Simulation report – prediction of survival probabilities

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1 Objective

To compare the predictive capabilities of survival probabilities between QRJM and JM using linear mixed model (LMJM) for data from different distribution features.

2 Simulation procedure

1. Define different simulation scenarios in terms of the distribution of random error and simulate 100 data sets for each scenario (see below for the specification of scenarios). Each simulated data set has 600 subjects, 500 out of which will be used to fit the model for inference purpose and the rest 100 will be used to make predictions and validation.
2. Fit the data using QRJM and LMJM respectively and save the posterior samples of the model parameters.
3. Validation data preparation: choose a time t so that all the patients selected to for prediction will only have longitudinal measurements up to this time t.
4. Make predictions of subject-specific random effects: use saved posterior samples in step 2 and longitudinal measurements from step 3 to predict subject-specific random effects for every subject in the validation samples.
5. Calculate the predictions of survival probabilities for all the subjects in validation data for some time $u = t + \Delta t$ ($\Delta t > 0$).
6. Summarize the result: make Bland-Altman plots and calculate the MSE and bias for our predictions versus the gold standard, which is calculated from the true simulated values (i.e. the random effects and the parameters).

3 Simulation scenarios and results

$$\begin{cases} Y_{it} = \boldsymbol{X}_{it}^{\top}\boldsymbol{\beta} + \boldsymbol{H}_{it}^{\top}\boldsymbol{\delta} + \boldsymbol{Z}_{it}^{\top}\boldsymbol{u}_i + \varepsilon_{it}, \varepsilon_{it} \sim ALD(0, \sigma, \tau) \\ h(T_i|\mathcal{T}_{iT_i}, \boldsymbol{W}_i; \boldsymbol{\gamma}, \alpha_1, \alpha_2) = h_0(T_i)\exp(\boldsymbol{W}_i^{\top}\boldsymbol{\gamma} + \alpha(\boldsymbol{H}_{iT_i}^{\top}\boldsymbol{\delta} + \boldsymbol{Z}_{iT_i}^{\top}\boldsymbol{u}_i)) \end{cases} \tag{1}$$

There are three scenarios in the simulation study:

1. Scenarios One: data are generated using Model (1). Choose the $\tau = \mathbf{0.25}$ for the ALD distribution.

2. Scenarios Two: data are generated using Model (1). Choose $\tau =$**0.5** for the ALD distribution.
3. Scenario Three: data are generated using Model (1), but the random error follows standard normal distribution instead of ALD.

3.1 Inference results (from previous simulation)

Table 1: Inference result for Scenario One

	QRJM ($\tau = 0.25$), true model			QRJM ($\tau = 0.5$)			LMJM		
	bias	se	MSE	bias	se	MSE	bias	se	MSE
alpha	0.008	0.110	0.012	-0.003	0.131	0.017	-0.012	0.138	0.019
beta[1]	-0.001	0.101	0.010	1.697	0.156	2.904	2.683	0.174	7.227
beta[2]	-0.005	0.096	0.009	0.002	0.132	0.017	0.014	0.150	0.023
c	-0.007	0.090	0.008	-0.004	0.091	0.008	-0.007	0.090	0.008
delta[1]	0.002	0.085	0.007	0.019	0.113	0.013	0.029	0.129	0.018
delta[2]	0.009	0.092	0.009	0.018	0.110	0.012	0.038	0.128	0.018
gamma[1]	0.007	0.083	0.007	0.012	0.086	0.007	0.007	0.085	0.007
gamma[2]	-0.001	0.087	0.008	0.005	0.090	0.008	0.000	0.089	0.008
sigma	-0.001	0.034	0.001	-0.319	0.025	0.103	-	-	-

Table 2: Inference result for Scenario Two

	QRJM ($\tau = 0.5$), true model			LMJM		
	bias	se	MSE	bias	se	MSE
alpha	0.013	0.094	0.009	0.013	0.106	0.011
beta[1]	-0.007	0.089	0.008	-0.009	0.112	0.013
beta[2]	0.011	0.080	0.007	0.013	0.103	0.011
c	0.002	0.084	0.007	-0.001	0.086	0.007
delta[1]	-0.009	0.075	0.006	-0.006	0.092	0.009
delta[2]	0.002	0.082	0.007	0.006	0.097	0.009
gamma[1]	0.009	0.090	0.008	0.009	0.090	0.008
gamma[2]	0.001	0.086	0.007	0.002	0.087	0.008
sigma	0.003	0.037	0.001	-	-	-

