Supplementary Material

TABLES

Table S1. Simulation scenarios.

Sc.	α	γ	θ, β	True Model	Covariates
1	$\alpha_1 = \alpha_2 = 0.16$	$\gamma_1 = \gamma_2 = 1.25$	$\theta = \ln(2)$ $\beta_1 = \ln(2)$	$S_Z(t) = exp\left[-(\alpha t)^{\gamma} e^{\theta I_{TRT} + \beta_1 Z_1}\right]$	$Z_1 \sim Unif(0,2)$ $X_1 \sim Unif(0,2)$
2*	$\alpha_1 = 0.18$ $\alpha_2 = 0.20$	$\gamma_1 = 1.50$ $\gamma_2 = 0.75$	$\beta_1 = \ln(2)$	$S_z(t) = exp\left[-\left(\alpha_g t\right)^{\gamma_g} e^{\beta_1 Z_1}\right], g = 1,2$	$Z_1 \sim Unif(0,2)$ $X_1 \sim Unif(0,2)$
3*	$\alpha_1 = 0.18$ $\alpha_2 = 0.28$	$\gamma_1 = 1.25$ $\gamma_2 = 1.65$	$\beta_1 = \ln(2)$	$S_z(t) = exp\left[-\left(\alpha_g t\right)^{\gamma_g} e^{\beta_1 Z_1}\right], g = 1,2$	$Z_1 \sim Unif(0,2)$ $X_1 \sim Unif(0,2)$
4	$\alpha_1 = \alpha_2 = 0.16$	$\gamma_1 = \gamma_2 = 1.25$	$\theta = \ln(1.75)$ $\beta_1 = \ln(1.33)$ $\beta_2 = \ln(1.5)$	$S_z(t) = exp\left[-(\alpha t)^{\gamma} e^{\theta\, I_{TRT} + \beta_1 Z_1 + \beta_2 Z_2}\right]$	$Z_1 \sim N(0,1)$ $Z_2 \sim Bernoulli\ (p = 0.5)$ $X_1 \sim Unif(0,2)$
5	$\alpha_1 = \alpha_2 = 0.16$	$\gamma_1 = \gamma_2 = 1.25$	$\theta = \ln(1.75)$ $\beta_1 = \ln(2)$ $\beta_2 = \ln(1.50)$ $\beta_3 = \ln(1.25)$ $\beta_4 = \ln(0.75)$ $\beta_5 = \ln(0.50)$	$S_z(t) = exp\left[-(\alpha t)^{\gamma} e^{\theta\, I_{TRT} + \beta_1 Z_1 + \cdots + \beta_5 Z_5}\right]$	$\{Z_1, \dots, Z_5\} \sim$ $MVN\left(\begin{pmatrix}1\\0\\0\\0\\0\end{pmatrix}, \begin{pmatrix}1 & 0 & 0 & 0 & 0\\ 0 & 1 & 0.1 & 0.2 & 0.3\\ 0 & 0.1 & 1 & 0.1 & 0.2\\ 0 & 0.2 & 0.1 & 1 & 0.1\\ 0 & 0.3 & 0.2 & 0.1 & 1\end{pmatrix}\right)$ $\{X_1, \dots, X_5\} \sim MVN(0, \Sigma)$

* Non-proportional hazards treatment effect;
I_{TRT} is the treatment group indicator; θ is the treatment effect for proportional hazards models
Z_j are the prognostic covariates with $\beta_j > 0$; X_j are unrelated covariates; Σ is same matrix as that for $Z_1, \dots, Z_5$

Table S2. Scenario 1: Proportional Hazards Treatment Effect
Cox Regression ($\theta = 0.6931$), Z_1 *prognostic*, X_1 *not prognostic*

