## Web-based Supplementary Materials for "Gene-based Association Analysis for Censored Traits Via Fixed Effect Functional Regressions"

## Appendix A. More Simulation Results

In this supplementary section, more simulation results are provided. When some causal variants are rare and some are common, the empirical type I error results are presented in Tables A.1, A.3, and A.5, and the empirical power comparison are presented in Figures A.1, A.3, and A.5. When all causal variants are rare, the empirical type I error results are presented in Tables A.2, A.4, and A.6, and the empirical power comparison are presented in Figures A.2, A.4, and A.6, and the empirical power comparison are presented in Figures A.2, A.4, and A.6. Three sets of parameters are used in the simulations:

- In Tables A.1 and A.2 and Figures A.1 and A.2, the order of B-spline basis was 4, and the number of B-spline basis functions was K = K<sub>β</sub> = 6; the number of Fourier basis functions was K = K<sub>β</sub> = 7.
- 2. In Tables A.3 and A.4 and Figures A.3 and A.4, the order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ .
- 3. In Tables A.5 and A.6 and Figures A.5 and A.6, the order of B-spline basis was 4, and the number of B-spline basis functions was K = K<sub>β</sub> = 12; the number of Fourier basis functions was K = K<sub>β</sub> = 13.

For the first two sets of parameters, 12 independent randomly seeded simulations were implemented to calculate the empirical type I error rates:  $10^5$  phenotype-genotype datasets in each simulation were generated to fit the proposed Cox models and to calculate the test statistics and related *p*-values for each combination of a sample size and a censoring scheme. The total number of simulations is  $1.2 \times 10^6$  in Tables A.1 and A.2. However, the computation of some simulations can not go through due to the failure of model convergence. Thus, the total number of simulations ranges from  $10^6$ (or 600,000) to  $1.2 \times 10^6$  in Table A.3 (or Table A.4). After the simulations were complete, an empirical type I error rate was calculated as the proportion of the total *p*-values which were smaller than a given  $\alpha$  level.

For the third set of parameters, 24 independent randomly seeded simulations were implemented to calculate the empirical type I error rates:  $10^5$  phenotype-genotype datasets in each simulation were generated to fit the proposed Cox models and to calculate the test statistics and related *p*-values for each combination of a sample size and a censoring scheme. However, the computation of some simulations can not go through due to the failure of model convergence. Thus, the total number of simulations ranges from 0 to  $2.4 \times 10^6$ . After the simulations were complete, an empirical type I error rate was calculated as the proportion of the total *p*-values which were smaller than a given  $\alpha$  level. If the total number of simulations is 0, no type I error rate is available.

The empirical power levels in Figures A.1 and A.2 are slightly lower than those of Figures 1 and 2. On the other hand, the empirical power levels in Figures Figures A.3, A.4, A.5, and A.6 are similar to those of Figures 1 and 2. Therefore, the range of parameters  $8 \le K = K_{\beta} \le 13$  should be fine to use in fitting the proposed Cox models, in terms of controlling type I error rates well and good power. Table A.1: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When All Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fourier basis functions was  $K = K_{\beta} = 7$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014)

