Appendix C. Varying Numbers of Regular Visits

3 Appendix C: Varying numbers of regular visits

We simulated responses Y from generalized linear mixed models with normal and binary outcomes and selected the data available for analysis (the observed data) according to an outcome-dependent visit process model. For each of 1000 subjects, we generated 151 longitudinal normal or binary responses from generalized linear mixed models with random slopes and intercepts, to resemble three years of potential weekly measurements:

$$\begin{aligned} y_{it} \mid \mathbf{b}_i, \mathbf{x}_{it}, \mathbf{z}_{it} &\sim f_{y|b,x,z}, i = 1, \ldots, m = 1000;\ t = 1, \ldots, 151, \\ g\{\mathrm{E}(y_{it}|\mathbf{b}_i, \mathbf{x}_{it}, \mathbf{z}_{it})\} &= \mathbf{x}_{it}^T \boldsymbol{\beta} + \mathbf{z}_{it}^T \mathbf{b}_i \equiv \eta_{it}, \\ \mathbf{b}_i &\sim \mathcal{N}(0, \Sigma_b), \end{aligned} \tag{5}$$

where $\mathbf{x}_{it}^T$ and $\mathbf{z}_{it}^T$ are known covariate row vectors relating the fixed and random effects, respectively, to the conditional mean of the outcome. Also $var(b_{0i}) = \sigma_0^2, var(b_{1i}) = \sigma_1^2, cov(b_{0i}, b_{1i}) = \sigma_{01}$, and $g(\cdot)$ is the known link function. Specifically, the linear predictor, η_{it}, included an intercept β_0, time effect β_t, group effect β_G, and a group by time interaction β_I, as well as random intercepts, $\beta_0 + b_{0i}$ and slopes, $\beta_t + b_{1i}$, with time,

$$\eta_{it} = (\beta_0 + b_{0i}) + (\beta_t + b_{1i}) X_{time,it} + \beta_G X_{group,i} + \beta_I X_{time,it} \times X_{group,i}. \tag{6}$$

X_{time} ranged from -0.5 to $+0.5$ in 150 equal steps. $X_{group} = 1$ for 300 subjects and $X_{group} = -1$ for the remaining 700 subjects. GLMMs with the linear predictor in (6) are the simplest forms that still capture the essence of a longitudinal model, namely within-subject trends in the response and differences in trends between groups of subjects.

The normal response, linear mixed effects model simulations used fixed effects parameters $\beta_0 = 0,\ \beta_G = 1,\ \beta_t = 2,\ \beta_I = 3$, covariance parameters $\sigma_0^2 = \sigma_1^2 = 1$, $\sigma_{01} = 0.5$ and a residual variance of 1. The binary response, mixed effects logistic model simulations used fixed effects parameters $\beta_0 = -1,\ \beta_G = 0.5,\ \beta_t = 1,\ \beta_I = 0.5$ and covariance parameters $\sigma_0^2 = \sigma_1^2 = 1$, and $\sigma_{01} = 0.5$.

3.1 Outcome-dependent visit processes

We select the data available for analysis (observed data) from the potential responses generated using (5) according to an outcome-dependent visit process. Let R_{it} be a binary indicator with $R_{it} = 1$ indicating that Y_{it} is observed and is 0 otherwise. We consider two models for the probability that $R_{it} = 1$. In model 1, $\Pr(R_{it} = 1)$ depends on the linear predictor of Y_{it} conditional on the random effects via a logistic model:

$$\text{logit}\{\Pr(R_{it} = 1 \mid b_i)\} = \mu_{it} + \gamma_Y \text{std}(\eta_{it}), \tag{7}$$

where std$(\cdot)$ of (7) denotes a variable standardized to have mean $= 0$ and variance $= 1$. We note that one could also specify models similar to (7) where the distribution of R_{it} depends directly on the random intercepts and slopes. In model 2, $\Pr(R_{it} = 1)$ depends on the value of Y at time $t - 1$, i.e. the lag 1 Y_{it}, which may be unobserved, via a logistic model:

$$\text{logit}\{\Pr(R_{it} = 1 \mid Y_i)\} = \mu_{it} + \gamma_Y \text{std}(Y_{i,t-1}). \tag{8}$$

We selected observed responses according to outcome-dependent visit processes that varied in the strength of outcome-dependence (magnitude of γ_Y in (7) or (8)) and the pattern (mix) of irregular and regular visit times. We generated regular visits by setting μ_{it} in (7) or (8) to values that produced the desired number of visits, using numerical methods and created an indicator variable $X_{regular}$ that indicated whether a visit was regular or irregular. We generated data according to five different visit patterns to explore potential reductions in bias resulting from adding regular visits to patterns where all the visits were irregular and potential efficiency gains resulting from adding irregular visits to patterns where all the visits were regular. Subjects in clinic-based longitudinal studies may provide outcomes and predictors at unscheduled visits which may be outcome-dependent in addition to their regularly scheduled visits and it would be worthwhile to include information from these unscheduled visits if it increased estimation efficiency without substantially increasing bias. Three visit patterns selected an average of 6.4

observations per subject. In the first pattern, all visits were regular, while in the second, all visits were irregular. The third pattern had a mixture of visit types, 2.8 irregular and 3.6 regular. The fourth pattern selected an average of 3.6 regular visits to allow us to assess the effect of adding the 2.8 irregular visits in pattern 3. The fifth pattern selected an average of 3.6 irregular visits to allow us to assess differences in parameter estimates between patterns where all the visits were either regular or all were irregular (by comparing patterns 4 and 5).

