Supplementary Material

Technical Appendix and Additional Figures and Tables for

The Added Value of New Covariates to the Brier Score in Cox Survival Models

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The asymptotic distribution for the estimated difference in expected Brier scores

$$n^{1/2}\left[D_n(t;\hat{\boldsymbol{\theta}}_t) - \Delta(t;\boldsymbol{\theta}_t)\right] \tag{A.1}$$

where

$$D_n^2(t;\hat{\boldsymbol{\theta}}_t) = n^{-1}\sum_i \left\{ \hat{S}_t(\boldsymbol{x}_i,\boldsymbol{z}_i) - \frac{\sum_j K_h(\hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_i, \hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_j)\hat{S}_t(\boldsymbol{x}_i,\boldsymbol{z}_j)}{\sum_j K_h(\hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_i, \hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_j)} \right\}^2 \tag{A.2}$$

$\hat{\boldsymbol{\theta}}_t = (\hat{\alpha}_t, \hat{\boldsymbol{\beta}}_t, \hat{\boldsymbol{\gamma}}_t)$ are the $\sqrt{n}$ consistent (pointwise in t) time-varying coefficient solutions to the estimating equations derived in Peng and Huang (2007)

$$\hat{S}_t(\boldsymbol{x},\boldsymbol{z}) = \exp[-\exp(\hat{\alpha}_t + \hat{\boldsymbol{\beta}}_t^T\boldsymbol{x} + \hat{\boldsymbol{\gamma}}_t^T\boldsymbol{z})] \qquad \boldsymbol{\theta}_t = \lim_{n\to\infty}(\hat{\alpha}_t, \hat{\boldsymbol{\beta}}_t, \hat{\boldsymbol{\gamma}}_t)$$

$$\hat{\pi}_t(\boldsymbol{x}) = \frac{\sum_j K_h(\hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}, \hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_j)\hat{S}_t(\boldsymbol{x},\boldsymbol{z}_j)}{\sum_j K_h(\hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_i, \hat{\boldsymbol{\beta}}_t^T\boldsymbol{x}_j)} \qquad \Delta(t;\boldsymbol{\theta}_t) = \lim_{n\to\infty} D_n(t;\hat{\boldsymbol{\theta}}_t).$$

The following conditions are applied in the derivations:

(C1) The linear combination $\boldsymbol{\beta}_t^T\boldsymbol{x}$ lies in a bounded interval.

(C2) The kernel function K is a univariate density function, symmetric about zero.

(C3) The bandwidth h is chosen so that as $n \to \infty$, $nh^8 \to 0$.

(C4) The survival function $\pi_t(\boldsymbol{x})$, based on $\boldsymbol{x}$ alone, is twice continuously differentiable with a bounded second derivative.

The following lemmas are used to derive the asymptotic distribution in the Theorem.

Lemma 1: The asymptotic moments of $D_n^2(t;\boldsymbol{\theta}_t)$ are:

$$\mathrm{E}[D_n^2(t;\boldsymbol{\theta}_t)] = \Delta^2(t;\boldsymbol{\theta}_t) + O(h^4)$$

$$\mathrm{var}[D_n^2(t;\boldsymbol{\theta}_t)] = n^{-1}\mathrm{var}\left\{[S_t(\boldsymbol{X},\boldsymbol{Z}) - \pi_t(\boldsymbol{X})]^2\right\} + O(n^{-2}h^{-1}) + O(n^{-1}h^4)$$

Proof: From projection theory (Figure 1),

$$S_t(\boldsymbol{X},\boldsymbol{Z}) = \pi_t(\boldsymbol{X}) + \epsilon_t; \qquad \mathrm{E}[\epsilon_t|\boldsymbol{x}] = 0,$$

and therefore from (A.2), $D_n^2(t;\boldsymbol{\theta}_t) = n^{-1}\sum_i \hat{\epsilon}_{it}^2$.

The moments now follow directly from Hall and Marron (1990).

Lemma 2: $n^{1/2}\left[D_n(t;\boldsymbol{\theta}_t) - \Delta(t;\boldsymbol{\theta}_t)\right]$ is an asymptotic normal mean zero U-statistic of degree 3.

Proof:

$$D_n^2(t;\boldsymbol{\theta}_t) = n^{-1}\sum_i \left[S_t(\boldsymbol{x}_i,\boldsymbol{z}_i) - \frac{r_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{r_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}\right]^2$$

where $r_t^{(l)}(\boldsymbol{\beta}_t^T\boldsymbol{x}) = n^{-1}\sum_j S_t^l(\boldsymbol{x},\boldsymbol{z}_j)K_h(\boldsymbol{\beta}_t^T\boldsymbol{x},\boldsymbol{\beta}_t^T\boldsymbol{x}_j)$

and $\rho_t^{(l)}(\boldsymbol{\beta}_t^T\boldsymbol{x}) = \lim_{n\to\infty} r_t^{(l)}(\boldsymbol{\beta}_t^T\boldsymbol{x})$.

A two-term Taylor expansion of the ratio produces

$D_n^2(t;\boldsymbol{\theta}_t) =$

$$n^{-1}\sum_i\left[\left(S_t(\boldsymbol{x}_i,\boldsymbol{z}_i) - \frac{\rho_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}\right) - \left(\frac{r_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)} - \frac{\rho_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)r_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{[\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)]^2}\right)\right]^2 + O_p(n^{-1}h^{-1}+h^4)$$

$$= n^{-3}\sum_i\sum_j\sum_k u_{ij}u_{ik} + O_p(n^{-1}h^{-1}+h^4)$$

where $$u_{ij} = S_t(\boldsymbol{x}_i,\boldsymbol{z}_i) - \frac{\rho_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)} - \frac{K_h(\boldsymbol{\beta}_t^T\boldsymbol{x}_i,\boldsymbol{\beta}_t^T\boldsymbol{x}_j)}{\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}\left(S_t(\boldsymbol{x}_i,\boldsymbol{z}_j) - \frac{\rho_t^{(1)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}{\rho_t^{(0)}(\boldsymbol{\beta}_t^T\boldsymbol{x}_i)}\right).$$

It follows using conditions (C1-C4) that $D_n^2(t;\boldsymbol{\theta}_t)$ is an asymptotic U-statistic with degree 3 and

$$n^{1/2}\left\{D_n^2(t;\boldsymbol{\theta}_t) - \mathrm{E}\left[D_n^2(t;\boldsymbol{\theta}_t)\right]\right\} \xrightarrow{D} N(0,W).$$

$$n^{1/2}\left\{\mathrm{E}\left[D_n^2(t;\boldsymbol{\theta}_t)\right] - \Delta^2(t;\boldsymbol{\theta}_t)\right\} \xrightarrow{p} 0.$$

Therefore, by Slutsky's theorem and the delta method,

$$n^{1/2}\left\{D_n(t;\boldsymbol{\theta}_t) - \Delta(t;\boldsymbol{\theta}_t)\right\}$$

is asymptotically normal with mean zero.