Sample	The	Number	Nominal		Cox			
Size	Censoring	of	Level	Basis of both	<b>GVF</b> and $\beta(u)$	Basis of bet	a-Smooth Only	SKAT
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
			0.05	0.05296	0.05309	0.05296	0.05309	0.06914
1.000			$10^{-3}$	0.00111	0.00000	0.00200	0.00000	0.00182
	$\infty$	1,200,000	$10^{-4}$	0.00012	0.00012	0.00012	0.00012	0.00021
			$10^{-5}$	$1.166 \times 10^{-5}$	$1.58 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.58 \times 10^{-5}$	$2.75 \times 10^{-5}$
			0.05	0.05322	0.05346	0.05322	0.05346	0.07243
			$10^{-3}$	0.00114	0.00117	0.00114	0.00117	0.00185
	U(0, 10)	1,200,000	$10^{-4}$	0.00012	0.00013	0.00012	0.00013	0.00019
			$10^{-5}$	$1.08 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.08 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.50 \times 10^{-5}$
1,000			0.05	0.05360	0.05363	0.05360	0.05363	0.07733
			$10^{-3}$	0.00112	0.00000	0.00000	0.00000	0.00199
	U(0,5)	1,200,000	$10^{-4}$	0.00112	0.00120	0.00112	0.00120	0.00133
			$10^{-5}$	$1.50 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.50 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.83 \times 10^{-5}$
			0.05	0.05447	0.05441	0.05447	0.05441	0.08145
			$10^{-3}$	0.00447	0.00119	0.00447	0.00119	0.00146
	U(0,3)	1,200,000	$10^{-4}$	0.00125	0.00113	0.00125	0.00113	0.00130
			$10^{-5}$	$1.22 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.22 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.82 \times 10^{-5}$
			10	1.55 × 10	1.07 × 10	1.33 × 10	1.07 × 10	$1.03 \times 10$
			0.05	0.00101	0.00194	0.00101	0.00194	0.00213
	$\infty$	1,200,000	10 3	0.00111	0.00109	0.00111	0.00109	0.00142
			10 *	0.00011	0.00012	0.00011	0.00012	0.00016
			10-5	$1.58 \times 10^{-3}$	$1.42 \times 10^{-3}$	$1.58 \times 10^{-5}$	$1.42 \times 10^{-3}$	$2.08 \times 10^{-5}$
			0.05	0.05155	0.05173	0.05155	0.05173	0.06411
	U(0, 10)	1.200.000	10-3	0.00110	0.00107	0.00110	0.00107	0.00153
			10-4	0.00014	0.00013	0.00014	0.00013	0.00015
2.000			10-5	$1.58 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.58 \times 10^{-5}$	$1.17 \times 10^{-5}$	$2.33 \times 10^{-5}$
_,000			0.05	0.05169	0.05193	0.05169	0.05193	0.06785
	U(0.5)	1 200 000	$10^{-3}$	0.00109	0.00106	0.00109	0.00106	0.00156
	0 (0, 3)	1,200,000	$10^{-4}$	0.00012	0.00010	0.00012	0.00010	0.00016
			$10^{-5}$	$1.92 \times 10^{-5}$	$1.42 \times 10^{-5}$	$1.92 \times 10^{-5}$	$1.42 \times 10^{-5}$	$2.58 \times 10^{-5}$
	U(0,3)	1,200,000	0.05	0.05232	0.05174	0.05232	0.05174	0.07222
			$10^{-3}$	0.00113	0.00115	0.00113	0.00115	0.00164
			$10^{-4}$	0.00012	0.00012	0.00012	0.00012	0.00017
			$10^{-5}$	$1.25 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.25 \times 10^{-5}$
	$\infty$		0.05	0.05118	0.05148	0.05118	0.05148	0.05969
			$10^{-3}$	0.00102	0.00106	0.00102	0.00106	0.00137
		1,200,000	$10^{-4}$	0.00011	0.00010	0.00011	0.00010	0.00012
			$10^{-5}$	$9.17 \times 10^{-6}$	$7.50 \times 10^{-6}$	$9.17 \times 10^{-6}$	$7.50 \times 10^{-6}$	$1.67 \times 10^{-5}$
	U(0,10)		0.05	0.05126	0.05120	0.05126	0.05120	0.06066
			$10^{-3}$	0.00109	0.00103	0.00109	0.00103	0.00139
		1,200,000	$10^{-4}$	0.00011	0.00012	0.00011	0.00012	0.00016
			$10^{-5}$	$9.17 \times 10^{-6}$	$1.08 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.08 \times 10^{-5}$	$1.83 \times 10^{-5}$
3,000			0.05	0.05120	0.05131	0.05120	0.05131	0.06287
			$10^{-3}$	0.00120	0.00104	0.00120	0.00104	0.00201
	U(0,5)	1,200,000	10-4	0.00104	0.00104	0.00104	0.00104	0.00145
			$10^{-5}$	$1.17 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.83 \times 10^{-5}$
			10	0.05125	0.05196	0.05195	0.05196	0.06795
			10-3	0.00100	0.00106	0.00100	0.00106	0.00156
	U(0,3)	1,200,000	10-4	0.00104	0.00100	0.00104	0.00100	0.0012
			10	1.00012	$1.00 \times 10^{-5}$	1.00012	$1.00 \times 10^{-5}$	0.00010
				1.20 × 10 °	1.00 X 10 ~	1.20 × 10 °	1.00 × 10 ~	1.55 × 10 °
			0.05	0.05041	0.05061	0.05041	0.05061	0.05753
	$\infty$	1,200.000	10 0	0.00102	0.00106	0.00102	0.00106	0.00127
		, .,	10-4	0.00009	0.00010	0.00009	0.00010	0.00014
	L		10-5	$9.17 \times 10^{-6}$	$1.00 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.00 \times 10^{-5}$	$1.41 \times 10^{-5}$
			0.05	0.05076	0.05081	0.05076	0.05081	0.05863
	U(0, 10)	1.200.000	10-3	0.00105	0.00106	0.00105	0.00106	0.00131
			$10^{-4}$	0.00011	0.00012	0.00011	0.00012	0.00014
4,000			$10^{-5}$	$1.25 \times 10^{-5}$	$5.83 \times 10^{-6}$	$1.25 \times 10^{-5}$	$5.83 \times 10^{-6}$	$1.58 \times 10^{-5}$
1,000			0.05	0.05095	0.05088	0.05095	0.05088	0.06078
	U(0.5)	1 200 000	$10^{-3}$	0.00101	0.00104	0.00101	0.00104	0.00133
		1,200,000	$10^{-4}$	0.00011	0.00011	0.00011	0.00011	0.00012
			$10^{-5}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$1.58 \times 10^{-5}$
			0.05	0.05133	0.05106	0.05133	0.05106	0.06455
		1 200 000	$10^{-3}$	0.00105	0.00105	0.00105	0.00105	0.00136
		1,200,000	$10^{-4}$	0.00011	0.00011	0.00011	0.00011	0.00014
			$10^{-5}$	$5.00 \times 10^{-6}$	$6.67 \times 10^{-6}$	$5.00 \times 10^{-6}$	$6.67 \times 10^{-6}$	$1.75 \times 10^{-5}$

Table A.2: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When Only Rare Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fourier basis functions was  $K = K_{\beta} = 7$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014).

