Supplementary Material for "Considerations for Analysis of Time-to-Event Outcomes Measured with Error: Bias and Correction with SIMEX"

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Table 1: The quantiles, mean, and standard deviation (SD) for the error-prone event time divided by true event time $\left(\frac{T'}{T}\right)$ for $\beta = \log(1.5)$ and $n = 1000$.

Error Distribution	σ_ν^2	5^{th}	25^{th}	50^{th}	Mean	75^{th}	95^{th}	SD
Normal	0.25	0.460	0.715	1.013	1.146	1.410	2.407	0.608
	0.5	0.337	0.575	0.973	1.254	1.586	3.009	0.964
	1	0.190	0.531	1.100	1.687	2.078	5.021	1.949
	2	0.091	0.375	0.948	2.550	2.521	10.15	5.139
Shifted Gamma	0.25	0.518	0.700	0.927	1.208	1.367	2.753	0.938
	0.5	0.437	0.588	0.863	1.484	1.444	4.143	2.810
	1	0.392	0.493	0.772	2.970	1.609	8.798	14.76
	2	0.370	0.405	0.564	35.99	1.329	23.49	657.0

Table 2: The percent (%) bias (absolute bias for intercept α_0), average model standard error (ASE), empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets with $n = 1000$, exponential time, and shifted gamma error.

			Weibull Model				Cox Model
β	σ^2_ν		α_0	α_1	shape	β	β
log(1.5)	0.25	Bias	0.059	0.120	-12.51	-14.23	-18.39
		ASE	0.039	0.041	0.021	0.036	0.033
		ESE	0.040	0.042	0.000	0.038	0.034
		MSE	0.071	0.042	0.125	0.069	0.082
		CP	0.664	0.973	0.000	0.640	0.390
	0.5	Bias	0.119	0.020	-25.17	-26.58	-29.89
		ASE	0.046	0.055	0.020	0.041	0.033
		ESE	0.046	0.061	0.000	0.046	0.035
		MSE	0.127	0.061	0.252	0.117	0.126
		CP	0.252	0.964	0.000	0.262	0.058
	1	Bias	0.233	-0.220	-47.33	-43.70	-41.78
		ASE	0.061	0.087	0.016	0.049	0.032
		ESE	0.061	0.105	0.000	0.060	0.035
		MSE	0.240	0.105	0.473	0.187	0.173
		CP	0.020	0.959	0.000	0.074	0.001
	2	Bias	0.441	1.110	-61.09	-60.65	-50.90
		ASE	0.171	0.210	0.028	0.089	0.032
		ESE	0.095	0.203	0.000	0.077	0.035
		MSE	0.451	0.203	0.611	0.258	0.209
		CP	0.005	0.939	0.004	0.056	0.000
log(3)	0.25	Bias	0.059	0.040	-15.62	-14.34	-16.53
		ASE	0.039	0.042	0.021	0.042	0.040
		ESE	0.039	0.041	0.000	0.046	0.046
		MSE	0.073	0.041	0.156	0.164	0.187
		CP	0.636	0.978	0.000	0.052	0.021
	0.5	Bias	0.118	-0.030	-24.78	-26.43	-28.70
		ASE	0.046	0.055	0.020	0.046	0.038
		ESE	0.045	0.059	0.000	0.056	0.049
		MSE	0.126	0.059	0.248	0.296	0.319
		CP	0.264	0.974	0.000	0.000	0.000
	1	Bias	0.230	-0.050	-45.67	-43.38	-42.55
		ASE	0.061	0.088	0.017	0.052	0.035
		ESE	0.060	0.105	0.000	0.074	0.049
		MSE	0.238	0.105	0.457	0.482	0.470
		CP	0.024	0.968	0.000	0.000	0.000
	2	Bias	0.437	0.280	-59.46	-60.81	-53.65
		ASE	0.157	0.211	0.027	0.069	0.034
		ESE	0.094	0.200	0.000	0.089	0.047
		MSE	0.447	0.200	0.595	0.674	0.591
		CP	0.001	0.941	0.000	0.000	0.000

Table 3: The percent ($\%$) bias (absolute bias for intercept α_0), average model standard error (ASE), empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets with $n = 1000$, log-normal time, and mean zero normal error.

			Weibull Model				Cox Model
β	σ_ν^2		α_0	α_1	shape	β	β
log(3)	1	Bias	0.499	0.020	3.59	0.520	-3.510
		ASE	0.034	0.040	0.030	0.052	0.041
		ESE	0.034	0.042	0.000	0.055	0.053
		MSE	0.500	0.042	0.036	0.055	0.065
		CP	0.000	0.975	1.000	0.931	0.772

Table 4: The percent ($\%$) bias, average bootstrap standard error (ASE) for SIMEX, average model standard error (ASE) for naive, empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets for the SIMEX and naive methods with $n = 1000$, exponential time, baseline hazard of 0.1, a normal distribution for the additive error term, and 90% uniform censoring for the true event time.