Proof of Theorem: Decompose (A.1) as

$$n^{1/2}\left[D_n(t;\hat{\boldsymbol{\theta}}_t) - D_n(t;\boldsymbol{\theta}_t)\right] + n^{1/2}\left[D_n(t;\boldsymbol{\theta}_t) - \Delta(t;\boldsymbol{\theta}_t)\right].$$

Taylor expand the first term around $\hat{\boldsymbol{\theta}}_t = \boldsymbol{\theta}_t$

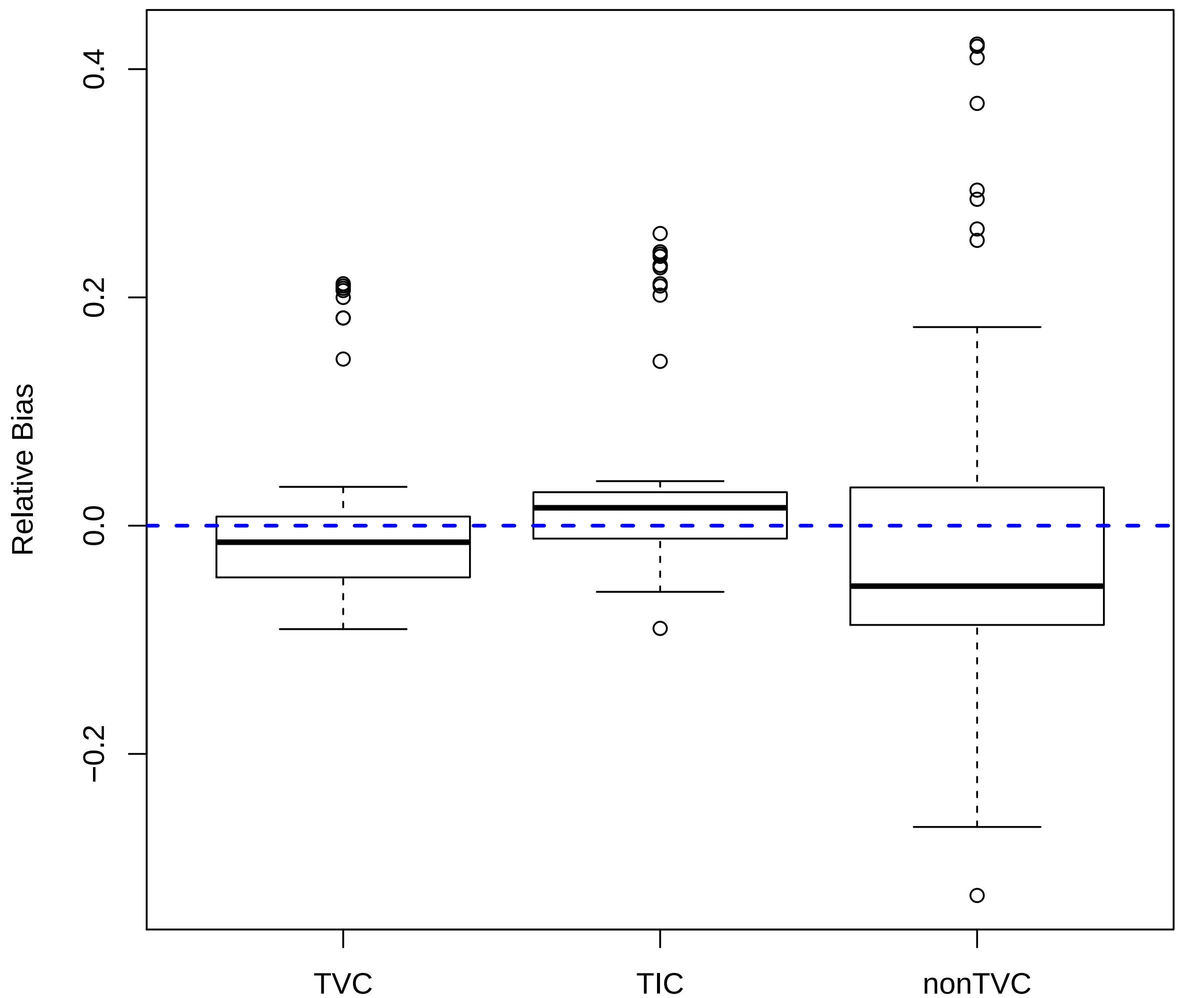
$$= \left[\frac{\partial}{\partial\boldsymbol{\eta}} D_n(t;\boldsymbol{\eta})\bigg|_{\boldsymbol{\eta}=\boldsymbol{\theta}_t}\right]^T \left[n^{1/2}(\hat{\boldsymbol{\theta}}_t - \boldsymbol{\theta}_t)\right] + n^{1/2}\left[D_n(t;\boldsymbol{\theta}_t) - \Delta(t;\boldsymbol{\theta}_t)\right] + o_p(1).$$

Since $[n^{1/2}(\hat{\boldsymbol{\theta}}_t - \boldsymbol{\theta}_t)]$ is asymptotically normal with mean zero (Peng and Huang 2007) and

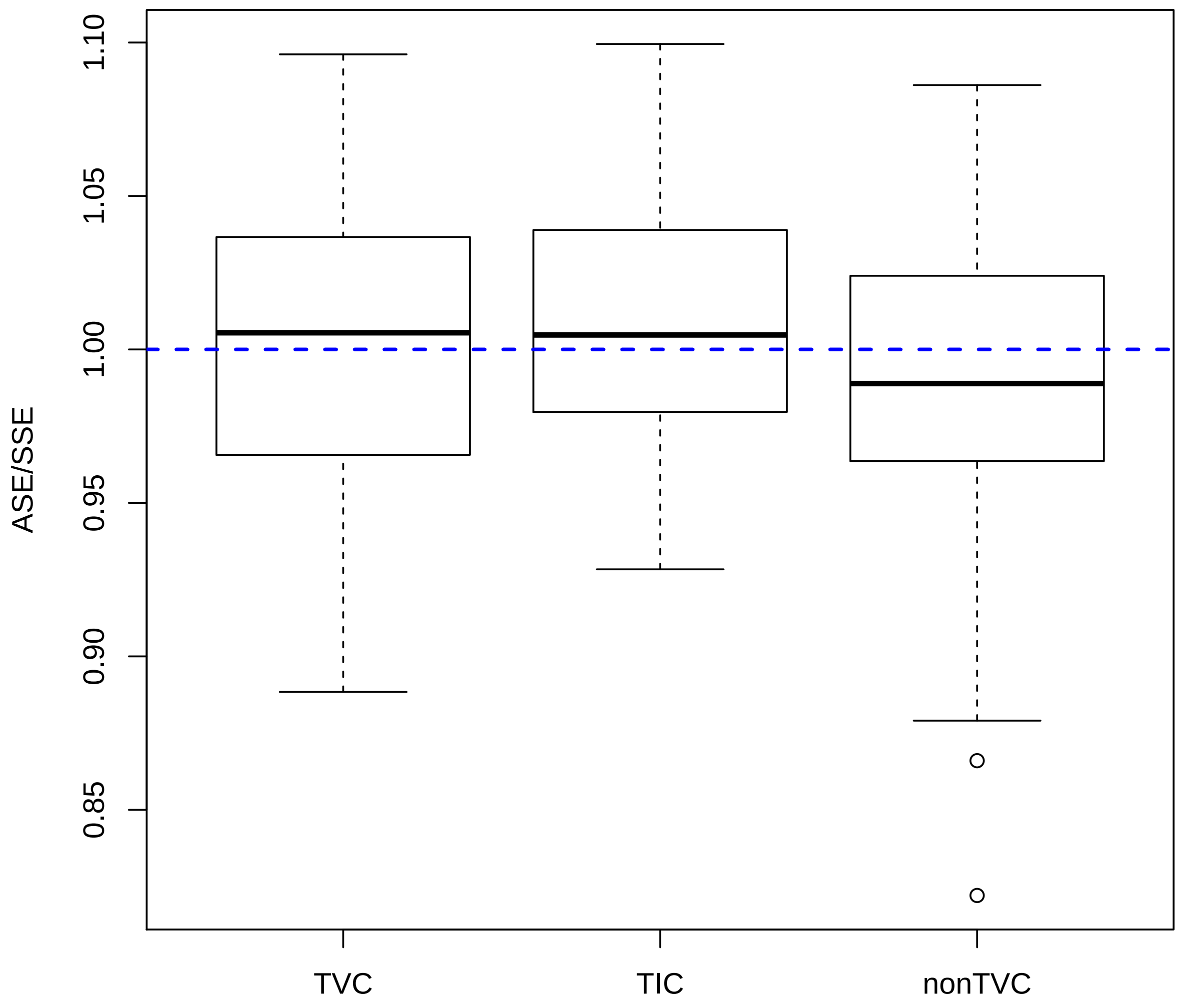
$$\left[\frac{\partial}{\partial\boldsymbol{\eta}} D_n(t;\boldsymbol{\eta})\bigg|_{\boldsymbol{\eta}=\boldsymbol{\theta}_t}\right] \xrightarrow{p} \boldsymbol{c}_1$$