Sample	The	Number	Nominal		Cox			
Size	Censoring	of	Level	Basis of bot	<b>h GVF</b> and $\beta(u)$	Basis of bet	a-Smooth Only	SKAT
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
			0.05	0.05393	0.05425	0.05393	0.05425	0.07166
1,000			$10^{-3}$	0.00120	0.00117	0.00120	0.00117	0.00196
	$\infty$	1,200,000	$10^{-4}$	0.00013	0.00012	0.00013	0.00012	0.00022
			$10^{-5}$	$1.17 \times 10^{-5}$	$6.67 \times 10^{-6}$	$1.17 \times 10^{-5}$	$6.67 \times 10^{-6}$	$2.75 \times 10^{-5}$
			0.05	0.05461	0.05480	0.05461	0.05480	0.07489
			$10^{-3}$	0.00115	0.00118	0.00115	0.00118	0.00200
	U(0, 10)	1,200,000	$10^{-4}$	0.00013	0.00014	0.00013	0.00014	0.00022
			$10^{-5}$	$1.50 \times 10^{-5}$	$1.92 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.92 \times 10^{-5}$	$1.58 \times 10^{-5}$
			0.05	0.05610	0.05561	0.05610	0.05561	0.08054
			$10^{-3}$	0.00010	0.00123	0.00010	0.00001	0.00001
	U(0,5)	1,200,000	$10^{-4}$	0.00120	0.00125	0.00120	0.00125	0.00210
			$10^{-5}$	$1.33 \times 10^{-5}$	$1.75 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.75 \times 10^{-5}$	$2.33 \times 10^{-5}$
			0.05	0.05917	0.05808	0.05918	0.05808	0.08462
			$10^{-3}$	0.00317	0.00000	0.00318	0.00000	0.00402
	U(0,3)	1,200,000	$10^{-4}$	0.00134	0.00134	0.00134	0.0015	0.00203
			$10^{-5}$	$1.50 \times 10^{-5}$	$1.42 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.42 \times 10^{-5}$	$2.00 \times 10^{-5}$
			10	0.05106	0.05208	0.05106	0.05208	2.00 × 10
			10-3	0.00104	0.03208	0.03190	0.05208	0.00348
	$\infty$	1,200,000	10 *	0.00104	0.00102	0.00104	0.00102	0.00130
			10 -	0.00012	0.00012	0.00012	0.00012	0.00016
			10-5	$1.58 \times 10^{-5}$	9.17 × 10 <sup>-0</sup>	$1.58 \times 10^{-5}$	$9.17 \times 10^{-6}$	$2.08 \times 10^{-3}$
			0.05	0.05254	0.05238	0.05254	0.05238	0.06542
	U(0, 10)	1.200.000	10-3	0.00109	0.00111	0.00109	0.00111	0.00161
	- (-) -)	,,	10-4	0.00012	0.00013	0.00012	0.00013	0.00017
2,000			$10^{-5}$	$1.75 \times 10^{-5}$	$1.42 \times 10^{-5}$	$1.75 \times 10^{-5}$	$1.42 \times 10^{-5}$	$2.33 \times 10^{-5}$
,			0.05	0.05310	0.05315	0.05310	0.05315	0.06932
	U(0,5)	1.200.000	$10^{-3}$	0.00115	0.00109	0.00115	0.00109	0.00163
	0 (0,0)	1,200,000	10-4	0.00011	0.00012	0.00011	0.00012	0.00017
			$10^{-5}$	$1.00 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.25 \times 10^{-5}$	$2.75 \times 10^{-5}$
	U(0,3)	1,200,000	0.05	0.05469	0.05404	0.05469	0.05404	0.07463
			$10^{-3}$	0.00122	0.00117	0.00122	0.00117	0.00173
			$10^{-4}$	0.00013	0.00013	0.00013	0.00013	0.00018
			$10^{-5}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.08 \times 10^{-5}$
	$\infty$		0.05	0.05182	0.05191	0.05182	0.05191	0.06058
		1 200 000	$10^{-3}$	0.00106	0.00108	0.00106	0.00108	0.00140
		1,200,000	$10^{-4}$	0.00011	0.00010	0.00011	0.00010	0.00015
			$10^{-5}$	$6.67 \times 10^{-6}$	$8.33 \times 10^{-6}$	$6.67 \times 10^{-6}$	$8.33 \times 10^{-6}$	$1.50 \times 10^{-5}$
	U(0, 10)		0.05	0.05151	0.05144	0.05151	0.05144	0.06161
		1 200 000	$10^{-3}$	0.00104	0.00104	0.00104	0.00104	0.00146
		1,200,000	$10^{-4}$	0.00010	0.00011	0.00010	0.00011	0.00015
			$10^{-5}$	$1.50 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.33 \times 10^{-5}$	$2.00 \times 10^{-5}$
3,000			0.05	0.05230	0.05190	0.05230	0.05190	0.06425
		1,200,000	$10^{-3}$	0.00112	0.00110	0.00112	0.00110	0.00150
	U(0,5)		$10^{-4}$	0.00010	0.00012	0.00010	0.00012	0.00019
			$10^{-5}$	$1.25 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.92 \times 10^{-5}$
			0.05	0.05353	0.05279	0.05353	0.05279	0.06887
		1,200,000	$10^{-3}$	0.00111	0.00108	0.00111	0.00108	0.00159
	U(0,3)		$10^{-4}$	0.00011	0.0010	0.00011	0.0010	0.00015
			10-5	$1.58 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.58 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.33 \times 10^{-5}$
			0.05	0.05100	0.05120	0.05100	0.05130	0.05825
			$10^{-3}$	0.00109	0.00100	0.03109	0.00108	0.00020
	$\infty$	1,200,000	10 - 4	0.00104	0.00108	0.00104	0.00108	0.00130
			10	1.58 × 10=5	1.50 × 10=5	$1.58 \times 10^{-5}$	1.50 × 10=5	$1.02 \times 10^{-5}$
			10 *	$1.38 \times 10^{-5}$	1.50 × 10 °	1.58 × 10 °	1.50 × 10 °	1.83 × 10 °
			0.05	0.05117	0.05089	0.00117	0.05089	0.05932
	U(0, 10)	1,200,000	10 0	0.00102	0.00113	0.00102	0.00111	0.00130
			10-4	0.00010	0.00011	0.00010	0.00011	0.00015
4,000			10=5	$1.42 \times 10^{-3}$	$1.42 \times 10^{-3}$	$1.42 \times 10^{-3}$	$1.42 \times 10^{-3}$	$1.42 \times 10^{-3}$
,			0.05	0.05171	0.05150	0.05171	0.05150	0.06173
	U(0,5)	1,200.000	10-3	0.00103	0.00106	0.00103	0.00106	0.00138
	- (-,-)	,,	10-4	0.00010	0.00012	0.00010	0.00012	0.00012
			10-5	$1.08 \times 10^{-5}$	$8.33 \times 10^{-6}$	$1.08 \times 10^{-5}$	$8.33 \times 10^{-6}$	$1.17 \times 10^{-5}$
			0.05	0.05215	0.05207	0.05215	0.05207	0.06585
	U(0,3)	1,200.000	10-3	0.00111	0.00108	0.00111	0.00108	0.00140
			10-4	0.00010	0.00010	0.00010	0.00010	0.00014
			$10^{-5}$	$1.33 \times 10^{-5}$	$1.50 \times 10^{-5}$	$  1.33 \times 10^{-5}$	$1.50 \times 10^{-5}$	$  1.58 \times 10^{-5}$



Figure A.1: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80%Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fourier basis functions was  $K = K_{\beta} = 7$ .



Figure A.2: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fourier basis functions was  $K = K_{\beta} = 7$ .