$\%$ Censored	σ_ν^2	Method	$\%$ Bias	ASE	ESE	MSE	CP
90	1	SIMEX	-11.59	0.125	0.122	0.168	0.834
		Naive	-13.55	0.101	0.101	0.169	1.000

Table 5: The percent ($\%$) bias, average bootstrap standard error (ASE) for SIMEX, average model standard error (ASE) for naive, empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets for the SIMEX and naive methods with $n = 1000$, exponential time, baseline hazard of 0.1, a normal distribution for the multiplicative error term, and 90% covariate-dependent censoring for the true event time.

$\%$ Censored	σ_ν^2	Method	$\%$ Bias	ASE	ESE	MSE	CP
90	0.5	SIMEX	-7.912	0.118	0.115	0.139	0.894
		Naive	-14.70	0.104	0.101	0.179	1.000

Table 6: The quantiles, interquartile range (IQR), and standard deviation (SD) for the ratio of the error-prone simulated event time and the true event time for virological failure $\left(\frac{T'_{\lambda b}}{T}\right)$ in the VCCC example.

λ	25^{th}	50^{th}	75^{th}	IQR	SD
0	1	1	1	0	32.06
0.5	0.669	1.026	1.543	0.874	38.57
1	0.570	1.002	1.784	1.214	48.40
1.5	0.499	1.020	2.064	1.565	68.25
2	0.452	0.991	2.239	1.787	56.29

Table 7: The hazard ratios (HR) and their corresponding bootstrap 95% confidence intervals for sex, a 100-unit increase in enrollment CD4, and a 10 year increase in age at enrollment for the time at first opportunistic infection post ART.

	Univariate		
	Sex	$100 \times$ CD4	$10 \times$ Age at Enrollment
True	0.951 (0.790,1.146)	0.781 (0.748,0.816)	1.146 (1.057,1.242)
Naive	1.053 (0.903,1.229)	0.840 (0.813,0.868)	1.153 (1.079,1.232)
SIMEX	1.078 (0.914,1.270)	0.846 (0.808,0.885)	1.177 (1.101,1.259)

	Multivariate		
	Sex	$100 \times$ CD4	$10 \times$ Age at Enrollment
True	0.822 (0.682,0.991)	0.782 (0.749,0.817)	1.113 (1.025,1.209)
Naive	0.928 (0.795,1.084)	0.843 (0.815,0.871)	1.121 (1.048,1.200)
SIMEX	0.908 (0.754,1.095)	0.845 (0.806,0.886)	1.145 (1.061,1.235)

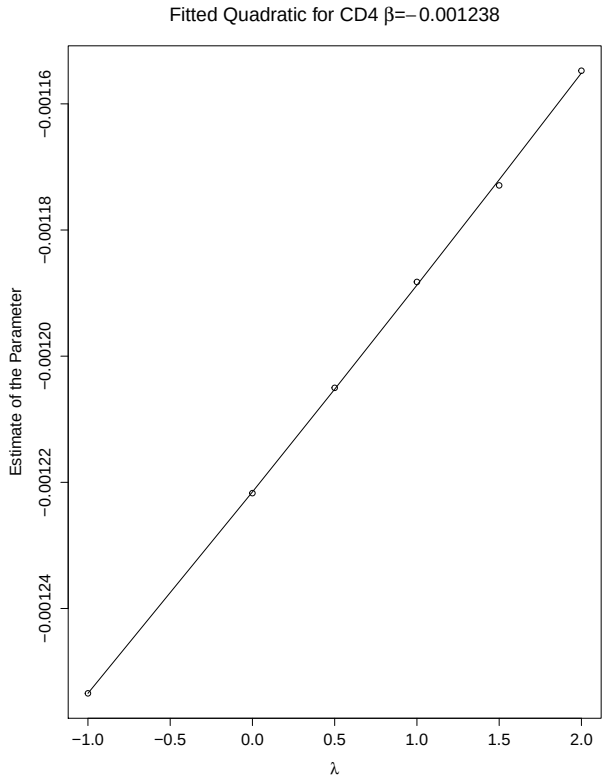
Table 8: The percent (%) bias, average bootstrap standard error (ASE) for SIMEX, average model standard error (ASE) for naive, empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets for the SIMEX and naive methods with exponential time and mixture gamma, mean zero normal, and shifted gamma error distributions.

Error Distribution	Covariate	Method	% Bias	ASE	ESE	MSE	CP
Mixed	CD4	SIMEX	-1.760	0.0001	0.0001	0.0001	0.316
		Naive	-12.40	0.0001	0.0001	0.0002	0.198
	Gender	SIMEX	-1.520	0.058	0.059	0.059	0.880
		Naive	-13.16	0.051	0.052	0.052	0.878
	Age	SIMEX	-3.050	0.003	0.003	0.003	0.624
		Naive	-14.99	0.002	0.002	0.002	0.623
Normal	CD4	SIMEX	-4.930	0.0001	0.0001	0.0001	0.299
		Naive	-11.82	0.0001	0.0001	0.0002	0.204
	Gender	SIMEX	-3.170	0.059	0.060	0.060	0.875
		Naive	-11.51	0.051	0.052	0.052	0.878
	Age	SIMEX	-2.580	0.003	0.003	0.003	0.634
		Naive	-10.51	0.002	0.002	0.002	0.636
Gamma	CD4	SIMEX	-6.620	0.0001	0.0001	0.0001	0.288
		Naive	-13.23	0.0001	0.0001	0.0002	0.180
	Gender	SIMEX	-7.880	0.058	0.059	0.059	0.896
		Naive	-14.94	0.051	0.052	0.053	0.892
	Age	SIMEX	-10.62	0.002	0.002	0.002	0.630
		Naive	-17.33	0.002	0.002	0.002	0.633