The simulations used a range of values for the outcome-dependence parameter, γ_Y =0, 0.32, 0.65, 0.97 in order to generate a range of settings from no outcome-dependence ($\gamma_Y = 0$) to strongly outcome-dependent ($\gamma_Y = 0.97$).

3.2 Fitted approaches

To each data set we fit the six approaches described in detail below: 1) three marginal models: an unweighted approach; weighted marginal models with weights that depend on the covariates X; and weighted marginal models with weights that depend on the covariates X and the last prior observed response Y; 2) joint models for responses and visit times that modeled the visit process in terms of the conditional linear predictor of Y as in (7); 3) standard mixed effects models; and 4) standard mixed effects models that additionally adjusted for the previous number of visits.

We implemented the inverse intensity rate ratio (IIRR)-weighted generalized estimating equations (GEE) approach described in the main summary report for longitudinal normal responses using weighted least squares. The covariate vector $W_i(t)$ included group, X_{group}, the regular visit indicator $X_{regular}$, and the group by regular visit indicator interaction for the first weighted approach and added dependence on the last prior observed response as a second weighted approach. We implemented the approach for binary responses analogously by weighting standard logistic models. We note that the GEE and mixed model approaches estimate different parameters and include the GEE approaches in our simulation studies in order to assess the effect of increasing the magnitude of outcome-dependence in the visit process.

We fit joint models for responses and visit times that we could implement with existing, widely available software, in this case PROC NLMIXED in SAS. Let V_{it} denote the time between the t^{th} and $(t+1)^{st}$ visits for the i^{th} subject, the inter-visit time, where $t = 0$ will correspond to the start of the study, time 0. The models contained a generalized linear mixed submodel for the response Y in (5) and a mixed effects gamma model for the inter-visit times of a subject. The linear predictor η_V for the fitted mixed effects gamma model corresponded to the model that generated visits according to the conditional linear predictor using (7). That is, the fitted gamma model had

$$\eta_{V_{it}} = \gamma_0 + \gamma\eta_{it}.$$

The linear predictor relates to the expected value of V through a log link:

$$E(V_{it}) = \mu_V = exp(\eta_{V_{it}}).$$

We based our choice of the form of the fitted joint models merely on convenience since we will not typically have the necessary information to correctly specify the visit process model. Thus, the joint models are misspecified to some degree.

To fit an analogous model where the linear predictor η_V depended on lagged responses we would need to include observed responses in the model for η_V. Since the parameters of the models for the response Y and inter-visit times V are distinct, the joint distribution of (Y, V) would factor so that maximum likelihood estimates obtained from the likelihood based on the responses Y alone would be identical to those obtained from the joint likelihood based on Y and V. Thus, we do not present results from joint model fits with dependence of the visit process on observed lag one dependence of the response. Instead, we fit joint models that assume that the visit process depends on the conditional linear predictor of Y as in (7) when in fact the visit process depended on the lag 1 response of Y.

We note that our choice of fitted models for the joint model simulations with visit process dependent on the linear predictor of the response (7) likely provides an optimistic view of the performance of the models since we correctly specify the form of the dependence of the visit process on the responses (i.e., we used a conditional linear predictor dependence joint model when the visit process was (7)) and we will typically not be able to do so in practice. Thus, our findings provide an assessment of performance in an idealized case.

We fit standard linear mixed and mixed effects logistic models using PROC MIXED and GLIMMIX with 12 quadrature points, respectively, in SAS as a third approach. We added the current cumulative number of visits by a subject to the standard mixed effects models of approach 3 as an additional approach.

Our original plan was to fit the joint model approach to each of the five patterns of irregular and regular visit times. However, despite much effort we were not able to obtain acceptable convergence rates for visit patterns involving only regular visits. For example, for normal responses with the 6.4 regular only visit pattern and $\gamma_Y = 0.97$ only 56% of the joint model fits converged. In the regular visit only setting, visit times are essentially deterministic and our attempts to model these visit time distributions as random variables resulted in substantial computational difficulties. Of course in practice it is most appropriate to fit a standard mixed effects model in settings where visit times are all regular, i.e. non-outcome-dependent; one would not fit a joint model in such settings. Thus, we only present findings from the joint model approach in the settings that involved at least some irregular visit times.

3.3 Results

The tables below present means of estimates of all the parameters, including the constant, β_0, group effect, β_g, time effect, β_t, and interaction effect, β_I of equation (6) for normal and binary responses with lag one dependence in the visit process (8) and conditional linear predictor dependence in the visit process (7) for standard generalized linear mixed models that ignore outcome-dependent visits (Avg ML), the inverse intensity rate ratio (IIRR)-weighted generalized estimating equations (GEE) approach with weights depending on both X and Y (Avg BZ_Y), and joint models for responses and visits (Avg JT_Y).