Table A.3: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When All Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014)

Sample	The	Number	Nominal Cox FR LRT Statistics					Cox
Size	Censoring		of Level		Basis of bot	h GVF and $\beta(u)$	Basis of bet	a-Smooth Only
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
			0.05	0.05415	0.05442	0.05415	0.05442	0.06914
	$\infty$		$10^{-3}$	0.00116	0.00115	0.00116	0.00115	0.00182
		1,200,000	$10^{-4}$	0.00013	0.00012	0.00013	0.00012	0.00021
1.000			$10^{-5}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$2.75 \times 10^{-5}$
			0.05	0.05475	0.05471	0.05475	0.05471	0.07243
			$10^{-3}$	0.00119	0.00119	0.00119	0.00119	0.00185
	U(0, 10)	1,200,000	$10^{-4}$	0.00013	0.00013	0.00013	0.00013	0.00019
			10-5	$1.33 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.33 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.50 \times 10^{-5}$
1,000			0.05	0.05555	0.05485	0.05556	0.05485	0.07733
		1 200 000	$10^{-3}$	0.00122	0.00116	0.00122	0.00116	0.00199
	U(0,5)	1,200,000	$10^{-4}$	0.00013	0.00011	0.00014	0.00011	0.00021
			$10^{-5}$	$1.67 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.75 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.83 \times 10^{-5}$
			0.05	0.05758	0.05629	0.05761	0.05629	0.08144
	U(0,2)	1 100 000	$10^{-3}$	0.00131	0.00126	0.00131	0.00126	0.00195
	U(0,3)	1,100,000	$10^{-4}$	0.00015	0.00014	0.00015	0.00014	0.00021
			$10^{-5}$	$1.91 \times 10^{-5}$	$1.45 \times 10^{-5}$	$1.91 \times 10^{-5}$	$1.45 \times 10^{-5}$	$1.91 \times 10^{-5}$
			0.05	0.05263	0.05252	0.05263	0.05252	0.06213
	~	1 200 000	$10^{-3}$	0.00112	0.00110	0.00112	0.00110	0.00142
		1,200,000	$10^{-4}$	0.00011	0.00013	0.00011	0.00013	0.00016
			$10^{-5}$	$9.17 \times 10^{-6}$	$1.42 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.42 \times 10^{-5}$	$2.08 \times 10^{-5}$
			0.05	0.05220	0.05215	0.05220	0.05215	0.06411
	U(0,10)	1 200 000	$10^{-3}$	0.00112	0.00108	0.00112	0.00108	0.00153
		1,200,000	$10^{-4}$	0.00012	0.00013	0.00012	0.00013	0.00015
2.000			$10^{-5}$	$1.75 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.75 \times 10^{-5}$	$1.33 \times 10^{-5}$	$2.33 \times 10^{-5}$
2,000			0.05	0.05298	0.05271	0.05298	0.05271	0.06786
	U(0,5)	1 100 000	10-3	0.00115	0.00107	0.00115	0.00107	0.00155
		,,	10-4	0.00013	0.00010	0.00013	0.00010	0.00016
			10-5	$1.36 \times 10^{-5}$	$1.27 \times 10^{-5}$	$1.36 \times 10^{-5}$	$1.27 \times 10^{-5}$	$2.72 \times 10^{-3}$
	U(0,3)	1,200,000	0.05	0.05381	0.05294	0.05382	0.05294	0.07222
			10-3	0.00121	0.00113	0.00121	0.00113	0.00164
			10 4	0.00014	0.00012	0.00014	0.00012	0.00017
			10 0	$1.33 \times 10^{-5}$	1.33 × 10 °	1.33 × 10 °	1.33 × 10 °	1.25 × 10 °
			0.05	0.05152	0.05148	0.05152	0.05148	0.05969
		1,200,000	$10^{-4}$	0.00107	0.00106	0.00107	0.00106	0.00137
		, ,	10 -	0.00012	0.00012	0.00012	0.00012	0.00012
			0.05	1.00 × 10	0.05144	1.00 × 10	0.05144	0.06066
	U(0, 10)	1,200,000	$10^{-3}$	0.00105	0.00144	0.00105	0.00144	0.00000
			$10^{-4}$	0.00103	0.00100	0.00103	0.00100	0.00139
			$10^{-5}$	$5.83 \times 10^{-6}$	$1.08 \times 10^{-5}$	$5.83 \times 10^{-6}$	$1.08 \times 10^{-5}$	$1.83 \times 10^{-5}$
3,000			0.05	$0.00 \times 10$ 0.05194	0.05131	0.05194	0.05131	0.06287
		1,200,000	$10^{-3}$	0.00109	0.00101	0.00109	0.00105	0.00145
	U(0,5)		$10^{-4}$	0.00009	0.00011	0.00009	0.00011	0.00018
			$10^{-5}$	$9.17 \times 10^{-6}$	$1.00 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.00 \times 10^{-5}$	$1.83 \times 10^{-5}$
			0.05	0.05273	0.05195	0.05273	0.05195	0.06735
	TT(O_O)	1 202 202	$10^{-3}$	0.00108	0.00110	0.00108	0.00110	0.00156
	U(0,3)	1,200,000	10-4	0.00012	0.00011	0.00012	0.00011	0.00016
			$10^{-5}$	$1.58 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.58 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.33 \times 10^{-5}$
			0.05	0.05087	0.05103	0.05087	0.05103	0.05753
		1 200 000	$10^{-3}$	0.00104	0.00106	0.00104	0.00106	0.00127
	$\infty$	1,200,000	$10^{-4}$	0.00010	0.00009	0.00010	0.00009	0.00014
			$10^{-5}$	$1.00 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.42 \times 10^{-5}$
			0.05	0.05109	0.05106	0.05109	0.05106	0.05863
	U(0, 10)	1 200 000	$10^{-3}$	0.00105	0.00108	0.00105	0.00108	0.00131
		1,200,000	$10^{-4}$	0.00014	0.00012	0.00014	0.00012	0.00014
4 000			$10^{-5}$	$8.33 \times 10^{-6}$	$6.67 \times 10^{-6}$	$8.33 \times 10^{-6}$	$6.67 \times 10^{-6}$	$1.58 \times 10^{-5}$
4,000			0.05	0.05148	0.05124	0.05148	0.05124	0.06078
	U(0.5)	1 200 000	$10^{-3}$	0.00106	0.00106	0.00106	0.00106	0.00133
		1,200,000	$10^{-4}$	0.00011	0.00011	0.00011	0.00011	0.00012
			$10^{-5}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$1.58 \times 10^{-5}$
			0.05	0.05198	0.05153	0.05198	0.05153	0.06455
	U(0,3)	1.200.000	$10^{-3}$	0.00108	0.00109	0.00108	0.00109	0.00136
			10-4	0.00010	0.00010	0.00010	0.00010	0.00014
			$  10^{-5}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$  1.75 \times 10^{-5}$

Table A.4: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When Only Rare Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014).

