

Supplementary material:
"A covariate-specific time dependent ROC curve for correlated survival data"

Alessandra Meddis, Paul Blanche, François C Bidard, Aurélien Latouche

1 Misspecification of frailty

1.1 Simulation section

Simulation study to illustrate the robustness of the method in case of misspecification of the frailty distribution. We generated data from a shared frailty model for the survival time and a negative binomial model for the biomarker, as described in the manuscript. We simulated data with $U_k \sim \chi^2(2)$ and $U_k \sim U[0, 10]$ and estimated the survival function with a shared gamma frailty model. We provide the results for the estimated covariate-specific time dependent AUC in Figures 1 and 2.

1.2 Application section

In the motivating example for non metastatic breast cancer, we assume a gamma distribution. To check for the adequacy of this assumption, we compare the estimated marginal survival function by a shared frailty model with the Kaplan-Meier estimator (Figure 3).

2 Results on the estimated parameters

We provide the coefficients estimated in the simulation study in the Table 1. As in the manuscript, β and γ are the coefficients of the shared frailty model with a Gamma frailty distribution with parameter θ ; the biomarker $Y|X$ follows a negative binomial distribution with set of parameter $\alpha = (d, \xi)$ where d is the dispersion parameter and ξ the regression coefficient for the covariate X .

	tvalue	estimate (sd)
β	0.8	0.799 (0.017)
γ	0.5	0.501 (0.051)
θ	1	1.028 (0.145)
d	0.5	0.501 (0.016)
ξ	0.4	0.399 (0.012)

Table 1: Results of simulation: parameters.

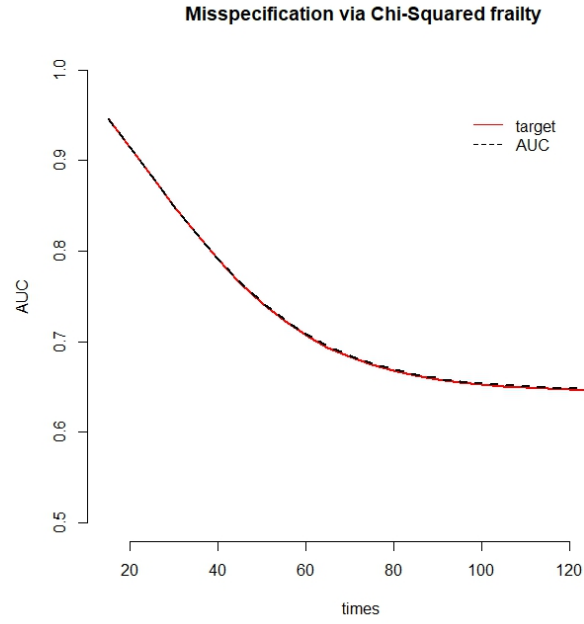


Figure 1: Simulation results for a misspecified frailty distribution. Data were generated with $U_k \sim \chi^2(2)$. The estimated covariate-specific $\text{AUC}(t)$ with a shared gamma frailty model is provided in black and the true value in red.

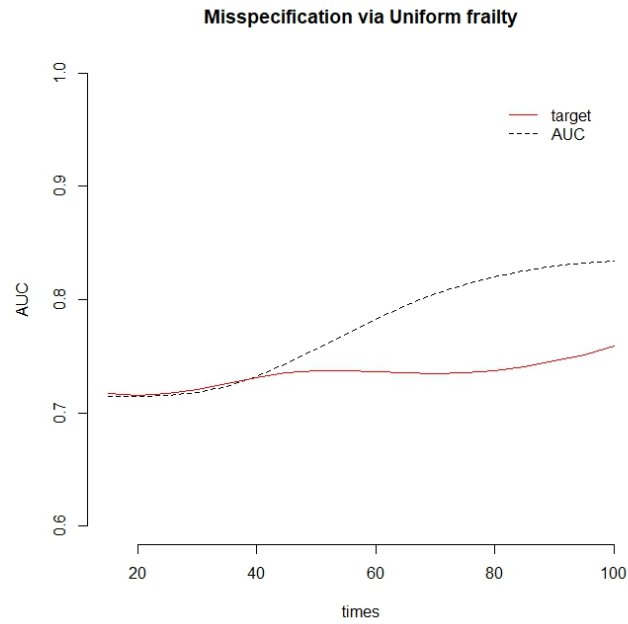


Figure 2: Simulation results for a misspecified frailty distribution. Data were generated with $U_k \sim [0, 10]$. The estimated covariate-specific $\text{AUC}(t)$ with a shared gamma frailty model (black line) and the true value (red line) are provided.

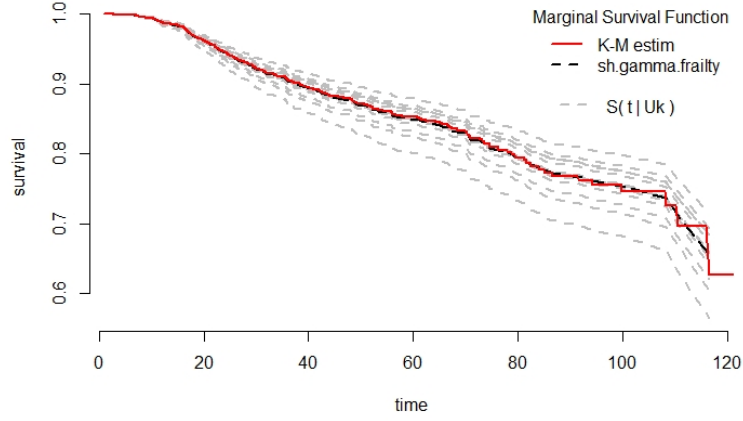


Figure 3: Marginal survival function estimated by the shared gamma frailty model (in black) and by the Kaplan-Meier estimator (in red). We also provide the estimated conditional survival functions for each cluster $S(t|U_k)$ (in gray).