 (3.32, 6.11)	5.00 (3.48, 6.47)	5.02 (3.57, 6.48)
	Patient CESD	0.87 (0.81, 0.93)	0.86 (0.80, 0.92)	0.88 (0.83, 0.94)
	Spouse CESD	0.14 (0.09, 0.19)	0.14 (0.08, 0.19)	0.13 (0.08, 0.18)
	Patient MPI	1.27 (0.84, 1.71)	1.12 (0.67, 1.60)	1.20 (0.85, 1.57)
	Spouse MPI	0.71 (0.49, 0.91)	0.68 (0.46, 0.87)	0.61 (0.39, 0.82)
	Cancer stage	−0.03 (−0.50, 0.50)	0.18 (−0.31, 0.65)	−0.08 (−0.57, 0.40)
Spouses	Intercept	6.40 (4.39, 8.41)	7.56 (5.35, 9.93)	7.52 (5.43, 9.55)
	Patient CESD	0.67 (0.62, 0.73)	0.67 (0.62, 0.72)	0.69 (0.64, 0.73)
	Spouse CESD	0.76 (0.71, 0.80)	0.75 (0.71, 0.81)	0.75 (0.71, 0.80)
	Patient MPI	0.51 (0.32, 0.71)	0.54 (0.35, 0.73)	0.53 (0.34, 0.72)
	Spouse MPI	0.79 (−0.05, 1.46)	0.54 (−0.03, 1.06)	0.45 (−0.23, 1.09)
	Cancer stage	−0.41 (−0.86, 0.02)	−0.38 (−0.81, 0.03)	−0.48 (−0.87, 0.08)

within dyads using random effects. In the model, we allow a subject's outcome to depend on not only his/her own characteristics but also the characteristics of the other member in the dyad. As a result, the parameters of the proposed model have appealing interpretations as "actor" and "partner" effects, which greatly facilitates the understanding of interdependence within a relationship and the design of more efficient prevention programs. To account for the nonignorable dropout, we adopt a discrete time survival model to link the dropout process with the longitudinal measurement process. We used the data augment method to address the complex missing data problem caused by dropout and interdependence within dyads. The simulation study shows that the proposed method yields consistent estimates with correct coverage rates. We apply our methodology to the longitudinal dyadic data collected from a breast cancer study. Our method identifies more "partner" effects than the methods that ignore the missing data, thereby providing extra insights into the interdependence of the dyads. For example, the methods that ignore the missing data suggest that the spouse's CESD related only to his own previous CESD scores, whereas the proposed method suggested that the spouse's CESD related not only to his own CESD but also to the patient's CESD and MPI level. This extra information can be useful for the design of more efficient depression prevention programs for breast cancer patients.

In the proposed dropout model (3.2), we assume that time-dependent covariates $\mathbf{X}_{kij}$ and Y_{kij}, $k = 1, 2$, have captured all important time-dependent factors that influence dropout. However, this assumption may not be always true. A more flexible approach is to include in the model a time-dependent random effect c_{ij} to represent all unmeasured time-variant factors that influence dropout. We can further

put a hierarchical structure on c_{ij} to shrink it toward a dyad-level time-invariant random effect c_i to account for the effects of unmeasured time-invariance factors on dropout. In addition, in (3.2), in order to allow members in a dyad to drop out at different times, we specify separate dropout models for each dyadic member, linked by a common random effect. Although the common random effect makes the members in a dyad more likely to drop out at the same time, it may not be the most effective modeling approach when dropout mostly occurs at the dyad level. In this case, a more effective approach is that, in addition to the dyad-level random effect, we further put hierarchical structure on the coefficients of common covariates (in the two dropout models) to shrink toward a common value to reflect that dropout is almost always at the dyad level.

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REFERENCES

AGRESTI, A. (2002). *Categorical Data Analysis*, 2nd ed. Wiley, New York. MR1914507

BADR, H., CARMACK, C. L., KASHY, D. A., CRISTOFANILLI, M. and REVENSON, T. A. (2010). Dyadic coping in metastatic breast cancer. *Health Psychol*. **29** 169–180.

COOK, W. L. and KENNY, D. A. (2005). The actor partner interdependence model: A model of bidirectional effects in developmental studies. *International Journal of Behavioral Development* **29** 101–109.

DANIELS, M. J. and HOGAN, J. W. (2000). Reparameterizing the pattern mixture model for sensitivity analyses under informative dropout. *Biometrics* **56** 1241–1248. MR1815627

DANIELS, M. J. and HOGAN, J. W. (2008). *Missing Data in Longitudinal Studies*: *Strategies for Bayesian Modeling and Sensitivity Analysis*. *Monographs on Statistics and Applied Probability* **109**. Chapman & Hall/CRC, Boca Raton, FL. MR2459796

DIGGLE, P. and KENWARD, M. G. (1994). Informative drop-out in longitudinal data analysis. *J. R. Stat. Soc. Ser. C. Appl. Stat.* **43** 49–73.