N	Model	"Bias" $(\hat{\beta})$	ESE	ASE	Coverage Rate	Power
100	Unadj	-.0557	.2415	.2334	93.3%	78.7%
	Adj:					
	Z_1	.0111	.2437	.2374	94.3%	85.3%
	X_1	-.0498	.2462	.2354	93.6%	78.2%
	Z_1, X_1	.0169	.2476	.2397	94.3%	85.3%
130	Unadj	-.0493	.2066	.2042	93.3%	88.7%
	Adj:					
	Z_1	.0148	.2086	.2073	94.9%	93.2%
	X_1	-.0454	.2087	.2056	93.2%	88.9%
	Z_1, X_1	.0189	.2109	.2087	94.8%	93.1%
150	Unadj	-.0507	.1974	.1900	93.2%	91.9%
	Adj:					
	Z_1	.0139	.1990	.1926	94.8%	96.5%
	X_1	-.0465	.2000	.1911	93.1%	92.0%
	Z_1, X_1	.0185	.2013	.1938	94.5%	96.1%

ESE: empirical standard error; ASE: average model-based standard error
Unadj: unadjusted; Adj: Adjusted

Table S3. Scenario 2: Non-proportional Hazards Treatment Effect (Early Difference) Cox Regression (Z_1 *prognostic*, X_1 *not prognostic*)

N	Model	ESE	ASE	Power
100	Unadj	.2395	.2330	61.5%
	Adj:			
	Z_1	.2489	.2371	73.9%
	X_1	.2448	.2352	62.3%
	Z_1, X_1	.2539	.2394	73.6%
130	Unadj	.2054	.2038	72.4%
	Adj:			
	Z_1	.2140	.2067	83.0%
	X_1	.2077	.2052	72.9%
	Z_1, X_1	.2174	.2082	83.5%
150	Unadj	.1908	.1895	79.8%
	Adj:			
	Z_1	.1930	.1918	88.7%
	X_1	.1926	.1905	79.9%
	Z_1, X_1	.1947	.1930	89.2%

ESE: empirical standard error; ASE: average model-based standard error;
Unadj: unadjusted; Adj: Adjusted

Table S4. Scenario 3: Non-proportional Hazards Treatment Effect (Late Difference)
Cox Regression (Z_1 *prognostic*, X_1 *not prognostic*)

N	Model	ESE	ASE	Power
150	Unadj	.1873	.1867	62.6%
	Adj:			
	Z_1	.1873	.1887	69.9%
	X_1	.1891	.1877	62.9%
	Z_1, X_1	.1891	.1898	69.5%
200	Unadj	.1590	.1613	75.4%
	Adj:			
	Z_1	.1613	.1628	81.7%
	X_1	.1604	.1620	75.0%
	Z_1, X_1	.1628	.1635	81.1%
250	Unadj	.1435	.1440	84.4%
	Adj:			
	Z_1	.1456	.1452	89.2%
	X_1	.1445	.1445	84.3%
	Z_1, X_1	.1467	.1457	88.9%

ESE: empirical standard error; ASE: average model-based standard error;
Unadj: unadjusted; Adj: Adjusted

Table S5. Scenario 4: Proportional Hazards Treatment Effect
Cox Regression (θ=0.5596) ($Z_1,\ Z_2\ prognostic,\ X_1\ not\ prognostic$)

N	**Model**	**"Bias" $(\hat{\beta})$**	**ESE**	**ASE**	**Coverage Rate**	**Power**
200	Unadj	-.0279	.1797	.1819	95.1%	84.4%
	Adj:					
	Z_1	-.0082	.1819	.1829	95.4%	86.4%
	X_1	-.0258	.1808	.1826	95.1%	84.3%
	Z_1, X_1	-.0060	.1831	.1836	95.3%	86.2%
	Z_2	-.0156	.1812	.1828	95.3%	85.6%
	Z_2, X_1	-.0135	.1825	.1835	95.2%	85.6%
	Z_1, Z_2	.0058	.1839	.1838	95.4%	87.6%
	Z_1, Z_2, X_1	.0081	.1852	.1846	95.2%	87.4%