converges in probability, the first term is an asymptotic mean zero normal random variable. In addition, Lemmas 1 and 2 demonstrate that the second term is asymptotically normal. Therefore,

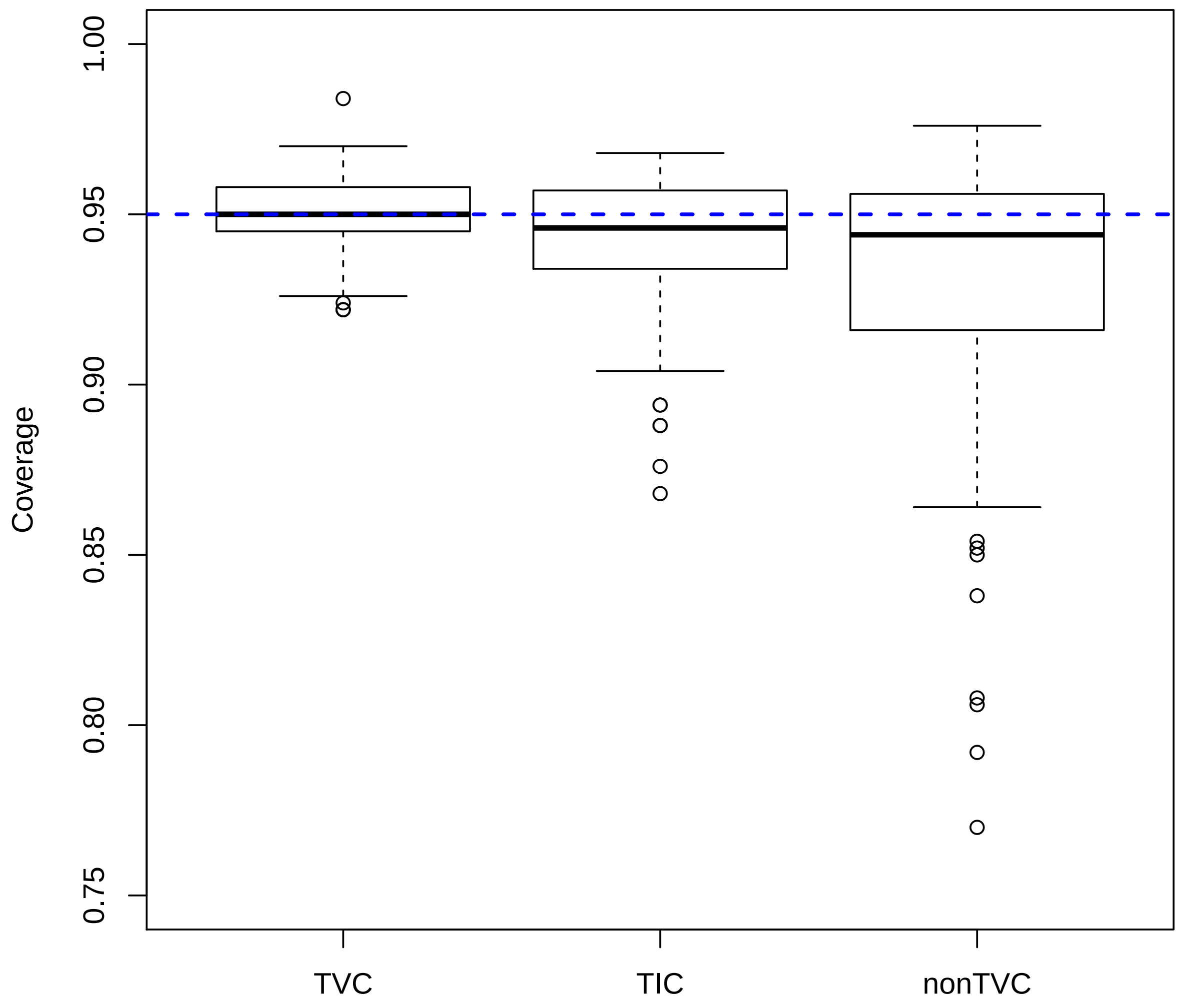
$$n^{1/2}\left[D_n(t;\hat{\boldsymbol{\theta}}) - \Delta(t;\boldsymbol{\theta}_t)\right] \xrightarrow{D} N(0,V).$$