Sample	The	Number	Nominal		Cox			
Size	Censoring	of	Level	Basis of bot	<b>h GVF</b> and $\beta(u)$	Basis of bet	a-Smooth Only	SKAT
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
[			0.05	0.05602	0.05629	0.05602	0.05629	0.07169
1,000			$10^{-3}$	0.00002	0.00023	0.00002	0.00023	0.07105
	$\infty$	1,100,000	$10^{-4}$	0.00120	0.00128	0.00120	0.00128	0.00135
			$10^{-5}$	0.00013	$1.72 \times 10^{-5}$	0.00013	$1.72 \times 10^{-5}$	$2.62 \times 10^{-5}$
			10	9.09 × 10	1.72 X 10	9.09 × 10	1.72 X 10	2.05 × 10
			0.00	0.00105	0.00070	0.00739	0.00070	0.07505
	U(0, 10)	900,000	10 °	0.00125	0.00127	0.00125	0.00127	0.00194
			10 1	0.00013	0.00014	0.00013	0.00014	0.00021
			10 0	1.78 × 10 °	1.89 × 10 °	1.78 × 10 °	1.89 × 10 °	$1.56 \times 10^{-6}$
			0.05	0.05950	0.05819	0.05951	0.05819	0.08059
	U(0,5)	800,000	10-3	0.00136	0.00129	0.00136	0.00129	0.00219
		,	10-4	0.00016	0.00015	0.00016	0.00015	0.00022
			10-5	$2.25 \times 10^{-5}$	$1.63 \times 10^{-5}$	$2.25 \times 10^{-3}$	$1.63 \times 10^{-3}$	$2.38 \times 10^{-3}$
			0.05	0.06461	0.06237	0.06476	0.06237	0.08430
	U(0,3)	600.000	10-3	0.00162	0.00154	0.00163	0.00154	0.00205
			10-4	0.00018	0.00016	0.00018	0.00016	0.00020
			$10^{-5}$	$1.67 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.67 \times 10^{-5}$	$2.00 \times 10^{-5}$	$2.00 \times 10^{-5}$
			0.05	0.05305	0.05299	0.05305	0.05299	0.06348
	$\sim$	1 200 000	$10^{-3}$	0.00109	0.00108	0.00109	0.00108	0.00150
		1,200,000	$10^{-4}$	0.00011	0.00011	0.00011	0.00011	0.00016
			$10^{-5}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$1.17 \times 10^{-5}$	$9.17 \times 10^{-6}$	$2.08 \times 10^{-5}$
			0.05	0.05369	0.05344	0.05369	0.05344	0.06542
	U(0, 10)	1 200 000	$10^{-3}$	0.00117	0.00118	0.00117	0.00118	0.00161
	0 (0, 10)	1,200,000	$10^{-4}$	0.00014	0.00011	0.00014	0.00011	0.00017
2 000			$10^{-5}$	$2.00 \times 10^{-5}$	$1.08 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.08 \times 10^{-5}$	$2.33 \times 10^{-5}$
2,000			0.05	0.05498	0.05432	0.05498	0.05432	0.06926
		1 100 000	$10^{-3}$	0.00123	0.00115	0.00123	0.00115	0.00163
	U(0,5)	1,100,000	$10^{-4}$	0.00013	0.00012	0.00013	0.00012	0.00017
			$10^{-5}$	$1.27 \times 10^{-5}$	$1.27 \times 10^{-5}$	$1.27 \times 10^{-5}$	$1.27 \times 10^{-5}$	$2.81 \times 10^{-5}$
	U(0,3)		0.05	0.05778	0.05608	0.05778	0.05608	0.07419
			$10^{-3}$	0.00126	0.00116	0.00126	0.00116	0.00159
		100,000	$10^{-4}$	0.00017	0.00011	0.00017	0.00011	0.00012
			$10^{-5}$	$1.00 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$2.00 \times 10^{-5}$	0
	$\infty$		0.05	0.05243	0.05223	0.05243	0.05223	0.06058
			$10^{-3}$	0.00110	0.00108	0.00110	0.00108	0.00140
		1,200,000	$10^{-4}$	0.00110	0.00100	0.00110	0.00100	0.00140
			$10^{-5}$	$1.08 \times 10^{-5}$	$5.83 \times 10^{-6}$	$1.08 \times 10^{-5}$	$5.83 \times 10^{-6}$	$1.50 \times 10^{-5}$
	U(0, 10)		0.05	0.05232	0.05180	0.05232	0.05180	0.06161
			$10^{-3}$	0.00202	0.00100	0.00202	0.00100	0.00101
		1,200,000	10 - 4	0.00103	0.00109	0.00109	0.00109	0.00140
			$10^{-5}$	$1.42 \times 10^{-5}$	$1.17 \times 10^{-5}$	$1.42 \times 10^{-5}$	$1.17 \times 10^{-5}$	$2.00 \times 10^{-5}$
3,000			10	1.42 × 10	1.17 × 10	1.42 × 10	1.17 × 10	2.00 × 10
		1,200,000	10-3	0.00000	0.05250	0.00000	0.05250	0.00425
	U(0,5)		10-4	0.00111	0.00110	0.00111	0.00110	0.00130
			10-5	0.00012	1.05 × 10=5	0.00012	0.00011	0.00019
			10 *	1.07 × 10 °	1.25 × 10 °	1.07 × 10 °	1.25 × 10 °	1.92 × 10 °
			0.05	0.05563	0.05398	0.05564	0.05398	0.06887
	U(0,3)	1,200,000	10 0	0.00119	0.00117	0.00119	0.00117	0.00159
			10 1	0.00011	0.00011	0.00011	0.00011	0.00015
			10 0	1.17 × 10 °	2.50 × 10 °	1.17 × 10 °	$2.50 \times 10^{-6}$	1.33 × 10 °
			0.05	0.05161	0.05148	0.05161	0.05148	0.05825
	~	1 200 000	$10^{-3}$	0.00109	0.00111	0.00109	0.00111	0.00130
			10-4	0.00012	0.00013	0.00012	0.00013	0.00014
			10-5	$1.67 \times 10^{-5}$	$1.83 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.83 \times 10^{-5}$	$1.83 \times 10^{-5}$
			0.05	0.05168	0.05131	0.05168	0.05131	0.05932
	U(0,10)	1,200,000	$10^{-3}$	0.00103	0.00107	0.00103	0.00107	0.00130
		1,200,000	$10^{-4}$	0.00011	0.00010	0.00011	0.00010	0.00015
4 000			$10^{-5}$	$1.25 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.42 \times 10^{-5}$
-,000			0.05	0.05270	0.05227	0.05270	0.05227	0.06173
	U(0.5)	1 200 000	$10^{-3}$	0.00110	0.00108	0.00110	0.00108	0.00138
		1,200,000	$10^{-4}$	0.00010	0.00011	0.00010	0.00011	0.00012
			$10^{-5}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$8.33 \times 10^{-6}$	$7.50 \times 10^{-6}$	$1.17 \times 10^{-5}$
			0.05	0.05379	0.05326	0.05379	0.05326	0.06585
	U(0,3)	1 200 000	$10^{-3}$	0.00114	0.00112	0.00114	0.00112	0.00140
		1,200,000	$10^{-4}$	0.00012	0.00012	0.00012	0.00012	0.00014
			$10^{-5}$	$1.58 \times 10^{-5}$	$1.08 \times 10^{-5}$	$1.58 \times 10^{-5}$	$1.08 \times 10^{-5}$	$1.58 \times 10^{-5}$