ESE: empirical standard error; ASE: average model-based standard error;
Unadj: unadjusted; Adj: Adjusted

FIGURES

Figure S1A. Scenario 5. ($\theta = \ln(1.75) = 0.5596$, $Z_1, \dots, Z_5$ prognostic, $X_1, \dots, X_5$ not prognostic)

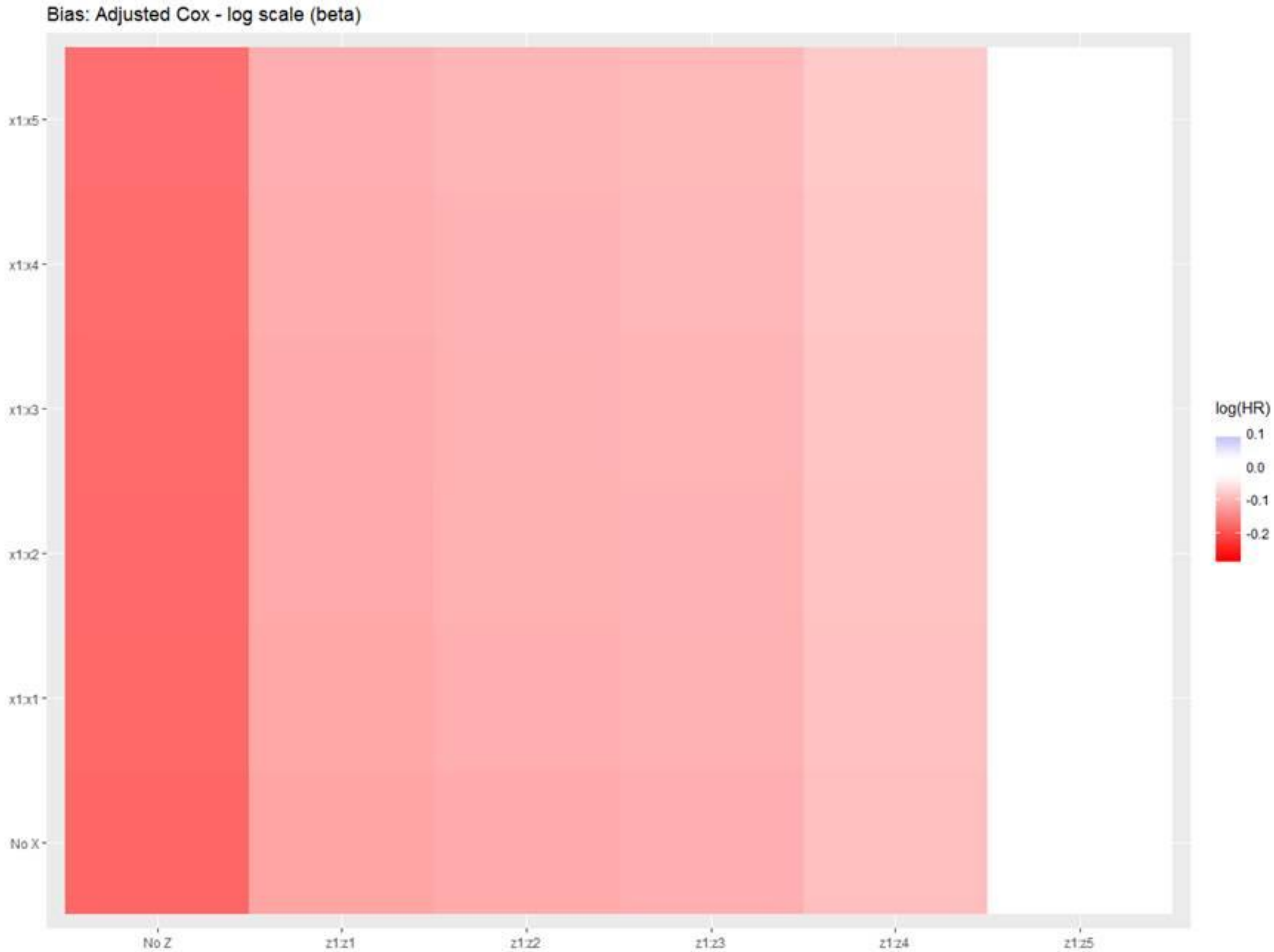