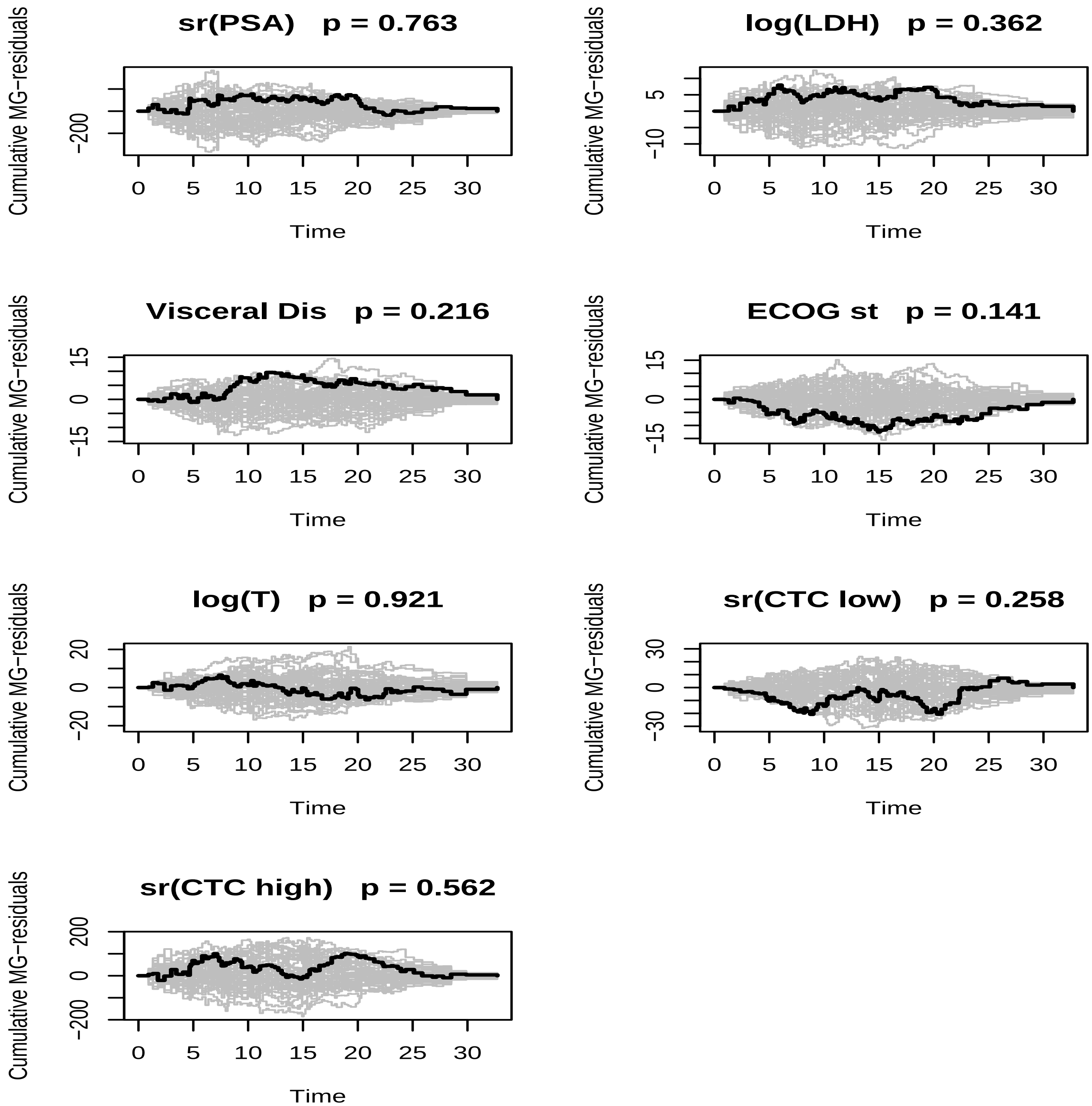
SUPPLEMENTAL FIGURE 1 Relative bias in the square root estimated difference in the expected Brier scores. Results from the 72 parameter combinations specified in Section 3 of the manuscript. Data generated from a time-varying coefficient Cox model (TVC), a time-invariant coefficient Cox model (TIC), a survival function which is not a time-varying coefficient Cox model (nonTVC).



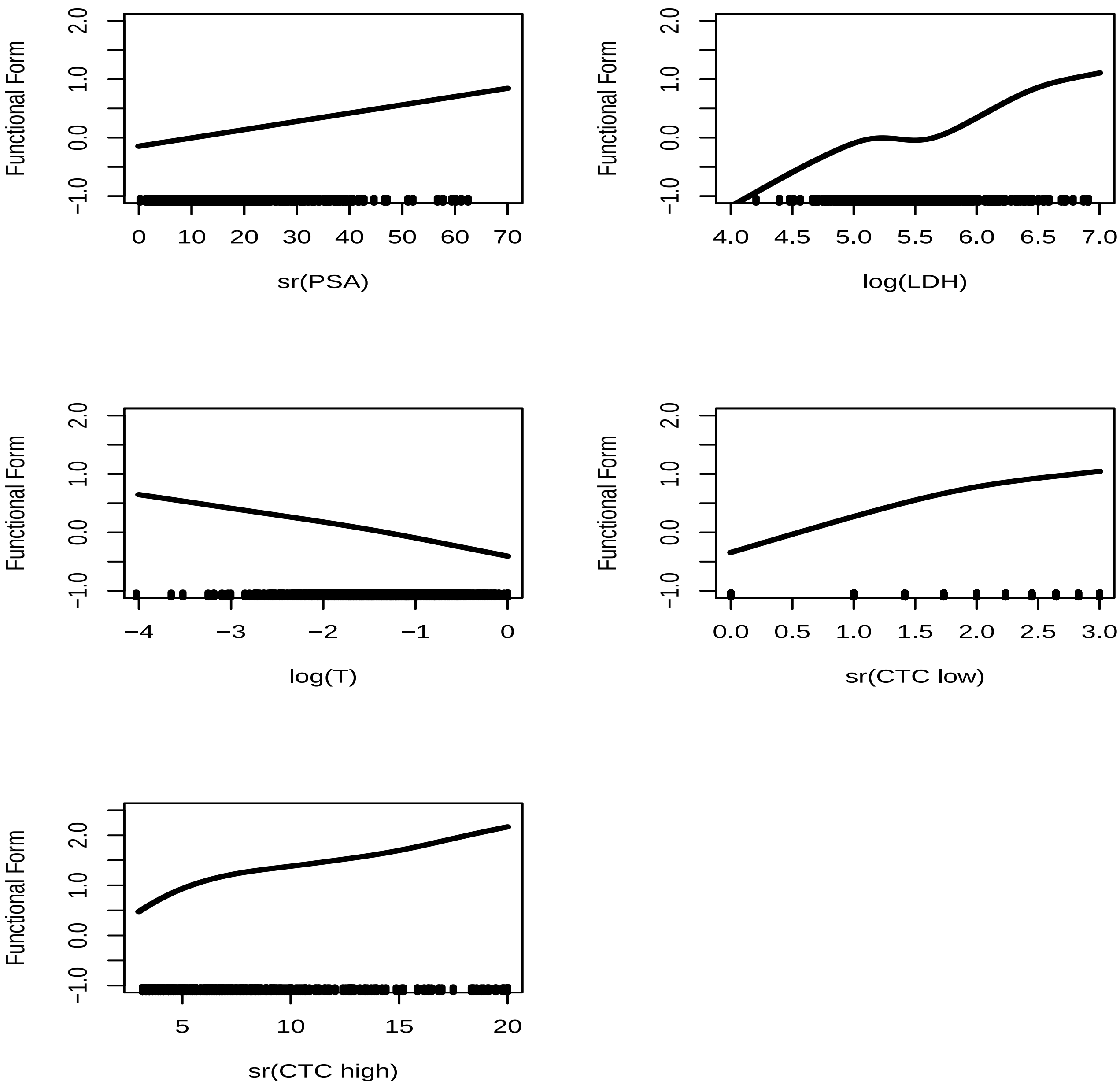
SUPPLEMENTAL FIGURE 2 Ratio of the average estimated standard error to the simulation standard error. Results from the 72 parameter combinations specified in Section 3 of the manuscript. Data generated from a time-varying coefficient Cox model (TVC), a time-invariant coefficient Cox model (TIC), a survival function which is not a time-varying coefficient Cox model (nonTVC).