The unweighted GEE approach and the IIRR approach with weights dependent on covariates alone produced magnitudes of bias similar to the IIRR approach with weights dependent on both covariates and responses. The linear mixed effects and mixed effects logistic models that additionally adjusted for the previous number of responses produced biased estimates in all settings with outcome-dependent visits, even those with a mixture of regular and irregular visits. This makes intuitive sense. Suppose that the visit process depends on the conditional linear predictor and that the response is increasing over time. Then the cumulative number of visits is correlated with the time effect but not part of the model, such as (5), that generated the response. Including the correlated visit count variable in models for the response produces bias in estimated time effects, as well as other covariate effects (see rows of data designated with MLN in the tables).

The additional simulation results in this Appendix are consistent with those presented in the main report and the theory. For normal responses, the tables show that estimates of the intercept, β_0, were biased for all six approaches when all visits were irregular. Bias was reduced substantially for ML estimators in the mixed visit pattern with both regular and irregular visits. Bias was also small for the joint model estimators. Bias reductions for this pattern were much smaller for the other four approaches.

3.4 Tables of means of parameter estimates

Table 13: Means of estimated intercepts, β_0, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_0 = 0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.00	0.21	0.40	0.59
	BZ	0.00	0.21	0.40	0.59
	BZY	0.03	0.30	0.56	0.81
	ML	0.00	0.05	0.10	0.18
	JTY	0.00	0.02	0.05	0.10
	MLN	0.00	-0.15	-0.12	0.06
6.4 irregular, 0 regular	GEE	0.00	0.21	0.42	0.61
	BZ	0.00	0.21	0.42	0.61
	BZY	0.02	0.31	0.61	0.89
	ML	0.00	0.08	0.16	0.26
	JTY	-0.00	0.04	0.10	0.19
	MLN	-0.00	-0.05	0.00	0.17
2.8 irregular, 3.6 regular	GEE	0.00	0.11	0.22	0.31
	BZ	0.00	0.07	0.14	0.21
	BZY	0.03	0.14	0.25	0.33
	ML	0.00	0.02	0.04	0.05
	JTY	-0.00	0.00	0.01	0.02
	MLN	-0.00	-0.19	-0.27	-0.17
0 irregular, 3.6 regular	GEE	-0.00	0.02	0.04	0.06
	BZ	-0.00	0.02	0.04	0.06
	BZY	0.02	0.05	0.08	0.10
	ML	-0.00	0.01	0.02	0.02
	JTY	*	*	*	*
	MLN	0.00	-0.18	-0.35	-0.51
0 irregular, 6.4 regular	GEE	-0.00	0.02	0.03	0.05
	BZ	-0.00	0.02	0.03	0.05
	BZY	0.04	0.06	0.08	0.09
	ML	-0.00	0.00	0.01	0.01
	JTY	*	*	*	*
	MLN	0.00	-0.28	-0.56	-0.82

* Convergence rates too low to provide meaningful summaries.

Table 14: Means of estimated group effects, β_g, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_g = 1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	1.00	1.00	0.99	0.96
	BZ	1.00	1.00	0.99	0.96
	BZY	1.00	1.00	0.98	0.95
	ML	1.00	0.99	0.96	0.91
	JTY	1.00	1.01	1.02	1.03
	MLN	1.00	0.97	0.91	0.87
6.4 irregular, 0 regular	GEE	1.00	1.00	0.99	0.97
	BZ	1.00	1.00	0.99	0.97
	BZY	1.00	0.99	0.98	0.94
	ML	1.00	0.98	0.94	0.88
	JTY	1.00	1.01	1.01	1.01
	MLN	1.00	0.97	0.92	0.87
2.8 irregular, 3.6 regular	GEE	1.00	1.01	1.03	1.07
	BZ	1.00	1.00	1.02	1.06
	BZY	1.00	1.01	1.03	1.07
	ML	1.00	1.00	1.00	0.99
	JTY	1.00	1.00	1.01	1.02
	MLN	1.00	0.98	0.95	0.95
0 irregular, 3.6 regular	GEE	1.00	1.00	0.99	0.97
	BZ	1.00	1.00	0.99	0.97
	BZY	1.00	1.00	0.99	0.98
	ML	1.00	1.00	0.99	0.99
	JTY	*	*	*	*
	MLN	1.00	1.00	0.99	0.99
0 irregular, 6.4 regular	GEE	1.00	1.00	0.99	0.98
	BZ	1.00	1.00	0.99	0.98
	BZY	1.00	1.00	0.99	0.98
	ML	1.00	1.00	1.00	1.00
	JTY	*	*	*	*
	MLN	1.00	1.00	0.99	0.99

* Convergence rates too low to provide meaningful summaries.

