Supplementary Material
Generalized inverse-Gaussian frailty models with application to TARGET neuroblastoma data

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In this Supplementary Material, we provide some additional theoretical and simulated results.

1 Additional theoretical results

Lemma 1. *Let* $\zeta(x) = K_\phi(\sqrt{x})/x^{\phi/2}$, *we have that* $\dfrac{\partial^k}{\partial x^k}\zeta(x) = \left(-\dfrac{1}{2}\right)^k \dfrac{K_{\phi+k}(\sqrt{x})}{x^{(\phi+k)/2}}$, *for* $k \in \mathbb{N}$.

Proof. Case $k = 1$. It can be shown that the derivative of the Bessel function with respect to its argument is

$$\frac{\partial}{\partial x}K_\phi(\sqrt{x}) = -\frac{1}{4\sqrt{x}}\left(K_{\phi+1}(\sqrt{x}) + K_{\phi-1}(\sqrt{x})\right).$$

Using this expression, we have that

$$\frac{\partial}{\partial x}\zeta(x) = -\frac{1}{2}\left(\phi\frac{K_\phi(\sqrt{x})}{x^{(\phi/2+1)}} + \frac{K_{\phi+1}(\sqrt{x}) + K_{\phi-1}(\sqrt{x})}{2x^{(\phi+1)/2}}\right).$$

At this point, we apply the recurrence identity on the Bessel function previously mentioned,

$$K_v(z) = \frac{z}{2v}\left(K_{v+1}(z) - K_{v-1}(z)\right), \tag{1}$$

and the former derivative simplifies to

$$\frac{\partial}{\partial x}\zeta(x) = -\frac{1}{2}\frac{K_{\phi+1}(\sqrt{x})}{x^{(\phi+1)/2}}.$$

Using this, we continue the demonstration by finding the second derivative of $\zeta(x)$ with respect to x. The result is as follows

$$\frac{\partial^2}{\partial x^2}\zeta(x) = -\frac{1}{2}\left(-\frac{K_{\phi+1}(\sqrt{x})(\phi+1)}{2x^{(\phi+3)/2}} - \frac{K_{\phi+2}(\sqrt{x}) + K_\phi(\sqrt{x})}{4x^{(\phi/2+1)}}\right).$$

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Using (1), the second derivative simplifies to

$$\frac{\partial^2}{\partial x^2}\zeta(x) = \frac{1}{4}\frac{K_{\phi+2}(\sqrt{x})}{x^{(\phi+2)/2}}.$$

To finish the proof by induction, we now assume as true the case $k-1$ and use it to prove the k-th order expression. If this is satisfied, then the result is true for all k. If the $\{k-1\}$-th derivative of $\zeta(x)$ with respect to x is given by

$$\frac{\partial^{k-1}}{\partial x^{k-1}}\zeta(x) = \left(-\frac{1}{2}\right)^{k-1}\frac{K_{\phi+k-1}(\sqrt{x})}{x^{(\phi+k-1)/2}},$$

then the k-th order derivative is

$$\frac{\partial^{k-1}}{\partial x^{k-1}}\zeta(x) = \left(-\frac{1}{2}\right)^{k-1}\left\{\frac{-K_{\phi+k-1}(\sqrt{x})(\phi+k-1)}{2x^{(\phi+k+1)/2}} - \frac{K_{\phi+k}(\sqrt{x})+K_{\phi+k-2}(\sqrt{x})}{4x^{(\phi+k)/2}}\right\}.$$

Here we use again (1), which provides $K_{\phi+k-1}(\sqrt{x}) = \frac{\sqrt{x}}{2(\phi+k-1)}[K_{\phi+k}(\sqrt{x}) - K_{\phi+k-2}(\sqrt{x})]$ and the result

$$\frac{\partial^{k}}{\partial x^{k}}\zeta(x) = \left(-\frac{1}{2}\right)^{k}\frac{K_{\phi+k}(\sqrt{x})}{x^{(\phi+k)/2}}.$$