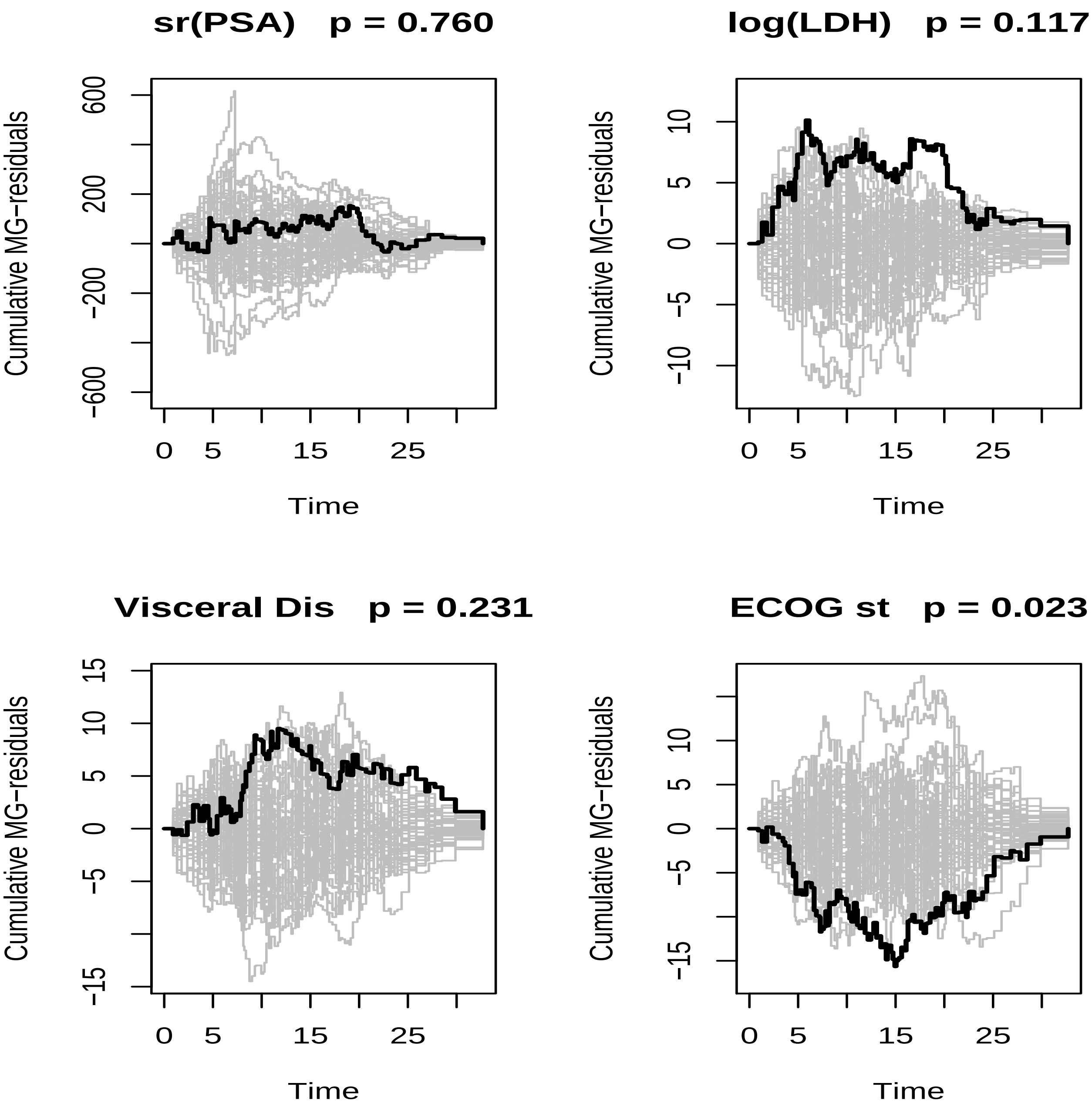
SUPPLEMENTAL FIGURE 3 Coverage probabilities from 95% confidence intervals. Results from the 72 parameter combinations specified in Section 3 of the manuscript. Data generated from a time-varying coefficient Cox model (TVC), a time-invariant coefficient Cox model (TIC), a survival function which is not a time-varying coefficient Cox model (nonTVC).



SUPPLEMENTAL FIGURE 4 Diagnostic plots based on cumulative martingale residuals to assess the proportional hazards assumption in the full model. sr(PSA) = square root prostate specific antigen; log(LDH) = log lactate dehydrogenase; sr(CTC) = square root circulating tumor cells; log(T) = log serum testosterone



SUPPLEMENTAL FIGURE 5 Diagnostic plots to assess the functional form for each continuous covariate in the full model.



SUPPLEMENTAL FIGURE 6 Diagnostic plots based on cumulative martingale residuals to assess the proportional hazards assumption in the subset model.

This section provides the information used to produce the simulation results in Tables S1-S4 that follow. For all simulations, the model used to estimate the full survival function was

$$S_t(x_1, x_2, z) = \exp\left[-\exp\left\{\alpha_t + \beta_{1t}x_1 + \beta_{2t}x_2 + \gamma z\right\}\right] \tag{A.3}$$

where the survival probabilities were evaluated at $t = 12$. The survival times were generated from a Weibull distribution $(\lambda, \nu(x_1, x_2))$. For Tables S1-S3, $\nu(x_1, x_2) = \nu$, corresponding to either a time-varying coefficient Cox model or a time-invariant coefficient Cox model. For Table S4, when the shape parameter is a function of the covariates $\nu(x_1, x_2) = -0.2x_1x_2\nu$, the additive covariate form of the Cox model (A.3) misspecifies the survival function. The covariate distributions for all simulations are: $(x_1, x_2) \sim$ exponential(1) and $\exp(\gamma z) \sim$ gamma(ϕ, ϕ).

The additional columns in Tables S1-S4 represent:

$\Delta(t) = \sqrt{E\left\{\pi_t(\boldsymbol{X}) - S_t(\boldsymbol{X}, \boldsymbol{Z})\right\}^2}$

PROP CENSOR: the average proportion censored

REL BIAS: $\left[\text{avg}\left(\hat{\Delta}(t)\right) - \Delta(t)\right] / \Delta(t)$

ASE: the average standard error of $\hat{\Delta}(t)$

ASE/SSE: the ratio of the average standard error to the simulation standard error

COV: 95% confidence interval coverage based on the square root reparameterization

Table S1: Simulations from correctly specified time-varying coefficient Cox model.

Data generated from survival model: $S_t(x_1, x_2, z) = \exp[-\exp\{\alpha_t + \beta_{1t}x_1 + \beta_{2t}x_2 + \gamma z\}]$

$\alpha_t = \log(\lambda t^\nu)$; $\beta_{jt} = \beta_j \log t$; $\beta_1 = \beta_2 = 1$

Projection method used to estimate $\hat{\pi}_t(x_1, x_2)$

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
0.75	0.5	0.05	0	0.212	0.024	1.000	0.940
0.75	0.5	0.05	0.25	0.208	0.024	1.022	0.922
0.75	0.5	0.05	0.5	0.182	0.024	1.022	0.932
0.75	0.5	0.05	0.75	-0.002	0.023	0.945	0.952
0.75	0.5	0.1	0	0.008	0.023	1.027	0.948
0.75	0.5	0.1	0.25	0.008	0.023	1.036	0.950
0.75	0.5	0.1	0.5	-0.024	0.023	0.987	0.950
0.75	0.5	0.1	0.75	-0.009	0.025	1.029	0.962
0.75	0.5	0.15	0	-0.012	0.024	1.034	0.968
0.75	0.5	0.15	0.25	-0.010	0.023	1.046	0.948
0.75	0.5	0.15	0.5	-0.031	0.022	1.068	0.968
0.75	0.5	0.15	0.75	-0.041	0.024	0.960	0.958
0.75	1	0.05	0	0.206	0.024	1.008	0.938
0.75	1	0.05	0.25	0.200	0.023	0.987	0.922
0.75	1	0.05	0.5	0.146	0.023	0.966	0.924
0.75	1	0.05	0.75	-0.012	0.022	0.941	0.954
0.75	1	0.1	0	0.012	0.023	1.086	0.960
0.75	1	0.1	0.25	-0.021	0.023	1.071	0.962
0.75	1	0.1	0.5	0.006	0.023	1.064	0.958
0.75	1	0.1	0.75	-0.003	0.025	1.029	0.952
0.75	1	0.15	0	0.002	0.024	1.026	0.960
0.75	1	0.15	0.25	-0.006	0.023	1.056	0.956
0.75	1	0.15	0.5	-0.021	0.022	1.093	0.984
0.75	1	0.15	0.75	-0.035	0.024	0.942	0.936
0.75	2	0.05	0	0.210	0.023	1.000	0.928
0.75	2	0.05	0.25	0.182	0.023	0.983	0.926
0.75	2	0.05	0.5	0.006	0.021	0.899	0.946
0.75	2	0.05	0.75	-0.040	0.022	0.932	0.968
0.75	2	0.1	0	0.010	0.022	1.028	0.950
0.75	2	0.1	0.25	-0.009	0.023	1.051	0.964
0.75	2	0.1	0.5	0.009	0.024	1.086	0.962
0.75	2	0.1	0.75	0.004	0.026	1.012	0.948
0.75	2	0.15	0	0.011	0.023	1.009	0.960
0.75	2	0.15	0.25	0.005	0.023	1.032	0.946
0.75	2	0.15	0.5	-0.011	0.023	1.096	0.970
0.75	2	0.15	0.75	-0.023	0.025	0.973	0.952