Table 3: Inference result for Scenario Three

	QRJM ($\tau = 0.5$)			LMJM, true model		
	bias	se	MSE	bias	se	MSE
alpha	-0.012	0.075	0.006	0.004	0.076	0.006
beta[1]	0.013	0.050	0.003	0.003	0.046	0.002
beta[2]	0.001	0.045	0.002	0.002	0.043	0.002
c	0.001	0.082	0.007	0.005	0.081	0.007
delta[1]	0.007	0.045	0.002	0.001	0.041	0.002
delta[2]	0.008	0.058	0.003	0.000	0.055	0.003
gamma[1]	-0.003	0.081	0.007	-0.007	0.080	0.006
gamma[2]	-0.002	0.085	0.007	-0.006	0.084	0.007
sigma	-	-	-	0.001	0.029	0.001

3.2 BA plots of predictions from the model vs. gold standard

Scenario One Only

1. $t = 0.25$

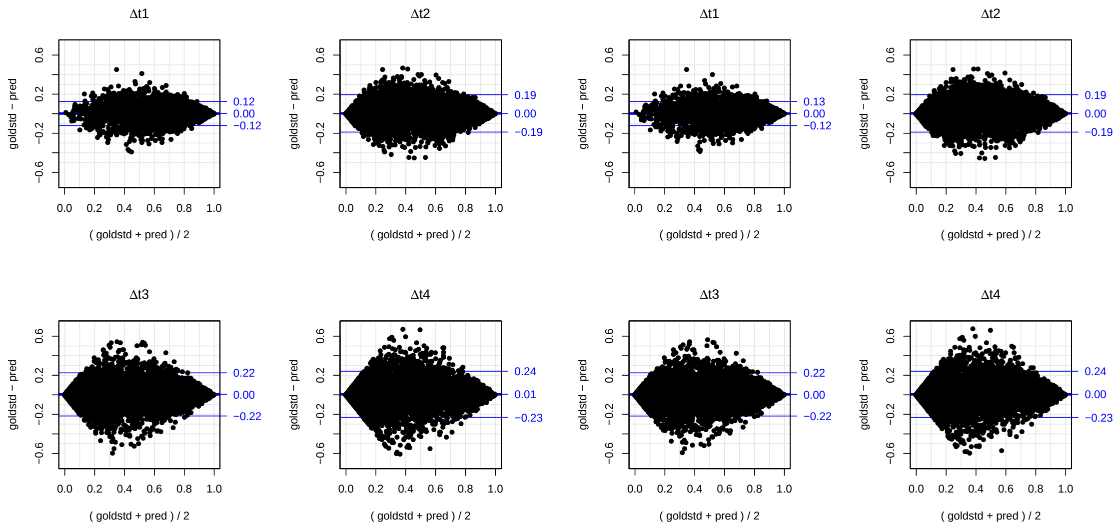

Figure 1: BA plot: predictions with first two longitudinal observations available: QRJM(left) and LMJM(right)