This completes the proof of Lemma 1. □

Consider $\mathrm{RFV}(s) = J''(-s/\mu)/J'(-s/\mu)^2$, where $J(s) = \log L(-s)$, $L(\cdot)$ is the Laplace transform and μ is the expected value of the GIG frailty distribution. The expressions required to calculate the RFV for the GIG frailty model are given by

$$\begin{aligned}\frac{\partial J(s)}{\partial s} &= \frac{\partial \log L(-s)}{\partial s} = \frac{\alpha^{-1}}{2(\alpha^{-1}(\alpha^{-1}-2s))^{3/2}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})}\times\\ &\{\alpha^{-1}(\alpha^{-1}-2s)K_{\lambda-1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})\\ &+2\lambda\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})\\ &+\alpha^{-1}(\alpha^{-1}-2s)K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})\},\end{aligned}$$

and

$$\begin{aligned}\frac{\partial J(s)^2}{\partial s^2} &= \frac{\partial \log L(-s)^2}{\partial s^2} = \frac{1}{4(\alpha^{-1}-2s)^2\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2}\times\\ &\{-(\alpha^{-1}(\alpha^{-1}-2s))^{3/2}K_{\lambda-1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2 + 2\alpha^{-1}(\alpha^{-1}-2s)\times\\ &[K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}) - \sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})]\times\\ &K_{\lambda-1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}) - 4\alpha^{-1}s\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2+\\ &8\lambda\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2+\\ &2\alpha^{-2}\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2+\\ &2\alpha^{-1}s\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2-\\ &\alpha^{-2}\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})^2+\\ &(\alpha^{-1}(\alpha^{-1}-2s))^{3/2}K_{\lambda-2}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})+\\ &2\alpha^{-2}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})-\\ &4\alpha^{-1}sK_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})K_{\lambda+1}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})-\\ &2\alpha^{-1}s\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})K_{\lambda+2}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})+\\ &\alpha^{-2}\sqrt{\alpha^{-1}(\alpha^{-1}-2s)}K_\lambda(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})K_{\lambda+2}(\sqrt{\alpha^{-1}(\alpha^{-1}-2s)})\}.\end{aligned}$$

2 Simulation studies

Simulation studies in this section aim to evaluate the performance, in terms of estimation, of the PE-GIG frailty models under misspecification of the frailty distribution. Different scenarios are assessed, where 1000 synthetic data sets are simulated with either a gamma, inverse-Gaussian (IG), generalized exponential (GE), or log-normal frailty. To each simulated data set, the IG, RIG, HYP, and PHYP frailty models are fitted with different numbers of change points for the piecewise constant hazard function. Additionally to the GIG class, the semiparametric versions of the gamma and generalized exponential frailty models, described in the literature, are fitted and compared. All scenarios employ total sample sizes of 200 and 500. The gamma, GE, and log-normal simulations are conducted with clusters formed by $n_i = 2$ individuals each, while the IG case explores the GIG class behavior under large clusters by setting $n_i = 10$ for all i. The IG scenario does not include the GE fit because the explicit expressions of this model are available for clusters up to size 2. The failure and censoring times are simulated as described in Subsection 4.1 of the paper with true value of the parameters being $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$. Fitting the IG, RIG, HYP, and PHYP models are done with 5 and 10 change points for the piecewise exponential baseline hazard function. The semiparametric versions of the gamma and GE models evaluated here are based on the Cox partial likelihood function, therefore, do not require this specification.

The parameter α represents the frailty variance only in the gamma and IG options. Hence, in each case an appropriate transformation of this parameter is calculated so that we obtain the frailty variance. This comparison is done as discussed by Barreto-Souza and Mayrink (2019), where it is noted that the model given by $h(t_{ij}|Z_i) = Z_i h_0(t_{ij}) \exp(x_{ij}^\top \beta)$ is equivalent to $h(t_{ij}|Z_i) = Z_i^* h_0^*(t_{ij}) \exp(x_{ij}^\top \beta)$, with $Z_i^* = Z_i/E(Z_i)$ having mean 1 and $h_0^*(t_{ij}) = h_0(t_{ij})E(Z_i)$. In other words, the comparison of the frailty variance should be done through the transformation $\text{Var}(Z_i^*) = \text{Var}(Z_i)/E(Z_i)^2$. The proper transformation for each model is done so that they are comparable and is reported in the column named "Var" in the forthcoming tables.