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
1.333	0.5	0.05	0	0.028	0.022	0.913	0.940
1.333	0.5	0.05	0.25	0.024	0.022	1.005	0.948
1.333	0.5	0.05	0.5	-0.006	0.021	0.921	0.948
1.333	0.5	0.05	0.75	-0.052	0.021	0.898	0.944
1.333	0.5	0.1	0	-0.037	0.023	0.996	0.952
1.333	0.5	0.1	0.25	-0.035	0.023	1.071	0.958
1.333	0.5	0.1	0.5	-0.016	0.023	0.987	0.942
1.333	0.5	0.1	0.75	-0.058	0.024	1.000	0.950
1.333	0.5	0.15	0	-0.081	0.021	1.045	0.936
1.333	0.5	0.15	0.25	-0.091	0.020	1.010	0.922
1.333	0.5	0.15	0.5	-0.079	0.022	1.037	0.942
1.333	0.5	0.15	0.75	-0.083	0.032	1.006	0.956
1.333	1	0.05	0	0.030	0.022	0.916	0.946
1.333	1	0.05	0.25	0.024	0.021	1.000	0.954
1.333	1	0.05	0.5	-0.056	0.021	0.963	0.964
1.333	1	0.05	0.75	-0.056	0.022	0.919	0.958
1.333	1	0.1	0	-0.034	0.022	0.965	0.948
1.333	1	0.1	0.25	-0.031	0.023	1.066	0.956
1.333	1	0.1	0.5	-0.013	0.023	0.987	0.954
1.333	1	0.1	0.75	-0.052	0.025	0.972	0.950
1.333	1	0.15	0	-0.062	0.021	1.015	0.948
1.333	1	0.15	0.25	-0.079	0.021	1.020	0.942
1.333	1	0.15	0.5	-0.067	0.023	1.051	0.952
1.333	1	0.15	0.75	-0.077	0.034	0.980	0.962
1.333	2	0.05	0	0.034	0.021	0.918	0.944
1.333	2	0.05	0.25	-0.022	0.021	0.916	0.952
1.333	2	0.05	0.5	-0.058	0.021	0.888	0.948
1.333	2	0.05	0.75	-0.048	0.022	0.921	0.956
1.333	2	0.1	0	-0.028	0.022	0.987	0.942
1.333	2	0.1	0.25	-0.020	0.023	1.079	0.958
1.333	2	0.1	0.5	0.001	0.024	0.980	0.948
1.333	2	0.1	0.75	-0.034	0.025	0.958	0.946
1.333	2	0.15	0	-0.043	0.021	1.040	0.966
1.333	2	0.15	0.25	-0.061	0.022	1.029	0.958
1.333	2	0.15	0.5	-0.052	0.025	1.061	0.964
1.333	2	0.15	0.75	-0.065	0.028	0.986	0.968

Table S2: Simulations from correctly specified time-varying coefficient Cox model.

Data generated from survival model: $S_t(x_1, x_2, z) = \exp\left[-\exp\left\{\alpha_t + \beta_{1t}x_1 + \beta_{2t}x_2 + \gamma z\right\}\right]$

$\alpha_t = \log(\lambda t^{\nu});$ $\beta_{jt} = \beta_j \log t;$ $\beta_1 = \beta_2 = 1$

Working Cox model used to estimate $\hat{\pi}_t(x_1, x_2)$

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
0.75	0.5	0.05	0	0.498	0.026	1.227	0.854
0.75	0.5	0.05	0.25	0.490	0.025	1.214	0.842
0.75	0.5	0.05	0.5	0.444	0.025	1.235	0.864
0.75	0.5	0.05	0.75	0.168	0.029	1.535	0.968
0.75	0.5	0.1	0	0.088	0.023	0.983	0.944
0.75	0.5	0.1	0.25	0.087	0.023	1.059	0.950
0.75	0.5	0.1	0.5	0.049	0.022	1.028	0.962
0.75	0.5	0.1	0.75	0.067	0.023	1.065	0.946
0.75	0.5	0.15	0	0.041	0.027	1.004	0.970
0.75	0.5	0.15	0.25	0.026	0.024	1.043	0.946
0.75	0.5	0.15	0.5	-0.003	0.023	1.051	0.960
0.75	0.5	0.15	0.75	-0.027	0.025	0.962	0.952
0.75	1	0.05	0	0.480	0.026	1.262	0.838
0.75	1	0.05	0.25	0.456	0.025	1.237	0.844
0.75	1	0.05	0.5	0.390	0.024	1.279	0.880
0.75	1	0.05	0.75	0.132	0.028	1.413	0.958
0.75	1	0.1	0	0.081	0.023	1.022	0.950
0.75	1	0.1	0.25	0.049	0.023	1.119	0.968
0.75	1	0.1	0.5	0.087	0.023	1.076	0.948
0.75	1	0.1	0.75	0.071	0.023	1.100	0.954
0.75	1	0.15	0	0.049	0.025	1.037	0.952
0.75	1	0.15	0.25	0.028	0.024	1.088	0.954
0.75	1	0.15	0.5	0.006	0.023	1.101	0.968
0.75	1	0.15	0.75	-0.018	0.026	0.945	0.934
0.75	2	0.05	0	0.460	0.025	1.258	0.866
0.75	2	0.05	0.25	0.420	0.024	1.218	0.868
0.75	2	0.05	0.5	0.234	0.024	1.150	0.928
0.75	2	0.05	0.75	0.144	0.024	1.286	0.966
0.75	2	0.1	0	0.063	0.022	1.074	0.948
0.75	2	0.1	0.25	0.056	0.022	1.062	0.954
0.75	2	0.1	0.5	0.094	0.023	1.145	0.956
0.75	2	0.1	0.75	0.095	0.024	1.017	0.932
0.75	2	0.15	0	0.055	0.024	1.077	0.944
0.75	2	0.15	0.25	0.045	0.023	0.979	0.944
0.75	2	0.15	0.5	0.021	0.023	1.088	0.956
0.75	2	0.15	0.75	-0.002	0.026	0.956	0.950

