

# Supplementary Materials for “Covariate-adjusted continuous biomarker assessment among subpopulations”

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Table S1: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.25, 0.75)^T$  by our proposed method and two existing methods (Pepe, 1998; Faraggi, 2003) are estimated and presented.

$n_1 = n_0$	Proposed method				Pepe (1998)				Faraggi (2003)			
	Bias	SD	SE	Cov	Bias	SD	SE	LCov	Bias	SD	SE	Cov
$\rho_0 = 0.95$												
100	252	1450	1530	95.7	302	1100	1050	93.0	1140	1050	959	73.7
200	155	1040	1080	95.1	119	749	728	93.5	1130	761	703	60.9
500	42	650	675	95.2	-24	466	449	94.1	1090	486	457	33.0
1000	20	453	471	95.0	-66	322	314	93.6	1090	342	325	9.5
5000	3	201	206	94.7	-95	143	139	88.8	1090	150	147	0.0
$\rho_0 = 0.90$												
100	165	1540	1600	97.5	281	1220	1140	93.0	900	1000	930	79.0
200	94	1090	1140	95.9	135	876	827	93.0	907	720	675	70.0
500	23	690	716	95.2	18	553	526	93.4	884	462	436	47.6
1000	8	483	501	94.9	-15	390	371	93.6	886	325	309	21.2
5000	5	215	221	95.2	-42	170	166	93.5	888	142	139	0.0
$\rho_0 = 0.85$												
100	92	1500	1560	98.0	253	1240	1130	93.0	541	921	860	85.0
200	55	1060	1110	96.5	158	901	838	92.7	553	655	619	80.6
500	3	682	704	94.7	64	582	547	93.3	539	420	398	70.0
1000	2	478	496	94.9	38	410	390	93.5	542	295	281	51.3
5000	2	211	219	95.6	20	180	175	93.8	546	129	126	1.7
$\rho_0 = 0.80$												
100	29	1400	1460	98.2	213	1160	1050	93.2	169	834	782	90.6
200	19	989	1040	96.5	143	859	793	93.0	185	588	559	90.0
500	-6	636	659	95.3	82	559	525	93.2	176	378	358	88.2
1000	-10	452	464	95.0	68	394	375	93.2	180	266	253	86.1
5000	3	200	206	95.4	60	174	170	92.4	184	116	114	62.3

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval.

Table S2: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.75, 0.25)^T$  by our proposed method and two existing methods (Pepe, 1998; Faraggi, 2003) are estimated and presented.

$n_1 = n_0$	Proposed method				Pepe (1998)				Faraggi (2003)			
	Bias	SD	SE	Cov	Bias	SD	SE	LCov	Bias	SD	SE	Cov
$\rho_0 = 0.95$												
100	326	1650	1660	94.4	1210	1210	1140	91.2	1090	1090	976	66.2
200	172	1170	1200	94.9	833	833	803	92.4	774	774	716	49.4
500	80	732	759	94.9	514	514	502	92.8	491	491	465	18.0
1000	32	519	532	94.7	363	363	351	93.1	349	349	331	2.4
5000	7	229	232	94.6	162	162	156	91.5	157	157	149	0.0
$\rho_0 = 0.90$												
100	144	1670	1690	97.3	1310	1310	1180	92.3	1000	1000	910	78.6
200	75	1190	1240	96.2	919	919	870	93.8	706	706	660	70.6
500	46	769	791	95.2	588	588	564	93.9	448	448	426	48.9
1000	20	548	561	94.5	418	418	399	93.6	319	319	302	23.4
5000	3	243	248	95.0	184	184	179	94.0	142	142	136	0.0
$\rho_0 = 0.85$												
100	-12	1540	1570	98.0	1260	1260	1110	93.5	898	898	820	88.9
200	21	1100	1140	96.3	899	899	838	93.8	626	626	590	88.3
500	14	698	728	95.4	575	575	553	93.9	398	398	378	85.2
1000	6	509	519	94.8	420	420	397	93.2	284	284	268	79.3
5000	0	224	230	94.8	187	187	179	91.5	126	126	120	38.0
$\rho_0 = 0.80$												
100	-74	1340	1390	97.5	1130	1130	993	93.4	797	797	730	92.2
200	-28	945	986	96.3	814	814	751	94.0	551	551	522	92.5
500	-14	599	623	95.5	524	524	499	93.3	351	351	333	90.6
1000	-1	438	440	93.9	385	385	359	92.3	251	251	236	85.2
5000	-2	192	196	94.7	170	170	163	88.0	111	111	106	55.6

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval.