2. $t = 0.50$

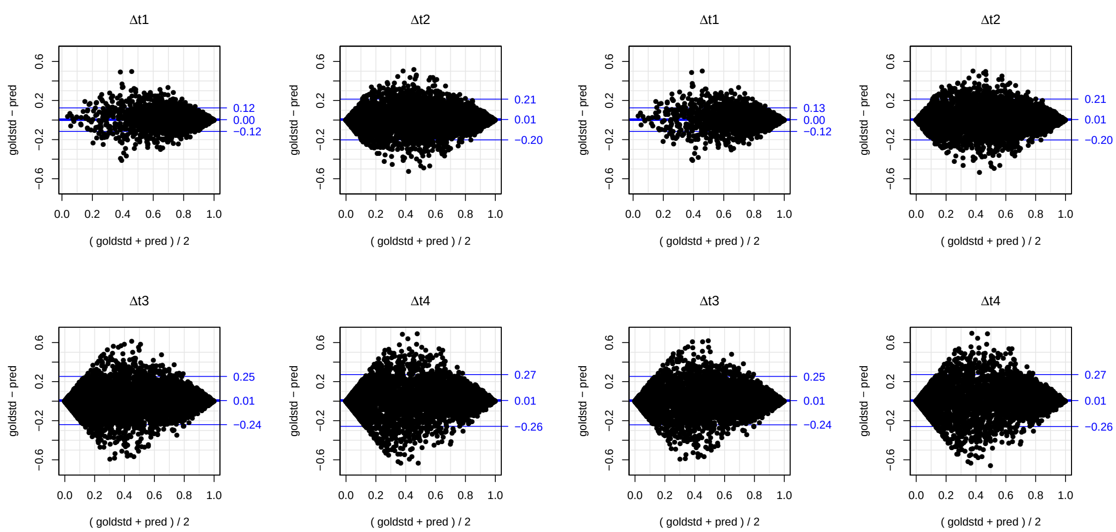

Figure 2: BA plot: predictions with first three longitudinal observations available: QRJM(left) and LMJM(right)

3. $t = 0.75$

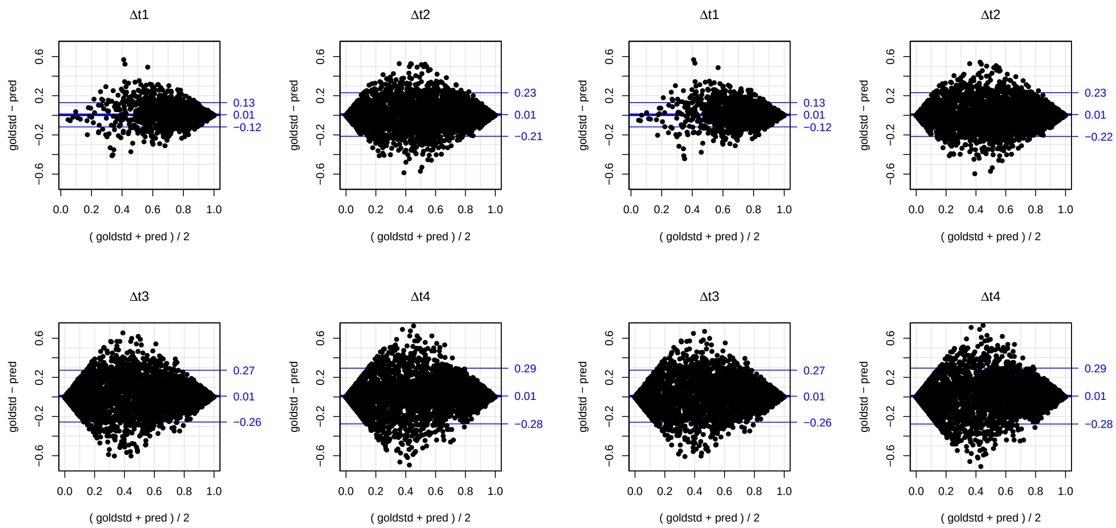

Figure 3: BA plot: predictions with first four longitudinal observations available: QRJM(left) and LMJM(right)

3.3 Predictive accuracy (for Scenario One only)

Table 4: MSE and bias (compared with gold standard) of predicted survival probabilities from two models

Scenario One		QRJM ($\tau = 0.25$)		QRJM ($\tau = 0.5$)		LMJM	
		MSE	Bias	MSE	Bias	MSE	Bias
t=0.25	Δt = 0.25	0.004	-0.002			0.004	-0.002
	Δt = 1	0.009	-0.003			0.009	-0.003
	Δt = 2	0.012	-0.004			0.012	-0.004
	Δt = 3	0.014	-0.005			0.014	-0.005
t=0.5	Δt =0.25	0.004	-0.004			0.004	-0.004
	Δt = 1	0.011	-0.005			0.011	-0.005
	Δt = 2	0.015	-0.006			0.015	-0.006
	Δt = 3	0.018	-0.007			0.018	-0.007
t=0.75	Δt =0.25	0.004	-0.005			0.004	-0.006
	Δt = 1	0.012	-0.008			0.013	-0.007
	Δt = 2	0.018	-0.008			0.018	-0.008
	Δt = 3	0.020	-0.009			0.021	-0.009