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
1.333	0.5	0.05	0	0.304	0.022	1.173	0.904
1.333	0.5	0.05	0.25	0.290	0.022	1.327	0.904
1.333	0.5	0.05	0.5	0.240	0.022	1.230	0.940
1.333	0.5	0.05	0.75	0.160	0.023	1.176	0.950
1.333	0.5	0.1	0	0.057	0.022	0.894	0.934
1.333	0.5	0.1	0.25	0.048	0.022	1.119	0.954
1.333	0.5	0.1	0.5	0.070	0.021	1.024	0.934
1.333	0.5	0.1	0.75	0.028	0.022	0.974	0.946
1.333	0.5	0.15	0	-0.052	0.022	0.948	0.960
1.333	0.5	0.15	0.25	-0.060	0.021	1.014	0.940
1.333	0.5	0.15	0.5	-0.037	0.023	1.065	0.964
1.333	0.5	0.15	0.75	0.007	0.043	1.159	0.956
1.333	1	0.05	0	0.298	0.022	1.165	0.894
1.333	1	0.05	0.25	0.286	0.021	1.313	0.932
1.333	1	0.05	0.5	0.214	0.021	1.189	0.940
1.333	1	0.05	0.75	0.150	0.023	1.258	0.954
1.333	1	0.1	0	0.052	0.021	0.986	0.936
1.333	1	0.1	0.25	0.059	0.021	1.081	0.944
1.333	1	0.1	0.5	0.082	0.022	1.039	0.930
1.333	1	0.1	0.75	0.028	0.023	0.991	0.948
1.333	1	0.15	0	-0.045	0.021	1.044	0.958
1.333	1	0.15	0.25	-0.057	0.021	1.024	0.944
1.333	1	0.15	0.5	-0.043	0.023	1.068	0.958
1.333	1	0.15	0.75	0.006	0.044	1.048	0.964
1.333	2	0.05	0	0.302	0.022	1.188	0.890
1.333	2	0.05	0.25	0.240	0.021	1.167	0.920
1.333	2	0.05	0.5	0.172	0.021	1.128	0.928
1.333	2	0.05	0.75	0.152	0.024	1.200	0.964
1.333	2	0.1	0	0.053	0.021	0.995	0.936
1.333	2	0.1	0.25	0.086	0.022	0.968	0.942
1.333	2	0.1	0.5	0.101	0.022	0.995	0.924
1.333	2	0.1	0.75	0.069	0.023	1.000	0.938
1.333	2	0.15	0	-0.029	0.021	1.055	0.974
1.333	2	0.15	0.25	-0.045	0.022	1.043	0.948
1.333	2	0.15	0.5	-0.033	0.026	1.114	0.970
1.333	2	0.15	0.75	-0.032	0.031	1.083	0.976

Table S3: Simulations from time invariant coefficient Cox model.

Data generated from survival model: $S_t(x_1, x_2, z) = \exp\left[-\exp\left\{\alpha_t + \beta_1 x_1 + \beta_2 x_2 + \gamma z\right\}\right]$

$$\alpha_t = \log(\lambda t^{\nu}); \qquad \beta_1 = \beta_2 = 1$$

Projection method used to estimate $\hat{\pi}_t(x_1, x_2)$

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
0.75	0.5	0.05	0	0.228	0.019	0.990	0.888
0.75	0.5	0.05	0.25	0.236	0.020	1.026	0.876
0.75	0.5	0.05	0.5	0.202	0.020	1.048	0.916
0.75	0.5	0.05	0.75	0.238	0.020	1.075	0.894
0.75	0.5	0.1	0	0.032	0.020	1.086	0.968
0.75	0.5	0.1	0.25	0.028	0.020	1.025	0.958
0.75	0.5	0.1	0.5	0.029	0.020	1.025	0.942
0.75	0.5	0.1	0.75	0.030	0.021	1.030	0.940
0.75	0.5	0.15	0	0.029	0.021	1.062	0.960
0.75	0.5	0.15	0.25	0.022	0.021	1.005	0.934
0.75	0.5	0.15	0.5	0.019	0.021	1.051	0.956
0.75	0.5	0.15	0.75	0.021	0.022	0.977	0.934
0.75	1	0.05	0	0.226	0.019	0.995	0.904
0.75	1	0.05	0.25	0.240	0.020	1.021	0.868
0.75	1	0.05	0.5	0.210	0.020	1.037	0.912
0.75	1	0.05	0.75	0.256	0.020	1.057	0.894
0.75	1	0.1	0	0.039	0.020	1.010	0.950
0.75	1	0.1	0.25	0.025	0.020	1.020	0.962
0.75	1	0.1	0.5	0.020	0.020	0.981	0.940
0.75	1	0.1	0.75	0.005	0.021	1.010	0.946
0.75	1	0.15	0	0.029	0.021	1.056	0.958
0.75	1	0.15	0.25	0.021	0.021	0.995	0.940
0.75	1	0.15	0.5	0.020	0.021	1.061	0.964
0.75	1	0.15	0.75	0.017	0.022	0.987	0.930
0.75	2	0.05	0	0.228	0.019	0.990	0.888
0.75	2	0.05	0.25	0.212	0.019	1.066	0.926
0.75	2	0.05	0.5	0.144	0.020	0.995	0.924
0.75	2	0.05	0.75	0.008	0.022	1.100	0.956
0.75	2	0.1	0	0.022	0.020	1.070	0.960
0.75	2	0.1	0.25	0.011	0.020	0.985	0.946
0.75	2	0.1	0.5	-0.030	0.021	1.000	0.954
0.75	2	0.1	0.75	0.005	0.022	0.948	0.918
0.75	2	0.15	0	0.029	0.021	1.056	0.958
0.75	2	0.15	0.25	0.023	0.021	0.991	0.946
0.75	2	0.15	0.5	0.024	0.022	1.059	0.958
0.75	2	0.15	0.75	0.014	0.024	0.960	0.934

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
1.333	0.5	0.05	0	0.032	0.018	0.968	0.940
1.333	0.5	0.05	0.25	0.014	0.018	0.958	0.932
1.333	0.5	0.05	0.5	0.020	0.018	0.989	0.950
1.333	0.5	0.05	0.75	0.028	0.019	0.969	0.954
1.333	0.5	0.1	0	-0.054	0.020	1.005	0.944
1.333	0.5	0.1	0.25	-0.052	0.021	1.041	0.962
1.333	0.5	0.1	0.5	-0.045	0.021	1.005	0.954
1.333	0.5	0.1	0.75	-0.036	0.021	0.968	0.940
1.333	0.5	0.15	0	-0.007	0.021	1.065	0.964
1.333	0.5	0.15	0.25	-0.011	0.021	0.977	0.948
1.333	0.5	0.15	0.5	-0.007	0.021	1.034	0.962
1.333	0.5	0.15	0.75	-0.008	0.028	0.965	0.948
1.333	1	0.05	0	0.032	0.018	0.968	0.940
1.333	1	0.05	0.25	0.006	0.019	1.022	0.940
1.333	1	0.05	0.5	0.028	0.019	1.016	0.956
1.333	1	0.05	0.75	0.010	0.019	0.960	0.942
1.333	1	0.1	0	-0.054	0.020	1.000	0.942
1.333	1	0.1	0.25	-0.046	0.021	1.025	0.966
1.333	1	0.1	0.5	-0.042	0.021	1.000	0.954
1.333	1	0.1	0.75	-0.022	0.022	0.973	0.942
1.333	1	0.15	0	-0.007	0.021	1.065	0.964
1.333	1	0.15	0.25	-0.013	0.021	0.972	0.938
1.333	1	0.15	0.5	-0.008	0.022	1.023	0.958
1.333	1	0.15	0.75	-0.005	0.031	0.928	0.946
1.333	2	0.05	0	0.032	0.018	0.968	0.940
1.333	2	0.05	0.25	-0.014	0.018	0.979	0.954
1.333	2	0.05	0.5	-0.058	0.018	0.958	0.934
1.333	2	0.05	0.75	-0.090	0.019	0.946	0.928
1.333	2	0.1	0	-0.053	0.020	1.000	0.942
1.333	2	0.1	0.25	-0.039	0.021	1.020	0.962
1.333	2	0.1	0.5	-0.024	0.022	1.005	0.956
1.333	2	0.1	0.75	-0.019	0.023	0.991	0.936
1.333	2	0.15	0	-0.008	0.021	1.065	0.964
1.333	2	0.15	0.25	-0.011	0.022	0.995	0.950
1.333	2	0.15	0.5	-0.010	0.023	1.050	0.966
1.333	2	0.15	0.75	0.001	0.035	0.983	0.946