Figure S1B. Scenario 5. ($\theta = \ln(1.75) = 0.5596,\ Z_1, \dots, Z_5$ prognostic, $X_1, \dots, X_5$ not prognostic)

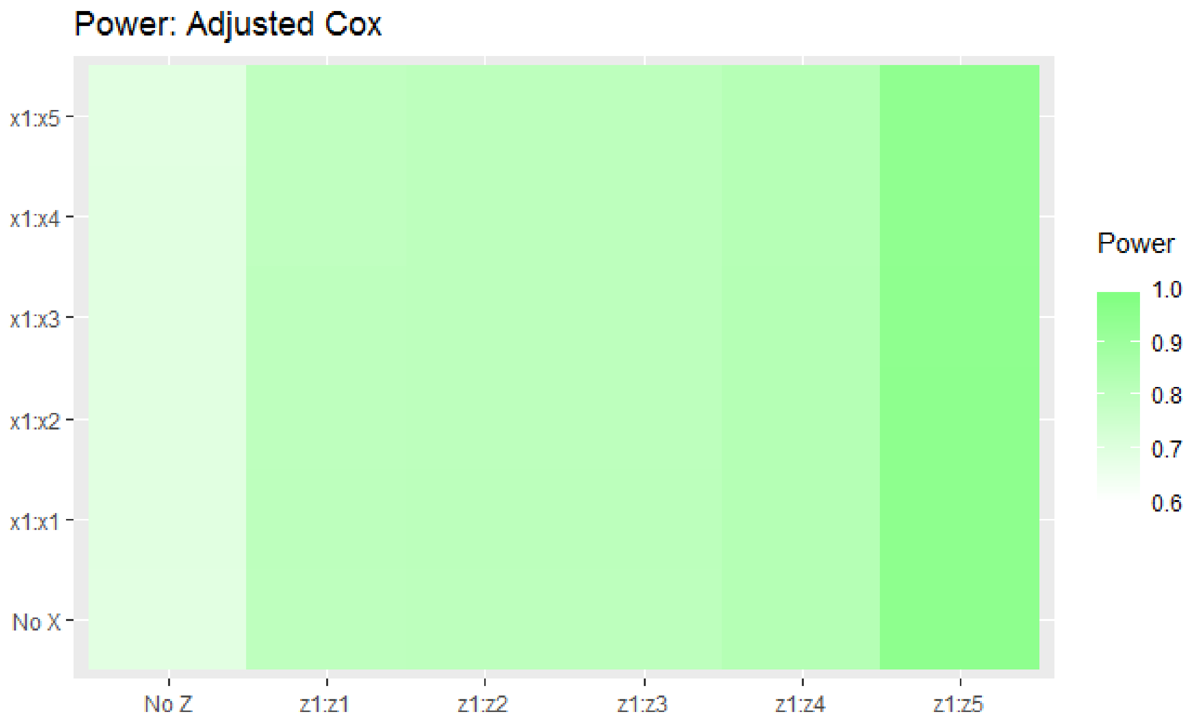

Figure S2. Scenario 5-revised. ($Z_1, \ldots, Z_5$ prognostic, $X_1, \ldots, X_5$ not prognostic). $\beta_1 = \ln(1.5)$, $\beta_2 = \ln(1.25)$, $\beta_3 = \ln(1.1)$, $\beta_4 = \ln(0.9)$, $\beta_5 = \ln(0.75)$