Table 15: Means of estimated time effects, β_t, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_t = 2.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	2.00	2.19	2.35	2.45
	BZ	2.00	2.19	2.35	2.45
	BZY	2.03	2.17	2.28	2.32
	ML	2.00	2.03	2.06	2.10
	JTY	2.00	1.97	1.93	1.93
	MLN	2.00	1.48	1.29	1.49
6.4 irregular, 0 regular	GEE	2.01	2.20	2.38	2.52
	BZ	2.01	2.20	2.38	2.52
	BZY	2.02	2.16	2.29	2.36
	ML	2.00	2.06	2.11	2.18
	JTY	2.00	1.96	1.92	1.93
	MLN	2.00	1.64	1.46	1.61
2.8 irregular, 3.6 regular	GEE	2.00	2.09	2.21	2.33
	BZ	2.00	2.06	2.14	2.24
	BZY	2.03	2.04	2.09	2.19
	ML	2.00	2.01	2.02	2.03
	JTY	2.01	2.05	2.08	2.09
	MLN	2.00	1.56	1.32	1.47
0 irregular, 3.6 regular	GEE	2.00	2.01	2.02	2.03
	BZ	2.00	2.01	2.02	2.03
	BZY	2.02	2.02	2.02	2.02
	ML	2.00	2.00	2.00	2.01
	JTY	*	*	*	*
	MLN	2.00	1.61	1.23	0.88
0 irregular, 6.4 regular	GEE	2.00	2.01	2.02	2.03
	BZ	2.00	2.01	2.02	2.03
	BZY	2.04	2.04	2.04	2.04
	ML	2.00	2.00	2.00	2.00
	JTY	*	*	*	*
	MLN	2.01	1.41	0.83	0.30

* Convergence rates too low to provide meaningful summaries.

Table 16: Means of estimated interaction effects, β_I, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_I = 3.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	3.00	3.00	2.97	2.89
	BZ	3.00	3.00	2.97	2.89
	BZY	3.00	3.02	2.99	2.88
	ML	3.00	2.99	2.95	2.89
	JTY	3.00	2.97	2.90	2.82
	MLN	3.00	2.88	2.62	2.47
6.4 irregular, 0 regular	GEE	3.00	3.01	3.00	2.94
	BZ	3.00	3.01	3.00	2.94
	BZY	3.00	3.01	2.98	2.87
	ML	3.00	2.99	2.94	2.87
	JTY	3.00	2.96	2.86	2.74
	MLN	3.00	2.91	2.66	2.48
2.8 irregular, 3.6 regular	GEE	3.00	3.02	3.07	3.15
	BZ	3.00	3.01	3.04	3.10
	BZY	3.00	3.02	3.08	3.15
	ML	3.00	3.00	3.00	2.99
	JTY	3.00	2.98	2.95	2.91
	MLN	3.00	2.95	2.81	2.76
0 irregular, 3.6 regular	GEE	3.00	2.99	2.96	2.92
	BZ	3.00	2.99	2.96	2.92
	BZY	3.00	2.98	2.94	2.90
	ML	3.00	2.99	2.98	2.96
	JTY	*	*	*	*
	MLN	3.00	2.99	2.97	2.94
0 irregular, 6.4 regular	GEE	3.00	2.99	2.96	2.93
	BZ	3.00	2.99	2.96	2.93
	BZY	3.00	2.99	2.96	2.92
	ML	3.00	3.00	2.99	2.98
	JTY	*	*	*	*
	MLN	3.00	2.99	2.96	2.93

* Convergence rates too low to provide meaningful summaries.

Table 17: Means of estimated intercepts, β_0, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_0 = 0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.00	0.18	0.34	0.50
	BZ	0.00	0.18	0.34	0.50
	BZY	0.03	0.26	0.48	0.69
	ML	0.00	0.04	0.08	0.14
	JTL	0.00	0.04	0.08	0.14
	MLN	-0.00	-0.13	-0.14	-0.03
6.4 irregular, 0 regular	GEE	-0.00	0.18	0.35	0.52
	BZ	-0.00	0.18	0.35	0.52
	BZY	0.02	0.27	0.52	0.76
	ML	-0.00	0.06	0.13	0.20
	JTL	0.00	0.07	0.13	0.21
	MLN	-0.00	-0.05	-0.03	0.09
2.8 irregular, 3.6 regular	GEE	0.00	0.09	0.19	0.27
	BZ	0.00	0.06	0.12	0.18
	BZY	0.03	0.12	0.21	0.29
	ML	0.00	0.02	0.03	0.04
	JTL	0.00	0.02	0.03	0.04
	MLN	0.00	-0.16	-0.25	-0.22
0 irregular, 3.6 regular	GEE	-0.00	0.02	0.03	0.05
	BZ	- 0.00	0.02	0.03	0.05
	BZY	0.02	0.05	0.07	0.09
	ML	- 0.00	0.01	0.01	0.02
	JTL	*	*	*	*
	MLN	0.00	-0.15	-0.30	-0.43
0 irregular, 6.4 regular	GEE	0.00	0.02	0.03	0.04
	BZ	0.00	0.02	0.03	0.04
	BZY	0.04	0.06	0.07	0.08
	ML	0.00	0.00	0.01	0.01
	JTL	*	*	*	*
	MLN	0.00	-0.24	-0.48	-0.70

* Convergence rates too low to provide meaningful summaries.