2.1 Gamma data

In Tables 1 and 2 we present the results of the described simulation study for the gamma scenario. The empirical mean and standard deviation (SD) of the parameter estimates under the IG, RIG, HYP, PHYP, and semiparametric gamma and GE models are provided.

Model	Cut points	β_1 Mean	β_1 SD	β_2 Mean	β_2 SD	**Var** Mean	**Var** SD
Semi. Gamma	-	1.288	0.160	-0.857	0.263	0.592	0.098
Semi. GE	-	1.396	0.169	-0.927	0.278	0.767	0.032
PE - IG	$k = 5$	1.307	0.167	-0.862	0.267	1.541	0.452
	$k = 10$	1.361	0.175	-0.900	0.279	1.866	0.591
PE - RIG	$k = 5$	1.408	0.184	-0.927	0.280	1.153	0.221
	$k = 10$	1.482	0.195	-0.981	0.297	1.272	0.219
PE - HYP	$k = 5$	1.365	0.176	-0.898	0.274	1.388	0.355
	$k = 10$	1.434	0.188	-0.946	0.290	1.608	0.408
PE - PHYP	$k = 5$	1.383	0.172	-0.914	0.274	0.865	0.091
	$k = 10$	1.427	0.174	-0.949	0.284	0.894	0.069

Table 1: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and GE models. Data generated from the gamma frailty model with sample size $m = 200$. Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

Model	Cut points	β_1 Mean	β_1 SD	β_2 Mean	β_2 SD	**Var** Mean	**Var** SD
Semi. Gamma	-	1.290	0.100	-0.863	0.160	0.609	0.061
Semi. GE	-	1.393	0.105	-0.929	0.169	0.769	0.019
PE - IG	$k = 5$	1.294	0.103	-0.860	0.163	1.480	0.266
	$k = 10$	1.345	0.109	-0.897	0.171	1.782	0.348
PE - RIG	$k = 5$	1.395	0.114	-0.923	0.171	1.149	0.140
	$k = 10$	1.471	0.122	-0.978	0.182	1.275	0.140
PE - HYP	$k = 5$	1.350	0.109	-0.894	0.168	1.351	0.217
	$k = 10$	1.418	0.117	-0.942	0.178	1.570	0.252
PE - PHYP	$k = 5$	1.381	0.107	-0.915	0.168	0.882	0.054
	$k = 10$	1.425	0.107	-0.951	0.174	0.909	0.037

Table 2: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and GE models. Data generated from the gamma frailty model with sample size $m = 500$. Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

In can be seen that the correctly specified gamma model underestimates the frailty variance under both sample sizes. This was observed by Barreto-Souza and Mayrink (2019) in their simulations studies, where it is pointed out that a difficulty in estimating α under a correctly specified gamma frailty model is likely due to the flat shape of its associated Q-function. Notably, the PHYP and GE models are favorable in estimating this quantity, producing mean estimates with smaller bias than the gamma model, and small variation. Moreover, under both sample sizes, the estimation of the covariate effects is excellent under all members of the GIG class, especially when $k = 10$.

2.2 Generalized exponential data

Results for simulation studied conducted under GE data are provided in Tables 3 and 4, where we report the empirical mean and standard deviation of the parameter estimates.

		β_1		β_2		**Var**	
Model	**Cut points**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Semi. Gamma	-	1.304	0.150	-0.869	0.245	0.645	0.113
Semi. GE	-	1.391	0.155	-0.924	0.257	0.770	0.035
PE - IG	$k = 5$	1.335	0.156	-0.885	0.255	1.602	0.478
	$k = 10$	1.407	0.170	-0.938	0.271	2.064	0.676
PE - RIG	$k = 5$	1.423	0.170	-0.938	0.263	1.163	0.219
	$k = 10$	1.483	0.181	-0.982	0.277	1.257	0.218
PE - HYP	$k = 5$	1.388	0.164	-0.917	0.261	1.407	0.354
	$k = 10$	1.448	0.177	-0.960	0.275	1.595	0.399
PE - PHYP	$k = 5$	1.393	0.158	-0.921	0.254	0.876	0.085
	$k = 10$	1.426	0.161	-0.949	0.262	0.895	0.068