Figure A.3: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80%Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ .



Figure A.4: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ .

Table A.5: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When All Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014)

Sample	The	Number	Nominal		Cox			
Size	Censoring	of	Level	Basis of both GVF and $\beta(u)$   Basis of beta-Smooth Only				SKAT
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
			0.05	0.05748	0.05719	0.05752	0.05719	0.06950
1.000			$10^{-3}$	0.00127	0.00127	0.00127	0.00127	0.00185
	$\infty$	900,000	$10^{-4}$	0.00013	0.00013	0.00013	0.00013	0.00021
			10-5	$1.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$2.67 \times 10^{-5}$
1,000			0.05	0.05906	0.05809	0.05911	0.05809	0.07252
		100.000	$10^{-3}$	0.00136	0.00142	0.00137	0.00142	0.00187
	U(0, 10)	100,000	$10^{-4}$	0.00015	0.00013	0.00015	0.00013	0.00015
			$10^{-5}$	$2.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.00 \times 10^{-5}$
			0.05	0.05390	0.05347	0.05390	0.05347	0.06203
		1 000 000	10-3	0.00116	0.00116	0.00116	0.00116	0.00146
	$\infty$	1,800,000	$10^{-4}$	0.00012	0.00012	0.00012	0.00012	0.00016
			10-4	0.00012	0.00012	0.00012	0.00012	0.00016
			$10^{-5}$	$1.88 \times 10^{-5}$	$1.38 \times 10^{-5}$	$1.88 \times 10^{-5}$	$1.38 \times 10^{-5}$	$2.11 \times 10^{-5}$
0.000			0.05	0.05463	0.05405	0.05464	0.05405	0.06406
2,000	U(0, 10)	000.000	$10^{-3}$	0.00121	0.00122	0.00121	0.00122	0.00152
	U(0, 10)	800,000	$10^{-4}$	0.00012	0.00010	0.00012	0.00010	0.00016
			$10^{-5}$	$1.25 \times 10^{-5}$	$8.75 \times 10^{-6}$	$1.25 \times 10^{-5}$	$8.75 \times 10^{-6}$	$1.75 \times 10^{-5}$
			0.05	0.05610	0.05516	0.05614	0.05516	0.06826
		100.000	$10^{-3}$	0.00119	0.00115	0.00119	0.00115	0.00150
	U(0,5)	400,000	$10^{-4}$	0.00013	0.00012	0.00013	0.00012	0.00018
			$10^{-5}$	$1.00 \times 10^{-5}$	0	$1.00 \times 10^{-5}$	0	$2.25 \times 10^{-5}$
	$\infty$	2,200,000	0.05	0.05270	0.05233	0.05270	0.05233	0.05952
			$10^{-3}$	0.00112	0.00110	0.00112	0.00110	0.00137
			$10^{-4}$	0.00010	0.00011	0.00010	0.00011	0.00013
			$10^{-5}$	$1.27 \times 10^{-5}$	$1.36 \times 10^{-5}$	$1.27 \times 10^{-5}$	$1.36 \times 10^{-5}$	$1.86 \times 10^{-5}$
	U(0, 10)	0 100 000	0.05	0.05289	0.05256	0.05289	0.05256	0.06040
			$10^{-3}$	0.00113	0.00111	0.00113	0.00111	0.00136
		2,100,000	$10^{-4}$	0.00011	0.00010	0.00011	0.00010	0.00014
2 000			$10^{-5}$	$1.14 \times 10^{-5}$	$1.19 \times 10^{-5}$	$1.14 \times 10^{-5}$	$1.19 \times 10^{-5}$	$1.38 \times 10^{-5}$
3,000			0.05	0.05411	0.05309	0.05412	0.05309	0.06313
	U(0.5)	1 000 000	$10^{-3}$	0.00117	0.00113	0.00117	0.00113	0.00145
	0 (0, 5)	1,900,000	$10^{-4}$	0.00012	0.00011	0.00012	0.00011	0.00016
			$10^{-5}$	$1.00 \times 10^{-5}$	$1.10 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.10 \times 10^{-5}$	$1.36 \times 10^{-5}$
		600,000	0.05	0.05641	0.05476	0.05646	0.05476	0.06780
	U(0,3)		$10^{-3}$	0.00119	0.00110	0.00119	0.00110	0.00155
			$10^{-4}$	0.00010	0.00011	0.00010	0.00011	0.00017
			$10^{-5}$	$1.00 \times 10^{-5}$	$5.00 \times 10^{-6}$	$1.00 \times 10^{-5}$	$5.00 \times 10^{-6}$	$1.33 \times 10^{-5}$
		2,200,000	0.05	0.05188	0.05172	0.05188	0.05172	0.05752
	$\sim$		$10^{-3}$	0.00107	0.00106	0.00107	0.00106	0.00127
	~		$10^{-4}$	0.00011	0.00012	0.00011	0.00012	0.00015
			$10^{-5}$	$1.40 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.40 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.13 \times 10^{-5}$
			0.05	0.05217	0.05182	0.05217	0.05182	0.05861
	U(0, 10)	2 400 000	$10^{-3}$	0.00114	0.00113	0.00114	0.00113	0.00132
	0 (0,10)	2,400,000	$10^{-4}$	0.00013	0.00011	0.00013	0.00011	0.00014
4,000			10 <sup>-5</sup>	$8.75 \times 10^{-6}$	$1.62 \times 10^{-5}$	$8.75 \times 10^{-6}$	$1.62 \times 10^{-5}$	$1.67 \times 10^{-5}$
1,000			0.05	0.05282	0.05225	0.05283	0.05225	0.06079
	U(0,5)	1 600 000	10-3	0.00110	0.00107	0.00110	0.00107	0.00134
		1,000,000	$10^{-4}$	0.00010	0.00012	0.00010	0.00012	0.00014
			10-5	$1.25 \times 10^{-5}$	$1.18 \times 10^{-5}$	$1.25 \times 10^{-5}$	$1.18 \times 10^{-5}$	$1.56 \times 10^{-5}$
			0.05	0.05435	0.05318	0.05437	0.05318	0.06459
	U(0,3)	3) 1 400 000	10-3	0.00124	0.00120	0.00125	0.00120	0.00138
			10-4	0.00013	0.00013	0.00013	0.00013	0.00014
			$  10^{-5}$	$1.14 \times 10^{-5}$	$  1.07 \times 10^{-5}$	$  1.14 \times 10^{-5}$	$1.07 \times 10^{-5}$	$1.85 \times 10^{-5}$