Table 18: Means of estimated group effects, β_g, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_g = 1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	1.00	1.00	0.99	0.97
	BZ	1.00	1.00	0.99	0.97
	BZY	1.00	1.00	0.99	0.96
	ML	1.00	0.99	0.97	0.93
	JTL	1.00	0.99	0.97	0.93
	MLN	1.00	0.98	0.93	0.90
6.4 irregular, 0 regular	GEE	1.00	1.00	0.99	0.98
	BZ	1.00	1.00	0.99	0.98
	BZY	1.00	1.00	0.98	0.96
	ML	1.00	0.99	0.96	0.91
	JTL	1.00	0.99	0.96	0.91
	MLN	1.00	0.98	0.94	0.89
2.8 irregular, 3.6 regular	GEE	1.00	1.01	1.03	1.05
	BZ	1.00	1.00	1.02	1.04
	BZY	1.00	1.01	1.02	1.05
	ML	1.00	1.00	1.00	1.00
	JTL	1.00	1.00	1.00	1.00
	MLN	1.00	0.99	0.97	0.95
0 irregular, 3.6 regular	GEE	1.00	1.00	0.99	0.98
	BZ	1.00	1.00	0.99	0.98
	BZY	1.00	1.00	0.99	0.99
	ML	1.00	1.00	0.99	0.99
	JTL	*	*	*	*
	MLN	1.00	1.00	0.99	0.99
0 irregular, 6.4 regular	GEE	1.00	1.00	0.99	0.98
	BZ	1.00	1.00	0.99	0.98
	BZY	1.00	1.00	0.99	0.99
	ML	1.00	1.00	1.00	1.00
	JTL	*	*	*	*
	MLN	1.00	1.00	0.99	0.99

* Convergence rates too low to provide meaningful summaries.

Table 19: Means of estimated time effects, β_t, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_t = 2.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	2.00	2.16	2.30	2.40
	BZ	2.00	2.16	2.30	2.40
	BZY	2.03	2.15	2.25	2.30
	ML	2.00	2.03	2.05	2.07
	JTL	2.00	2.02	2.04	2.07
	MLN	2.00	1.57	1.32	1.40
6.4 irregular, 0 regular	GEE	2.00	2.17	2.33	2.45
	BZ	2.00	2.17	2.33	2.45
	BZY	2.01	2.14	2.25	2.32
	ML	2.00	2.05	2.09	2.14
	JTL	2.00	2.05	2.09	2.13
	MLN	2.00	1.71	1.49	1.52
2.8 irregular, 3.6 regular	GEE	2.00	2.07	2.17	2.27
	BZ	2.00	2.05	2.11	2.19
	BZY	2.04	2.04	2.07	2.13
	ML	2.00	2.01	2.02	2.03
	JTL	2.00	2.01	2.02	2.03
	MLN	2.00	1.64	1.38	1.39
0 irregular, 3.6 regular	GEE	2.00	2.01	2.02	2.02
	BZ	2.00	2.01	2.02	2.02
	BZY	2.02	2.02	2.02	2.02
	ML	2.00	2.00	2.01	2.01
	JTL	*	*	*	*
	MLN	2.00	1.67	1.35	1.06
0 irregular, 6.4 regular	GEE	2.00	2.01	2.01	2.02
	BZ	2.00	2.01	2.01	2.02
	BZY	2.04	2.04	2.04	2.04
	ML	2.00	2.00	2.00	2.00
	JTL	*	*	*	*
	MLN	2.00	1.49	0.99	0.53

* Convergence rates too low to provide meaningful summaries.

Table 20: Means of estimated interaction effects, β_I, from six approaches fitted to data simulated from linear mixed effects models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_I = 3.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	3.01	3.00	2.99	2.93
	BZ	3.01	3.00	2.99	2.93
	BZY	3.01	3.02	3.01	2.94
	ML	3.00	2.99	2.96	2.92
	JTL	3.00	2.99	2.96	2.91
	MLN	3.00	2.92	2.71	2.55
6.4 irregular, 0 regular	GEE	3.00	3.01	3.00	2.97
	BZ	3.00	3.01	3.00	2.97
	BZY	3.01	3.02	2.99	2.93
	ML	3.00	2.99	2.95	2.90
	JTL	3.00	2.99	2.95	2.90
	MLN	3.00	2.94	2.75	2.56
2.8 irregular, 3.6 regular	GEE	3.00	3.01	3.05	3.11
	BZ	3.00	3.00	3.03	3.07
	BZY	3.00	3.01	3.05	3.11
	ML	3.00	3.00	3.00	2.99
	JTL	3.00	3.00	3.00	2.99
	MLN	3.00	2.96	2.86	2.78
0 irregular, 3.6 regular	GEE	2.99	2.99	2.96	2.93
	BZ	2.99	2.99	2.96	2.93
	BZY	3.00	2.99	2.96	2.92
	ML	2.99	2.99	2.98	2.97
	JTL	*	*	*	*
	MLN	2.99	2.99	2.97	2.95
0 irregular, 6.4 regular	GEE	3.00	2.99	2.97	2.95
	BZ	3.00	2.99	2.97	2.95
	BZY	3.00	2.99	2.97	2.94
	ML	3.00	3.00	2.99	2.98
	JTL	*	*	*	*
	MLN	3.00	2.99	2.97	2.95

* Convergence rates too low to provide meaningful summaries.