Table S3: Estimation and inference results under the second simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.25, 0.75)^T$  by our proposed method and two existing methods (Pepe, 1998; Faraggi, 2003) are estimated and presented.

$n_1 = n_0$	Proposed method				Pepe (1998)				Faraggi (2003)			
	Bias	SD	SE	Cov	Bias	SD	SE	LCov	Bias	SD	SE	Cov
$\rho_0 = 0.95$												
100	535	1870	1920	91.6	638	1440	1300	92.0	232	1130	1040	92.3
200	292	1330	1360	91.4	339	998	934	92.9	127	793	746	92.8
500	68	797	845	90.9	125	609	583	94.0	41	489	470	93.1
1000	-1	564	589	92.1	65	426	411	93.7	18	346	332	93.4
5000	-61	252	258	90.8	12	189	184	93.8	4	153	149	93.4
$\rho_0 = 0.90$												
100	246	2100	2080	91.8	416	1670	1470	93.0	102	1480	1310	92.0
200	112	1580	1560	91.8	232	1210	1110	93.1	65	1070	983	92.6
500	14	996	1040	91.2	76	776	741	94.0	13	680	646	93.3
1000	-31	730	739	92.0	34	561	530	93.4	2	485	463	93.1
5000	-38	327	331	92.3	9	251	240	93.7	1	217	209	93.5
$\rho_0 = 0.85$												
100	10	1930	1920	91.2	186	1540	1350	92.8	-29	1410	1230	92.2
200	2	1440	1430	92.3	110	1120	1030	93.3	-2	1020	930	92.6
500	14	907	935	92.6	37	723	685	93.9	-14	648	613	93.2
1000	1	658	669	92.5	10	518	495	93.9	-12	461	440	93.1
5000	20	293	297	93.0	2	232	223	93.7	-1	206	199	93.2
$\rho_0 = 0.80$												
100	-105	1580	1640	93.3	48	1270	1140	93.2	-104	1190	1040	92.5
200	-45	1150	1180	92.6	36	928	851	94.1	-42	843	771	92.7
500	12	709	741	92.6	2	587	559	94.1	-27	535	505	93.0
1000	30	500	523	92.4	-4	419	402	93.6	-18	379	361	93.0
5000	46	224	230	91.3	1	187	181	93.4	-2	169	162	93.0

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval.

Table S4: Estimation and inference results under the second simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.75, 0.25)^T$  by our proposed method and two existing methods (Pepe, 1998; Faraggi, 2003) are estimated and presented.

$n_1 = n_0$	Proposed method				Pepe (1998)				Faraggi (2003)			
	Bias	SD	SE	Cov	Bias	SD	SE	LCov	Bias	SD	SE	Cov
$\rho_0 = 0.95$												
100	463	1300	1390	89.8	992	992	914	93.1	733	733	679	91.4
200	217	822	895	92.9	621	621	603	94.0	476	476	456	92.8
500	75	471	503	94.4	362	362	349	94.1	286	286	273	93.2
1000	39	317	339	95.3	245	245	241	94.2	198	198	191	93.1
5000	-8	140	142	94.7	109	109	104	93.5	89	88.6	83.8	92.7
$\rho_0 = 0.90$												
100	315	1790	1790	95.8	1460	1460	1280	92.8	1250	1250	1100	91.8
200	146	1270	1300	95.5	1010	1010	941	93.7	876	876	812	92.7
500	11	805	825	95.7	643	643	603	93.6	553	553	522	93.3
1000	0	569	584	95.3	446	446	431	93.9	391	391	373	93.2
5000	-44	256	258	94.6	202	202	192	93.4	178	178	168	92.7
$\rho_0 = 0.85$												
100	74	1960	1940	98.0	1610	1610	1400	92.9	1450	1450	1260	92.0
200	62	1440	1460	96.8	1160	1160	1060	93.4	1030	1030	949	92.6
500	-3	926	945	95.1	740	740	699	94.0	659	659	621	93.4
1000	17	656	674	95.1	521	521	501	93.9	469	469	446	93.4
5000	-14	302	301	93.9	241	241	226	92.9	214	214	202	92.7
$\rho_0 = 0.80$												
100	-76	1920	1910	98.7	1550	1550	1360	93.0	1430	1430	1240	92.1
200	26	1390	1410	97.0	1130	1130	1030	93.3	1020	1020	934	92.6
500	11	878	914	95.5	722	722	680	93.6	648	648	612	93.5
1000	46	631	647	94.6	507	507	488	94.0	462	462	439	93.5
5000	39	289	288	93.6	233	233	221	93.5	211	211	199	92.8

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval.