DIGGLE, P. J., HEAGERTY, P. J., LIANG, K.-Y. and ZEGER, S. L. (2002). *Analysis of Longitudinal Data*, 2nd ed. *Oxford Statistical Science Series* **25**. Oxford Univ. Press, Oxford. MR2049007

FAREWELL, D. M. (2010). Marginal analyses of longitudinal data with an informative pattern of observations. *Biometrika* **97** 65–78. MR2594417

FOLLMANN, D. and WU, M. (1995). An approximate generalized linear model with random effects for informative missing data. *Biometrics* **51** 151–168. MR1341233

GLYNN, R. J., LAIRD, N. M. and RUBIN, D. B. (1986). Selection modelling versus mixture modelling with nonignorable nonresponse. In *Drawing Inferences from Self-selected Samples* (H. Wainer, ed.) 115–142. Springer, New York.

GOTTMAN, J. M. (1981). *Time–Series Analysis*: *A Comprehensive Introduction for Social Scientists*. Cambridge Univ. Press, Cambridge.

HOGAN, J. W. and LAIRD, N. M. (1997). Mixture models for the joint distribution of repeated measures and event times. *Stat. Med.* **16** 239–257.

HOGAN, J. W., LIN, X. and HERMAN, B. (2004). Mixtures of varying coefficient models for longitudinal data with discrete or continuous nonignorable dropout. *Biometrics* **60** 854–864. MR2133537

IBRAHIM, J. G. and MOLENBERGHS, G. (2009). Missing data methods in longitudinal studies: A review. *TEST* **18** 1–43. MR2495958

KALBFLEISCH, J. D. and LAWLESS, J. F. (1985). The analysis of panel data under a Markov assumption. *J. Amer. Statist. Assoc.* **80** 863–871. MR0819585

KENDALL, M. and ORD, J. K. (1990). *Time Series*, 3rd ed. Edward Arnold, London. MR1074771

KENNY, D. A., KASHY, D. A. and COOK, W. L. (2006). *Dyadic Data Analysis*. Guilford Press, New York.

KILPATRICK, M. G., KRISTJANSON, L. J., TATARYN, D. J. and FRASER, V. H. (1998). Information needs of husbands of women with breast cancer. *Oncology Nursing Forum* **25** 1595–1601.

LITTLE, R. J. A. (1993). Pattern-mixture models for multivariate incomplete data. *J. Amer. Statist. Assoc.* **88** 125–134.

LITTLE, R. J. A. (1994). A class of pattern-mixture models for normal incomplete data. *Biometrika* **81** 471–483. MR1311091

LITTLE, R. J. A. (1995). Modeling the drop-out mechanism in repeated-measures studies. *J. Amer. Statist. Assoc.* **90** 1112–1121. MR1354029

LITTLE, R. (2009). Selection and pattern-mixture models. In *Longitudinal Data Analysis* (G. Fitzmaurice, M. Davidian, G. Verbeke and G. Molenberghs, eds.) 409–431. CRC Press, Boca Raton, FL. MR1500128

LITTLE, R. J. A. and RUBIN, D. B. (2002). *Statistical Analysis with Missing Data*, 2nd ed. Wiley, Hoboken, NJ. MR1925014

MOLENBERGHS, G. and KENWARD, M. G. (2007). *Missing Data in Clinical Studies*. Wiley, New York.

ROBERTS, C., COX, C., SHANNON, V. and WELLS, N. (1994). A closer look at social support as a moderator of stress in breast cancer. *Health Social Work* **19** 157–164.

ROBINS, J. M., ROTNITZKY, A. and ZHAO, L. P. (1995). Analysis of semiparametric regression models for repeated outcomes in the presence of missing data. *J. Amer. Statist. Assoc.* **90** 106–121. MR1325118

ROTNITZKY, A., ROBINS, J. M. and SCHARFSTEIN, D. O. (1998). Semiparametric regression for repeated outcomes with nonignorable nonresponse. *J. Amer. Statist. Assoc.* **93** 1321–1339. MR1666631

ROTNITZKY, A., SCHARFSTEIN, D., SU, T.-L. and ROBINS, J. (2001). Methods for conducting sensitivity analysis of trials with potentially nonignorable competing causes of censoring. *Biometrics* **57** 103–113. MR1833295

ROY, J. (2003). Modeling longitudinal data with nonignorable dropouts using a latent dropout class model. *Biometrics* **59** 829–836. MR2025106

SCHARFSTEIN, D. O., ROTNITZKY, A. and ROBINS, J. M. (1999). Adjusting for nonignorable drop-out using semiparametric nonresponse models. *J. Amer. Statist. Assoc.* **94** 1096–1146. MR1731478

TANNER, M. A. and WONG, W. H. (1987). The calculation of posterior distributions by data augmentation. *J. Amer. Statist. Assoc.* **82** 528–550. MR0898357

TSONAKA, R., RIZOPOULOS, D., VERBEKE, G. and LESAFFRE, E. (2010). Nonignorable models for intermittently missing categorical longitudinal responses. *Biometrics* **66** 834–844. MR2758219

VERBEKE, G. and MOLENBERGHS, G. (2000). *Linear Mixed Models for Longitudinal Data*. Springer, New York. MR1880596

WU, M. C. and BAILEY, K. R. (1989). Estimation and comparison of changes in the presence of informative right censoring: Conditional linear model. *Biometrics* **45** 939–955. MR1029611

WU, M. C. and CARROLL, R. J. (1988). Estimation and comparison of changes in the presence of informative right censoring by modeling the censoring process. *Biometrics* **44** 175–188. MR0931633

YUAN, Y. and LITTLE, R. J. A. (2009). Mixed-effect hybrid models for longitudinal data with nonignorable dropout. *Biometrics* **65** 478–486. MR2751471

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