Table 21: Means of estimated intercepts, β_0, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_0 = -1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	-0.84	-0.60	-0.38	-0.17
	BZ	-0.84	-0.60	-0.38	-0.17
	BZY	-0.83	-0.57	-0.32	-0.08
	ML	-1.00	-0.85	-0.71	-0.57
	JTY	-1.00	-0.98	-0.94	-0.88
	MLN	-1.00	-1.33	-1.26	-0.98
6.4 irregular, 0 regular	GEE	-0.84	-0.60	-0.37	-0.15
	BZ	-0.84	-0.60	-0.37	-0.15
	BZY	-0.83	-0.53	-0.25	0.01
	ML	-1.00	-0.81	-0.64	-0.48
	JTY	-1.00	-0.94	-0.85	-0.76
	MLN	-1.00	-1.12	-1.04	-0.81
2.8 irregular, 3.6 regular	GEE	-0.84	-0.72	-0.59	-0.47
	BZ	-0.84	-0.76	-0.68	-0.62
	BZY	-0.83	-0.73	-0.63	-0.54
	ML	-1.00	-0.93	-0.86	-0.82
	JTY	-1.02	-0.96	-0.91	-0.88
	MLN	-1.00	-1.46	-1.63	-1.52
0 irregular, 3.6 regular	GEE	-0.84	-0.82	-0.80	-0.79
	BZ	-0.84	-0.82	-0.80	-0.79
	BZY	-0.84	-0.80	-0.78	-0.76
	ML	-1.01	-0.98	-0.96	-0.95
	JTY	*	*	*	*
	MLN	-1.00	-1.31	-1.58	-1.80
0 irregular, 6.4 regular	GEE	-0.84	-0.82	-0.81	-0.79
	BZ	-0.84	-0.82	-0.81	-0.79
	BZY	-0.83	-0.80	-0.79	-0.77
	ML	-1.00	-0.99	-0.97	-0.96
	JTY	*	*	*	*
	MLN	-1.01	-1.61	-2.14	-2.55

* Convergence rates too low to provide meaningful summaries.

Table 22: Means of estimated group effects, β_g, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_g = 0.5$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.42	0.41	0.40	0.39
	BZ	0.42	0.41	0.40	0.39
	BZY	0.42	0.41	0.39	0.36
	ML	0.50	0.49	0.46	0.42
	JTY	0.50	0.50	0.50	0.48
	MLN	0.50	0.43	0.33	0.27
6.4 irregular, 0 regular	GEE	0.42	0.41	0.40	0.40
	BZ	0.42	0.41	0.40	0.40
	BZY	0.42	0.41	0.38	0.36
	ML	0.51	0.49	0.46	0.43
	JTY	0.50	0.50	0.49	0.46
	MLN	0.51	0.45	0.36	0.30
2.8 irregular, 3.6 regular	GEE	0.41	0.42	0.43	0.45
	BZ	0.41	0.41	0.42	0.44
	BZY	0.42	0.42	0.42	0.42
	ML	0.50	0.50	0.50	0.50
	JTY	0.49	0.46	0.45	0.45
	MLN	0.50	0.46	0.39	0.34
0 irregular, 3.6 regular	GEE	0.41	0.40	0.40	0.39
	BZ	0.41	0.40	0.40	0.39
	BZY	0.42	0.41	0.41	0.40
	ML	0.50	0.50	0.49	0.48
	JTY	*	*	*	*
	MLN	0.50	0.49	0.48	0.46
0 irregular, 6.4 regular	GEE	0.41	0.41	0.40	0.40
	BZ	0.41	0.41	0.40	0.40
	BZY	0.42	0.41	0.41	0.40
	ML	0.50	0.50	0.49	0.49
	JTY	*	*	*	*
	MLN	0.50	0.49	0.47	0.45

* Convergence rates too low to provide meaningful summaries.

Table 23: Means of estimated time effects, β_t, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_t = 1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.95	1.13	1.28	1.40
	BZ	0.95	1.13	1.28	1.40
	BZY	0.96	1.03	1.10	1.15
	ML	1.01	1.13	1.24	1.32
	JTY	1.00	0.97	0.94	0.95
	MLN	1.01	-0.06	-0.35	-0.14
6.4 irregular, 0 regular	GEE	0.95	1.13	1.31	1.45
	BZ	0.95	1.13	1.31	1.45
	BZY	0.96	1.02	1.10	1.17
	ML	1.02	1.19	1.33	1.43
	JTY	1.00	0.95	0.91	0.94
	MLN	1.02	0.39	0.08	0.16
2.8 irregular, 3.6 regular	GEE	0.94	1.01	1.11	1.22
	BZ	0.94	0.98	1.04	1.10
	BZY	0.94	0.91	0.90	0.91
	ML	1.01	1.05	1.09	1.13
	JTY	1.13	1.37	1.39	1.33
	MLN	1.00	-0.04	-0.56	-0.51
0 irregular, 3.6 regular	GEE	0.94	0.95	0.96	0.95
	BZ	0.94	0.95	0.96	0.95
	BZY	0.95	0.94	0.93	0.91
	ML	1.01	1.03	1.04	1.04
	JTY	*	*	*	*
	MLN	1.02	0.36	-0.22	-0.71
0 irregular, 6.4 regular	GEE	0.94	0.95	0.95	0.95
	BZ	0.94	0.95	0.95	0.95
	BZY	0.95	0.95	0.94	0.93
	ML	1.00	1.01	1.02	1.02
	JTY	*	*	*	*
	MLN	1.00	-0.25	-1.36	-2.22

* Convergence rates too low to provide meaningful summaries.