Table S5: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.50, 0.50)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	Proposed method					Inácio de Carvalho et al. (2013)				
	Bias (SD)	SE	Cov	Time <sub>CI</sub>	Time <sub>CB</sub>	Bias (SD)	SE	Cov	Time <sub>CI</sub>	Time <sub>CB</sub>
$\rho_0 = 0.95$										
100	214.3 (1470)	1170	96.2	0.385	27	854.0 (1100)	1050	90.8	24.4	221
200	40.2 (984)	767	97.8	0.425	79	505.5 (790)	739	92.4	28.8	226
500	2.5 (683)	465	95.8	0.527	264	234.6 (559)	456	94.0	42.0	242
1000	14.4 (478)	325	95.6	0.785	743	138.9 (400)	325	95.4	62.3	267
5000	12.2 (203)	140	95.2	3.070	11453	72.1 (176)	147	95.4	228.8	460
$\rho_0 = 0.90$										
100	202.0 (1500)	1190	96.6	0.383	30	774.2 (1200)	1020	89.0	24.2	220
200	14.1 (1020)	806	97.6	0.419	87	438.0 (870)	742	92.0	28.6	227
500	7.3 (693)	492	96.2	0.530	231	182.3 (603)	477	95.2	41.7	242
1000	17.1 (501)	341	95.6	0.746	757	117.9 (450)	341	95.2	61.3	266
5000	10.9 (218)	149	96.0	2.921	11898	40.7 (191)	155	96.6	229.5	456
$\rho_0 = 0.85$										
100	131.0 (1510)	1110	97.8	0.379	30	593.4 (1160)	901	90.8	23.9	220
200	15.4 (1010)	771	97.4	0.417	80	328.1 (851)	672	92.6	28.5	227
500	13.3 (656)	474	96.4	0.535	232	138.1 (591)	445	94.8	41.3	243
1000	10.6 (519)	330	96.4	0.754	700	100.0 (461)	320	95.6	61.8	265
5000	10.7 (214)	145	95.0	3.020	11298	26.7 (190)	148	96.2	228.4	460
$\rho_0 = 0.80$										
100	100.0 (1470)	989	98.2	0.383	31	379.2 (1070)	763	90.8	24.1	221
200	4.2 (1000)	691	97.0	0.422	87	198.1 (782)	577	94.4	28.3	227
500	-3.6 (651)	425	95.2	0.545	269	83.6 (540)	388	95.0	40.7	241
1000	17.8 (506)	299	95.8	0.773	736	64.7 (430)	279	95.4	61.5	264
5000	8.6 (198)	130	95.6	3.030	11791	15.4 (178)	131	96.4	227.6	456

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Time<sub>CI</sub>, the averaged computational time of each iteration with second as the unit for confidence interval construction; Time<sub>CB</sub>, the averaged computational time of each iteration with second as the unit for confidence band construction.