Table A.6: Empirical Type I Error Rates of the Cox FR LRT Statistics and Cox SKAT LRT, When Only Rare Variants in 6 kb Regions Were Used to Generate Genotype Data. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ . The results of Cox SKAT LRT were from R SeqMeta package by Chen et al. (2014).

Sample	The	Number	Nominal		Cox			
Size	Censoring	of	Level	Basis of bot	Basis of both GVF and $\beta(u)$ Basis of beta-Smooth Only			
n	Scheme	Simulations	α	B-sp Basis	Fourier Basis	B-sp Basis	Fourier Basis	LRT
			0.05	0.06052	0.06091	0.06060	0.06091	0.07265
1.000			0.01	0.01358	0.01313	0.01360	0.01313	0.017
	$\infty$	100,000	$10^{-3}$	0.00154	0.00156	0.00155	0.00156	0.00184
1		,	$10^{-4}$	0.00014	0.00014	0.00015	0.00014	0.00024
			$10^{-5}$	0	0	0	0	$1.00 \times 10^{-5}$
			0.05	0.05758	0.05677	0.05758	0.05677	0.06718
1,500			0.01	0.01242	0.01204	0.01242	0.01204	0.01525
	$\infty$	400,000	$10^{-3}$	0.00136	0.00130	0.00136	0.00130	0.00166
			$10^{-4}$	0.00015	0.00015	0.00015	0.00015	0.00017
			$10^{-5}$	$7.50 \times 10^{-6}$	$1.00 \times 10^{-5}$	$7.50 \times 10^{-6}$	$1.00 \times 10^{-5}$	$1.50 \times 10^{-5}$
			0.05	0.05535	0.05486	0.05535	0.05486	0.06322
2,000			0.01	0.01160	0.01132	0.01160	0.01132	0.01379
	$\infty$	1,300,000	$10^{-3}$	0.00124	0.00114	0.00124	0.00114	0.00154
			$10^{-4}$	0.00013	0.00013	0.00013	0.00013	0.00016
			$10^{-5}$	$1.00 \times 10^{-5}$	$1.69 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.69 \times 10^{-5}$	$2.00 \times 10^{-5}$
			0.05	0.05473	0.05421	0.05473	0.05421	0.06183
			0.01	0.01144	0.01108	0.01144	0.01108	0.01340
	$\infty$	1,700,000	$10^{-3}$	0.00117	0.00120	0.00117	0.00120	0.00150
			$10^{-4}$	0.00013	0.00013	0.00013	0.00013	0.00017
2 500			$10^{-5}$	$1.76 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.76 \times 10^{-5}$	$1.00 \times 10^{-5}$	$1.35 \times 10^{-5}$
2,000			0.05	0.05497	0.05451	0.05497	0.05451	0.06253
			0.01	0.01143	0.01124	0.01143	0.01124	0.01343
	U(0, 10)	600,000	$10^{-3}$	0.00125	0.00123	0.00125	0.00123	0.00143
			$10^{-4}$	0.00014	0.00015	0.00014	0.00015	0.00014
			10 <sup>-5</sup>	$1.67 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.67 \times 10^{-5}$	$1.83 \times 10^{-5}$
	∞	1,900,000	0.05	0.05393	0.05334	0.05393	0.05334	0.06031
			0.01	0.01102	0.01088	0.01102	0.01088	0.01291
			$10^{-3}$	0.00117	0.00113	0.00117	0.00113	0.00139
			10-4	0.00012	0.00011	0.00012	0.00011	0.00014
			10 <sup>-5</sup>	$8.42 \times 10^{-6}$	$1.05 \times 10^{-3}$	$8.42 \times 10^{-6}$	$1.05 \times 10^{-3}$	$1.63 \times 10^{-3}$
			0.05	0.05388	0.05329	0.05388	0.05329	0.06133
3 000	U(0, 10)	1 000 000	0.01	0.01121	0.01095	0.01121	0.01095	0.01296
3,000		1,000,000	10 8	0.00121	0.00117	0.00121	0.00117	0.00142
			10 -	0.00012	0.00013	0.00012	0.00013	0.00015
			10 *	1.40 × 10 °	2.40 × 10 °	1.40 × 10 °	2.40 × 10 °	1.40 × 10 °
			0.05	0.03474	0.03400	0.03474	0.03400	0.00370
	U(0.5)	200,000	10-3	0.01139	0.01159	0.01140	0.01139	0.01575
	0 (0, 3)		$10^{-4}$	0.00119	0.00120	0.00119	0.00120	0.00134
			$10^{-5}$	$2.00 \times 10^{-5}$	$1.50 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.50 \times 10^{-5}$	$1.50 \times 10^{-5}$
			0.05	$2.00 \times 10$ 0.05271	0.05262	$2.00 \times 10$ 0.05271	0.05262	0.05809
			0.03	0.03271	0.03202	0.03271	0.03202	0.03003
	~	2 100 000	$10^{-3}$	0.01010	0.01074	0.01010	0.01074	0.01210
	~	2,100,000	$10^{-4}$	0.00111	0.00101	0.00111	0.00101	0.00120
			$10^{-5}$	$1.33 \times 10^{-5}$	$1.14 \times 10^{-5}$	$1.33 \times 10^{-5}$	$1.14 \times 10^{-5}$	$1.47 \times 10^{-5}$
			0.05	0.05325	0.05289	0.05325	0.05289	0.05914
			0.01	0.01101	0.01074	0.01101	0.01074	0.01244
4,000	U(0.10)	1,500.000	$10^{-3}$	0.00111	0.00111	0.00111	0.00111	0.00131
,	0 (0,10)	1,500,000	10-4	0.00010	0.00011	0.00010	0.00011	0.00014
			10-5	$1.26 \times 10^{-5}$	$1.53 \times 10^{-5}$	$1.26 \times 10^{-5}$	$1.53 \times 10^{-5}$	$1.93 \times 10^{-5}$
			0.05	0.05456	0.05328	0.05456	0.05328	0.06154
			0.01	0.01103	0.01093	0.01103	0.01093	0.01265
	U(0,5)	600,000	$10^{-3}$	0.00122	0.00113	0.00122	0.00113	0.00134
		, í	$10^{-4}$	0.00012	0.00012	0.00012	0.00012	0.00014
			$10^{-5}$	$1.83 \times 10^{-5}$	$2.00 \times 10^{-5}$	$1.83 \times 10^{-5}$	$2.00 \times 10^{-5}$	$2.00 \times 10^{-5}$