Table S4: Simulations from misspecified time-varying coefficient Cox model. Data generated from survival model: $S_t(x_1, x_2, z) = \exp[-\exp\{\alpha_t(x_1, x_2) + \beta_{1t}x_1 + \beta_{2t}x_2 + \gamma z\}]$

$$\alpha_t(x_1, x_2) = \log(\lambda t^{-0.2x_1x_2\nu}); \qquad \beta_{jt} = \beta_j \log t; \qquad \beta_1 = \beta_2 = 1$$

Projection method used to estimate $\hat{\pi}_t(x_1, x_2)$

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
0.75	0.5	0.05	0	0.028	0.020	0.981	0.956
0.75	0.5	0.05	0.25	0.050	0.021	0.962	0.950
0.75	0.5	0.05	0.5	0.018	0.020	0.967	0.950
0.75	0.5	0.05	0.75	-0.264	0.018	0.929	0.912
0.75	0.5	0.1	0	-0.055	0.022	0.991	0.954
0.75	0.5	0.1	0.25	-0.047	0.023	1.014	0.964
0.75	0.5	0.1	0.5	-0.086	0.022	0.953	0.940
0.75	0.5	0.1	0.75	-0.153	0.024	0.979	0.918
0.75	0.5	0.15	0	-0.052	0.025	1.033	0.970
0.75	0.5	0.15	0.25	-0.054	0.024	1.043	0.962
0.75	0.5	0.15	0.5	-0.047	0.024	0.967	0.946
0.75	0.5	0.15	0.75	-0.064	0.024	0.980	0.946
0.75	1	0.05	0	0.146	0.020	0.995	0.930
0.75	1	0.05	0.25	0.150	0.020	0.990	0.926
0.75	1	0.05	0.5	0.118	0.020	1.025	0.938
0.75	1	0.05	0.75	-0.154	0.019	0.879	0.934
0.75	1	0.1	0	-0.023	0.022	1.082	0.976
0.75	1	0.1	0.25	-0.026	0.023	1.061	0.958
0.75	1	0.1	0.5	-0.061	0.022	0.974	0.944
0.75	1	0.1	0.75	-0.104	0.024	1.030	0.968
0.75	1	0.15	0	-0.034	0.025	1.024	0.956
0.75	1	0.15	0.25	-0.047	0.025	1.021	0.938
0.75	1	0.15	0.5	-0.043	0.024	1.044	0.958
0.75	1	0.15	0.75	-0.055	0.024	1.013	0.948
0.75	2	0.05	0	0.410	0.021	1.030	0.808
0.75	2	0.05	0.25	0.422	0.021	1.046	0.792
0.75	2	0.05	0.5	0.420	0.021	0.963	0.770
0.75	2	0.05	0.75	0.370	0.021	0.926	0.806
0.75	2	0.1	0	0.164	0.023	0.947	0.852
0.75	2	0.1	0.25	0.172	0.023	1.018	0.850
0.75	2	0.1	0.5	0.152	0.023	0.991	0.872
0.75	2	0.1	0.75	0.174	0.024	1.035	0.866
0.75	2	0.15	0	0.005	0.026	1.024	0.964
0.75	2	0.15	0.25	0.012	0.025	1.008	0.958
0.75	2	0.15	0.5	0.012	0.024	1.000	0.938
0.75	2	0.15	0.75	0.002	0.023	0.983	0.956

ϕ	ν	$\Delta(t)$	prop censor	Rel Bias	ASE	ASE/SSE	Cov
1.333	0.5	0.05	0	-0.124	0.019	0.931	0.956
1.333	0.5	0.05	0.25	-0.088	0.019	0.927	0.950
1.333	0.5	0.05	0.5	-0.118	0.019	0.931	0.946
1.333	0.5	0.05	0.75	-0.324	0.017	0.822	0.868
1.333	0.5	0.1	0	-0.125	0.022	1.000	0.940
1.333	0.5	0.1	0.25	-0.119	0.023	1.013	0.938
1.333	0.5	0.1	0.5	-0.106	0.023	0.966	0.942
1.333	0.5	0.1	0.75	-0.114	0.024	1.013	0.954
1.333	0.5	0.15	0	-0.055	0.023	1.077	0.950
1.333	0.5	0.15	0.25	-0.065	0.021	1.049	0.942
1.333	0.5	0.15	0.5	-0.058	0.022	1.023	0.954
1.333	0.5	0.15	0.75	-0.065	0.032	0.988	0.960
1.333	1	0.05	0	-0.024	0.019	0.914	0.966
1.333	1	0.05	0.25	-0.040	0.019	0.896	0.946
1.333	1	0.05	0.5	-0.080	0.019	0.940	0.958
1.333	1	0.05	0.75	-0.212	0.018	0.866	0.908
1.333	1	0.1	0	-0.116	0.022	0.982	0.928
1.333	1	0.1	0.25	-0.080	0.022	0.961	0.944
1.333	1	0.1	0.5	-0.082	0.023	1.086	0.966
1.333	1	0.1	0.75	-0.067	0.024	1.026	0.960
1.333	1	0.15	0	-0.078	0.023	0.970	0.920
1.333	1	0.15	0.25	-0.075	0.022	0.973	0.922
1.333	1	0.15	0.5	-0.074	0.022	1.058	0.956
1.333	1	0.15	0.75	-0.079	0.030	0.977	0.962
1.333	2	0.05	0	0.286	0.020	0.922	0.838
1.333	2	0.05	0.25	0.260	0.020	0.976	0.864
1.333	2	0.05	0.5	0.250	0.020	0.962	0.864
1.333	2	0.05	0.75	0.294	0.022	0.965	0.854
1.333	2	0.1	0	0.034	0.023	1.022	0.950
1.333	2	0.1	0.25	0.032	0.023	1.027	0.948
1.333	2	0.1	0.5	0.054	0.023	0.970	0.926
1.333	2	0.1	0.75	0.033	0.023	1.059	0.954
1.333	2	0.15	0	-0.108	0.023	1.018	0.914
1.333	2	0.15	0.25	-0.119	0.022	0.996	0.896
1.333	2	0.15	0.5	-0.119	0.022	0.986	0.900
1.333	2	0.15	0.75	-0.112	0.025	0.969	0.926

References

Hall, P. and Marron, J.S. (1990). On variance estimation in nonparametric regression. *Biometrika*, 77, 415-419.