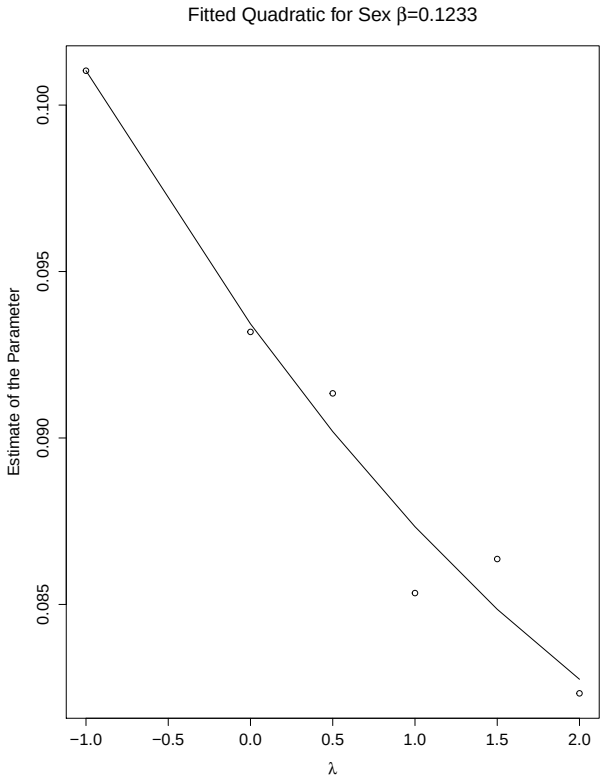
Table 9: The percent ($\%$) bias, average bootstrap standard error (ASE) for SIMEX, average model standard error (ASE) for naive, empirical standard error (ESE), mean squared error (MSE), and coverage probabilities (CP) are given for 2000 simulated data sets for the SIMEX and naive methods with $n = 1000$, exponential time, and a left-skewed gamma error distribution.

β	σ_ν^2	Method	$\%$ Bias	ASE	ESE	MSE	CP
log(1.5)	0.5	SIMEX	4.838	0.045	0.046	0.050	0.928
		Naive	-17.79	0.033	0.033	0.079	0.399
	1	SIMEX	12.38	0.051	0.051	0.072	0.828
		Naive	-22.07	0.033	0.033	0.095	0.22
log(3)	0.5	SIMEX	3.762	0.058	0.059	0.072	0.891
		Naive	-17.08	0.040	0.041	0.192	0.008
	1	SIMEX	9.189	0.064	0.066	0.121	0.656
		Naive	-22.24	0.040	0.039	0.247	0.000

Figure 1: The quadratic approximations of the β parameters as a function of λ for CD4 (a), sex (b), and age at enrollment (c), extrapolated to $\lambda = -1$.



(a)



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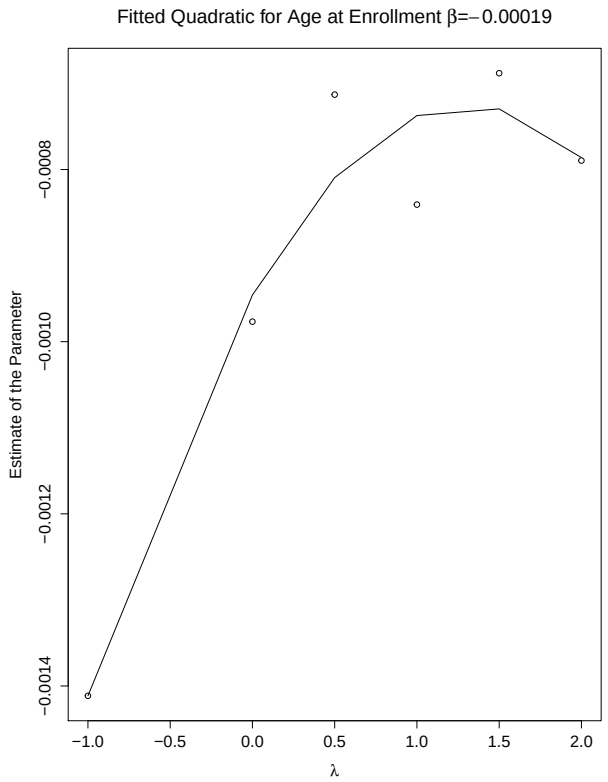

(c)