Figure A.5: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of **2,000.** When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80%Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ . 13



Figure A.6: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ .

## Web-based Supplementary Materials for "Gene-based Association Analysis for Censored Traits Via Fixed Effect Functional Regressions"

## Appendix B. More Simulation Results

In this **Supplementary Materials**, Appendix B, three more settings were considered: 30%, 40%, and 50% of variants were causal in the 6 kb subregion. When some causal variants are rare and some are common,  $c = \log(1.75)$ ,  $\log(1.50)$ , and  $\log(1.25)$  if 30%, 40%, and 50% of the variants were causal, respectively. When all causal variants are rare,  $c = \log(2.5)$ ,  $\log(2.0)$ , and  $\log(1.5)$  if 30%, 40%, and 50% of the variants were causal, respectively.

In Figures B.1, B.2, B.3, B.4, B.5, B.6, Figures B.7, and B.8, the range of parameters K and  $K_{\beta}$  are from 6 to 13 as those in the main text and **Supplementary Materials**, Appendix A. If some causal variants are rare and some are common, the Cox FR LRT statistics have higher or similar power as Cox SKAT LRT. If all causal variants are rare, the Cox FR LRT statistics have higher or similar or similar power as Cox SKAT LRT except when 50%/50% causal variants had negative/positive effects. The Cox FR LRT statistics have higher power than Cox BT LRT in all the figures.

The power levels of Cox SKAT LRT are higher than those of Cox BT LRT except when 50% variants are causal and all causal variants had positive effects [graph (c1) in Figures B.1, B.2, B.3, B.4, B.5, B.6, B.7, and B.8]. This is consistent with the results of Chen et al. (2014).



Figure B.1: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fouriers basis functions was  $K = K_{\beta} = 7$ .



Figure B.2: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of Bspline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 6$ ; the number of Fourier basis functions was  $K = K_{\beta} = 7$ . 17



Figure B.3: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fouries basis functions was  $K = K_{\beta} = 9$ .



Figure B.4: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of Bspline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 8$ ; the number of Fourier basis functions was  $K = K_{\beta} = 9$ . 19



Figure B.5: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 10$ ; the number of Fourier basis functions was  $K = K_{\beta} = 11$ .



Figure B.6: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 10$ ; the number of Fourier basis functions was  $K = K_{\beta} = 11$ . 21



Figure B.7: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When Some Causal Variants are Rare and Some are Common and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ .



Figure B.8: The Empirical Power of the Cox FR LRT Statistics of the Cox Models (4) and (5) and Cox SKAT LRT and Cox BT LRT by Chen et al. (2014) at  $\alpha = 0.001$ , When All Causal Variants are Rare and a Sample Size of 2,000. When Neg pct = 0, All Causal Variants Had Positive Effects; When Neg pct = 20, 20%/80% Causal Variants Had Negative/Positive Effects; When Neg pct = 50, 50%/50% Causal Variants Had Negative/Positive Effects. The order of B-spline basis was 4, and the number of B-spline basis functions was  $K = K_{\beta} = 12$ ; the number of Fourier basis functions was  $K = K_{\beta} = 13$ . 23