Table 5: AUC, AARD and MRD of predicted survival probabilities

Scenario One		AUC			AARD			MRD		
		gold standard	QRJM	LMJM	gold standard	QRJM	LMJM	gold standard	QRJM	LMJM
t=0.25	Δt =0.25	0.825	0.823	0.823	0.170	0.178	0.178	0.252	0.250	0.250
	$\Delta t = 1$	0.874	0.870	0.870	0.517	0.511	0.510	0.428	0.418	0.418
	$\Delta t = 2$	0.911	0.905	0.905	0.651	0.638	0.638	0.509	0.492	0.491
	$\Delta t = 3$	0.930	0.923	0.923	0.701	0.684	0.683	0.549	0.527	0.526
t=0.5	$\Delta t = 0.25$	0.815	0.814	0.814	0.169	0.176	0.176	0.204	0.208	0.208
	$\Delta t = 1$	0.868	0.864	0.864	0.530	0.527	0.527	0.411	0.403	0.403
	$\Delta t = 2$	0.907	0.901	0.901	0.643	0.630	0.630	0.512	0.493	0.492
	$\Delta t = 3$	0.927	0.920	0.919	0.686	0.668	0.665	0.559	0.536	0.534
t=0.75	Δt =0.25	0.816	0.816	0.816	0.178	0.199	0.200	0.185	0.190	0.190
	$\Delta t = 1$	0.870	0.866	0.866	0.546	0.541	0.542	0.410	0.402	0.402
	$\Delta t = 2$	0.908	0.902	0.901	0.644	0.628	0.627	0.519	0.501	0.499
	$\Delta t = 3$	0.927	0.920	0.920	0.686	0.664	0.662	0.572	0.548	0.546

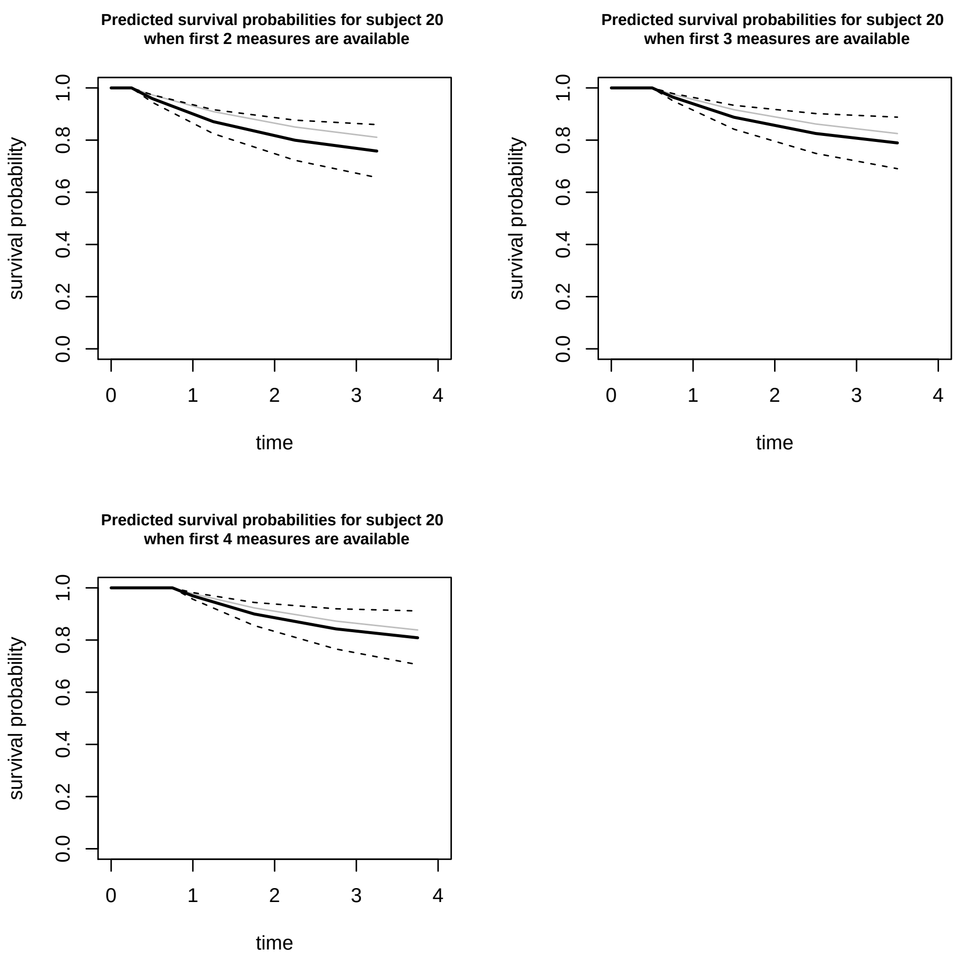

Figure 4: Dynamic predictions from increasing number of longitudinal observations (subject 20)