Table 3: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and generalized exponential models. Data generated from the generalized exponential frailty model with total sample size equal to 200 ($m = 100$ with $n_i = 2 \forall i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

Model	Cut points	β_1 Mean	SD	β_2 Mean	SD	**Var** Mean	SD
Semi. Gamma	-	1.311	0.100	-0.876	0.152	0.655	0.067
Semi. GE	-	1.394	0.104	-0.928	0.160	0.771	0.021
PE - IG	$k = 5$	1.397	0.105	-0.925	0.159	3.683	1.154
	$k = 10$	1.382	0.107	-0.921	0.165	1.847	0.345
PE - RIG	$k = 5$	1.417	0.112	-0.936	0.163	1.159	0.137
	$k = 10$	1.479	0.117	-0.982	0.172	1.259	0.134
PE - HYP	$k = 5$	1.382	0.107	-0.914	0.161	1.376	0.211
	$k = 10$	1.443	0.113	-0.957	0.170	1.565	0.234
PE - PHYP	$k = 5$	1.397	0.105	-0.925	0.159	0.892	0.051
	$k = 10$	1.431	0.106	-0.954	0.164	0.910	0.036

Table 4: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and generalized exponential models. Data generated from the generalized exponential frailty model with total sample size equal to 500 ($m = 250$ with $n_i = 2 \,\forall\, i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

In the GE scenario, the worst performance on the covariate effects estimation is due to the gamma frailty model, which displays an underestimation of β_1 and β_2 in comparison to the competing models. Although the frailty variance parameter is estimated with low variability under the correctly specified GE model, these are slightly biased on average. Meanwhile, the PHYP frailty fit produces parameter estimates that are considerably closer to the true value and have low variability, hence showing some advantage over the GE model.

2.3 Log-normal data

Results of misspecification simulation studies conducted with log-normal data are exhibited in Tables 5 and 6.

Model	Cut points	β_1 Mean	β_1 SD	β_2 Mean	β_2 SD	Var Mean	Var SD
Semi. Gamma	-	1.335	0.157	-0.887	0.230	0.442	0.092
Semi. GE	-	1.493	0.170	-0.988	0.251	0.739	0.032
PE - IG	$k = 5$	1.400	0.166	-0.926	0.239	1.124	0.413
	$k = 10$	1.464	0.176	-0.971	0.251	1.421	0.544
PE - RIG	$k = 5$	1.407	0.171	-0.928	0.241	0.782	0.200
	$k = 10$	1.466	0.179	-0.972	0.253	0.884	0.209
PE - HYP	$k = 5$	1.413	0.170	-0.933	0.241	0.947	0.289
	$k = 10$	1.478	0.181	-0.979	0.254	1.121	0.335
PE - PHYP	$k = 5$	1.390	0.168	-0.918	0.238	0.648	0.137
	$k = 10$	1.439	0.172	-0.955	0.247	0.704	0.130

Table 5: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and generalized exponential models. Data generated from the log-normal frailty model with total sample size equal to 200 ($m = 100$ with $n_i = 2\,\forall\, i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is approximately 1.718).

Model	Cut points	β_1 Mean	β_1 SD	β_2 Mean	β_2 SD	Var Mean	Var SD
Semi. Gamma	-	1.332	0.097	-0.891	0.148	0.454	0.058
Semi. GE	-	1.485	0.103	-0.988	0.162	0.741	0.020
PE - IG	$k = 5$	1.385	0.105	-0.921	0.154	1.080	0.250
	$k = 10$	1.451	0.113	-0.967	0.162	1.366	0.333
PE - RIG	$k = 5$	1.390	0.107	-0.922	0.154	0.774	0.128
	$k = 10$	1.451	0.113	-0.965	0.161	0.880	0.133
PE - HYP	$k = 5$	1.397	0.170	-0.928	0.155	0.926	0.179
	$k = 10$	1.463	0.115	-0.974	0.163	1.100	0.208
PE - PHYP	$k = 5$	1.377	0.105	-0.914	0.152	0.652	0.089
	$k = 10$	1.428	0.108	-0.952	0.158	0.713	0.083

Table 6: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma and generalized exponential models. Data generated from the log-normal frailty model with total sample size equal to 500 ($m = 250$ with $n_i = 2\,\forall\, i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is approximately 1.718).