Table 24: Means of estimated interaction effects, β_I, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on conditional linear predictors of the response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_I = 0.5$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.34	0.34	0.33	0.30
	BZ	0.34	0.34	0.33	0.30
	BZY	0.34	0.34	0.34	0.31
	ML	0.50	0.48	0.45	0.41
	JTY	0.50	0.47	0.44	0.41
	MLN	0.50	0.33	0.06	-0.08
6.4 irregular, 0 regular	GEE	0.35	0.34	0.33	0.31
	BZ	0.35	0.34	0.33	0.31
	BZY	0.34	0.33	0.32	0.30
	ML	0.51	0.49	0.46	0.41
	JTY	0.50	0.45	0.42	0.39
	MLN	0.51	0.37	0.14	-0.03
2.8 irregular, 3.6 regular	GEE	0.34	0.35	0.37	0.40
	BZ	0.34	0.35	0.36	0.38
	BZY	0.32	0.32	0.33	0.36
	ML	0.50	0.50	0.51	0.52
	JTY	0.47	0.45	0.47	0.49
	MLN	0.50	0.41	0.23	0.09
0 irregular, 3.6 regular	GEE	0.34	0.34	0.33	0.32
	BZ	0.34	0.34	0.33	0.32
	BZY	0.31	0.31	0.30	0.30
	ML	0.50	0.50	0.49	0.47
	JTY	*	*	*	*
	MLN	0.50	0.49	0.46	0.44
0 irregular, 6.4 regular	GEE	0.34	0.34	0.33	0.33
	BZ	0.34	0.34	0.33	0.33
	BZY	0.33	0.32	0.32	0.32
	ML	0.50	0.50	0.49	0.48
	JTY	*	*	*	*
	MLN	0.50	0.48	0.45	0.41

* Convergence rates too low to provide meaningful summaries.

Table 25: Means of estimated intercepts, β_0, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_0 = -1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	-0.84	-0.72	-0.60	-0.50
	BZ	-0.84	-0.72	-0.60	-0.50
	BZY	-0.83	-0.69	-0.56	-0.45
	ML	-1.00	-0.93	-0.86	-0.78
	JTL	-1.00	-0.93	-0.86	-0.78
	MLN	-1.00	-1.20	-1.32	-1.32
6.4 irregular, 0 regular	GEE	-0.84	-0.72	-0.60	-0.50
	BZ	-0.84	-0.72	-0.60	-0.50
	BZY	-0.83	-0.68	-0.52	-0.40
	ML	-1.00	-0.91	-0.81	-0.73
	JTL	-1.00	-0.91	-0.81	-0.72
	MLN	-1.00	-1.08	-1.11	-1.10
2.8 irregular, 3.6 regular	GEE	-0.84	-0.78	-0.72	-0.67
	BZ	-0.84	-0.80	-0.76	-0.73
	BZY	-0.82	-0.77	-0.73	-0.69
	ML	-1.00	-0.96	-0.93	-0.90
	JTL	-1.00	-0.97	-0.93	-0.90
	MLN	-1.00	-1.24	-1.44	-1.55
0 irregular, 3.6 regular	GEE	-0.84	-0.83	-0.82	-0.82
	BZ	-0.84	-0.83	-0.82	-0.82
	BZY	-0.83	-0.82	-0.81	-0.81
	ML	-1.01	-1.00	-0.99	-0.99
	JTL	*	*	*	*
	MLN	-1.00	-1.12	-1.19	-1.23
0 irregular, 6.4 regular	GEE	-0.84	-0.83	-0.83	-0.82
	BZ	-0.84	-0.83	-0.83	-0.82
	BZY	-0.82	-0.82	-0.81	-0.81
	ML	-1.00	-1.00	-0.99	-0.99
	JTL	*	*	*	*
	MLN	-0.99	-1.22	-1.37	-1.46

* Convergence rates too low to provide meaningful summaries.