In this scenario, we observed that the gamma and GE models underestimated the frailty variance, which is following the findings by Barreto-Souza and Mayrink (2019). All GIG special cases and the GE frailty model yielded very good estimates of the covariate effects, but they differ in terms of the frailty variance estimation. Notably, the model producing estimates of this quantity that are, on average, closest to the true value (1.718) is the IG, which achieves a very satisfactory result in comparison to the competing models when 10 cut points are specified.

2.4 Inverse-Gaussian data

Results from the IG case, provided in Tables 7 and 8, assess the misspecification of λ and performance of the GIG class under a larger cluster size.

		β_1		β_2		**Var**	
Model	**Cut points**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Semi. Gamma	-	1.471	0.134	-0.980	0.112	0.552	0.141
PE - IG	$k = 5$	1.450	0.130	-0.962	0.108	0.878	0.302
	$k = 10$	1.487	0.134	-0.992	0.112	0.978	0.353
PE - RIG	$k = 5$	1.449	0.130	-0.961	0.108	0.657	0.158
	$k = 10$	1.484	0.135	-0.990	0.112	0.702	0.167
PE - HYP	$k = 5$	1.452	0.130	-0.962	0.108	0.755	0.215
	$k = 10$	1.488	0.134	-0.992	0.112	0.822	0.238
PE - PHYP	$k = 5$	1.444	0.130	-0.958	0.108	0.573	0.114
	$k = 10$	1.478	0.134	-0.986	0.111	0.603	0.114

Table 7: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma models. Data generated from the inverse-Gaussian frailty model with total sample size equal to 200 ($m = 20$ with $n_i = 10 \, \forall \, i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

		β_1		β_2		**Var**	
Model	**Cut points**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Semi. Gamma	-	1.466	0.087	-0.980	0.071	0.557	0.096
PE - IG	$k = 5$	1.438	0.085	-0.958	0.069	0.867	0.200
	$k = 10$	1.480	0.087	-0.987	0.071	0.957	0.226
PE - RIG	$k = 5$	1.436	0.085	-0.956	0.069	0.658	0.107
	$k = 10$	1.477	0.088	-0.985	0.071	0.702	0.112
PE - HYP	$k = 5$	1.439	0.085	-0.958	0.069	0.753	0.145
	$k = 10$	1.480	0.088	-0.987	0.071	0.815	0.157
PE - PHYP	$k = 5$	1.432	0.084	-0.953	0.069	0.579	0.078
	$k = 10$	1.471	0.087	-0.981	0.071	0.608	0.077

Table 8: Empirical mean and standard deviation (SD) of the estimates for β_1, β_2 and the frailty variance under the IG, RIG, HYP, PHYP, and semiparametric gamma models. Data generated from the inverse-Gaussian frailty model with total sample size equal to 500 ($m = 50$ with $n_i = 10 \, \forall \, i$). Rows represent the fitted model. The true values of the parameters are $\beta_1 = 1.5$, $\beta_2 = -1$ and $\alpha = 1$ (true frailty variance is 1).

In this last scenario it is found that, as expected, all model parameters are well estimated under the correctly specified frailty distribution. Additionally, we found that the choice of λ does not largely influence the covariate effects, that are well estimated under all members of the GIG class. Instead, the choice of λ affects the frailty variance parameter, where models with λ further from the true value tended to underestimate this quantity. Even so, all GIG cases estimated this parameter with a smaller bias in comparison to the gamma frailty model.

References

BARRETO-SOUZA, W. & MAYRINK, V.D. (2019). Semiparametric generalized exponential frailty model for clustered survival data. *Annals of the Institute of Statistical Mathematics.* **71**, 679–701.