Table 26: Means of estimated group effects, β_g, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_g = 0.5$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.41	0.42	0.41	0.39
	BZ	0.41	0.42	0.41	0.39
	BZY	0.42	0.42	0.41	0.38
	ML	0.50	0.50	0.49	0.47
	JTL	0.51	0.50	0.49	0.47
	MLN	0.50	0.48	0.43	0.37
6.4 irregular, 0 regular	GEE	0.41	0.42	0.41	0.39
	BZ	0.41	0.42	0.41	0.39
	BZY	0.42	0.42	0.40	0.38
	ML	0.50	0.50	0.49	0.46
	JTL	0.51	0.51	0.49	0.47
	MLN	0.50	0.49	0.45	0.39
2.8 irregular, 3.6 regular	GEE	0.41	0.41	0.41	0.41
	BZ	0.41	0.41	0.41	0.41
	BZY	0.42	0.42	0.42	0.42
	ML	0.50	0.50	0.50	0.49
	JTL	0.50	0.50	0.50	0.49
	MLN	0.50	0.49	0.46	0.43
0 irregular, 3.6 regular	GEE	0.41	0.41	0.41	0.41
	BZ	0.41	0.41	0.41	0.41
	BZY	0.42	0.42	0.42	0.42
	ML	0.50	0.50	0.50	0.50
	JTL	*	*	*	*
	MLN	0.50	0.50	0.50	0.50
0 irregular, 6.4 regular	GEE	0.41	0.41	0.41	0.41
	BZ	0.41	0.41	0.41	0.41
	BZY	0.42	0.42	0.42	0.42
	ML	0.50	0.50	0.50	0.50
	JTL	*	*	*	*
	MLN	0.50	0.50	0.50	0.50

* Convergence rates too low to provide meaningful summaries.

Table 27: Means of estimated time effects, β_t, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_t = 1.0$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.94	1.03	1.08	1.11
	BZ	0.94	1.03	1.08	1.11
	BZY	0.95	0.98	0.97	0.94
	ML	1.00	1.07	1.12	1.15
	JTL	1.00	1.07	1.12	1.15
	MLN	1.00	0.43	-0.07	-0.32
6.4 irregular, 0 regular	GEE	0.94	1.03	1.08	1.11
	BZ	0.94	1.03	1.08	1.11
	BZY	0.94	0.96	0.95	0.93
	ML	1.01	1.09	1.16	1.20
	JTL	1.00	1.09	1.17	1.21
	MLN	1.01	0.67	0.35	0.14
2.8 irregular, 3.6 regular	GEE	0.94	0.97	0.99	1.01
	BZ	0.94	0.96	0.97	0.98
	BZY	0.94	0.92	0.90	0.87
	ML	1.00	1.03	1.04	1.05
	JTL	1.00	1.03	1.04	1.05
	MLN	1.00	0.47	-0.01	-0.31
0 irregular, 3.6 regular	GEE	0.93	0.94	0.95	0.95
	BZ	0.93	0.94	0.95	0.95
	BZY	0.94	0.94	0.94	0.94
	ML	1.01	1.02	1.03	1.03
	JTL	*	*	*	*
	MLN	1.02	0.78	0.62	0.53
0 irregular, 6.4 regular	GEE	0.94	0.95	0.95	0.95
	BZ	0.94	0.95	0.95	0.95
	BZY	0.95	0.95	0.95	0.95
	ML	1.00	1.01	1.01	1.02
	JTL	*	*	*	*
	MLN	1.02	0.55	0.25	0.07

* Convergence rates too low to provide meaningful summaries.

Table 28: Means of estimated interaction effects, β_I, from six approaches fitted to data simulated from mixed effects logistic models with informative visit processes dependent on a lag one response for four strengths of informativeness, γ_Y and five different visit patterns. True $\beta_I = 0.5$.

		γ_Y			
Visit Pattern	Approach	0	0.32	0.65	0.97
3.6 irregular, 0 regular	GEE	0.34	0.34	0.31	0.28
	BZ	0.34	0.34	0.31	0.28
	BZY	0.34	0.32	0.30	0.28
	ML	0.50	0.49	0.47	0.44
	JTL	0.50	0.49	0.47	0.43
	MLN	0.50	0.45	0.31	0.18
6.4 irregular, 0 regular	GEE	0.35	0.34	0.31	0.28
	BZ	0.35	0.34	0.31	0.28
	BZY	0.34	0.32	0.29	0.26
	ML	0.51	0.50	0.46	0.43
	JTL	0.50	0.49	0.45	0.42
	MLN	0.51	0.46	0.35	0.24
2.8 irregular, 3.6 regular	GEE	0.34	0.34	0.34	0.33
	BZ	0.34	0.34	0.34	0.34
	BZY	0.32	0.31	0.31	0.32
	ML	0.50	0.50	0.50	0.49
	JTL	0.50	0.50	0.49	0.49
	MLN	0.50	0.48	0.41	0.33
0 irregular, 3.6 regular	GEE	0.34	0.34	0.34	0.34
	BZ	0.34	0.34	0.34	0.34
	BZY	0.31	0.31	0.31	0.31
	ML	0.50	0.50	0.50	0.50
	JTL	*	*	*	*
	MLN	0.50	0.50	0.50	0.50
0 irregular, 6.4 regular	GEE	0.35	0.35	0.34	0.34
	BZ	0.35	0.35	0.34	0.34
	BZY	0.33	0.33	0.33	0.33
	ML	0.50	0.50	0.50	0.50
	JTL	*	*	*	*
	MLN	0.50	0.50	0.50	0.50

* Convergence rates too low to provide meaningful summaries.