Table S6: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.25, 0.25)^T$  and  $\mathbf{z} = (0.25, 0.75)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	$\mathbf{z} = (0.25, 0.25)^T$						$\mathbf{z} = (0.25, 0.75)^T$					
	Proposal			Inácio de Carvalho			Proposal			Inácio de Carvalho		
	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov
$\rho_0 = 0.95$												
100	370(1532)	1473	0.94	270(1070)	1131	0.94	160(1486)	1471	0.97	230(1137)	1149	0.98
200	180(1048)	1055	0.95	100(779)	842	0.99	130(1016)	1034	0.95	190(770)	856	0.98
500	100(543)	654	0.97	-13(488)	542	0.95	-59(606)	639	0.98	-1(485)	549	0.99
1000	-11(426)	467	0.98	-67(361)	390	0.96	60(438)	483	0.96	19(335)	407	0.98
5000	-11(191)	203	0.97	-6(166)	184	0.97	-1(202)	204	0.97	15(171)	187	0.96
$\rho_0 = 0.90$												
100	260(1585)	1505	0.94	110(1194)	1196	0.92	-92(1610)	1574	0.97	120(1225)	1256	0.95
200	200(1081)	1064	0.94	3(868)	891	0.98	98(1052)	1137	0.96	140(824)	938	0.96
500	46(686)	681	0.96	-91(546)	584	0.96	-85(631)	723	0.99	-36(532)	618	0.98
1000	1(476)	487	0.97	-140(409)	417	0.95	1(494)	492	0.95	3(401)	441	0.97
5000	-1(205)	214	0.92	-60(174)	192	0.97	-4(219)	225	0.97	-4(188)	200	0.95
$\rho_0 = 0.85$												
100	140(1467)	1468	0.98	-21(1184)	1156	0.92	-210(1403)	1578	0.98	21(1163)	1227	0.95
200	21(990)	1035	0.97	-43(859)	870	0.94	-69(1067)	1126	0.95	120(806)	912	0.97
500	-37(633)	684	0.98	-100(561)	582	0.95	-76(575)	724	0.98	-13(518)	618	0.98
1000	-29(496)	472	0.95	-130(430)	417	0.91	-13(505)	480	0.93	18(427)	439	0.97
5000	-12(209)	211	0.95	-68(179)	189	0.95	-6(212)	219	0.96	13(183)	200	0.99
$\rho_0 = 0.80$												
100	21(1458)	1386	0.97	-130(1109)	1079	0.92	-190(1420)	1524	0.97	-94(1054)	1137	0.93
200	-65(876)	976	0.97	-80(813)	808	0.95	-130(1029)	1056	0.95	55(750)	830	0.98
500	18(604)	656	0.96	-86(535)	548	0.96	-55(587)	677	0.98	-5(468)	574	0.98
1000	-25(456)	444	0.91	-110(420)	394	0.92	-54(485)	468	0.92	17(405)	406	0.97
5000	11(194)	197	0.96	-50(175)	179	0.95	4(182)	207	0.96	26(164)	187	0.98

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Inácio de Carvalho: the method by Inácio de Carvalho et al. (2013).

Table S7: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.75, 0.25)^T$  and  $\mathbf{z} = (0.75, 0.75)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	$\mathbf{z} = (0.75, 0.25)^T$						$\mathbf{z} = (0.75, 0.75)^T$					
	Proposal			Inácio de Carvalho			Proposal			Inácio de Carvalho		
	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov
$\rho_0 = 0.95$												
100	510(1694)	1704	0.98	610(1236)	1337	0.94	220(1558)	1712	0.98	610(1163)	1381	0.98
200	120(977)	1189	0.97	420(884)	1018	0.97	82(1017)	1217	0.97	490(928)	1048	0.96
500	130(714)	720	0.96	150(639)	654	0.95	-50(666)	750	0.98	220(560)	673	0.97
1000	-41(502)	539	0.96	4(430)	468	0.97	31(506)	523	0.96	130(450)	481	0.96
5000	49(243)	234	0.93	55(198)	215	0.95	57(213)	236	0.96	99(200)	222	0.96
$\rho_0 = 0.90$												
100	350(1582)	1701	0.95	390(1288)	1379	0.96	-24(1748)	1724	0.95	470(1253)	1415	0.98
200	140(1100)	1226	0.97	350(927)	1041	0.96	39(1189)	1314	0.96	460(997)	1089	0.97
500	41(702)	788	0.96	93(677)	692	0.95	-90(660)	818	0.99	190(620)	716	0.96
1000	-21(574)	560	0.93	-16(483)	508	0.97	-25(524)	569	0.96	140(524)	516	0.92
5000	48(242)	246	0.96	24(230)	229	0.96	44(250)	258	0.95	120(250)	240	0.9
$\rho_0 = 0.85$												
100	160(1388)	1558	0.97	150(1190)	1252	0.96	-210(1623)	1609	0.97	220(1152)	1270	0.98
200	160(1040)	1155	0.97	220(852)	929	0.96	79(1012)	1202	0.98	320(889)	958	0.97
500	20(632)	735	0.99	20(608)	641	0.95	-21(656)	742	0.99	110(575)	652	0.96
1000	-78(485)	522	0.96	-33(452)	470	0.97	-67(556)	534	0.96	99(485)	473	0.94
5000	38(231)	229	0.94	7(232)	214	0.91	43(251)	236	0.94	110(240)	221	0.9
$\rho_0 = 0.80$												
100	-51(1382)	1361	0.97	-52(1033)	1072	0.95	-250(1432)	1429	0.95	-24(975)	1072	0.98
200	110(930)	993	0.98	69(731)	775	0.97	63(909)	995	0.97	150(721)	780	0.97
500	-51(592)	635	0.98	-43(490)	550	0.98	-110(603)	634	0.98	8(484)	546	0.97
1000	-17(430)	457	0.96	-56(380)	400	0.97	-45(458)	461	0.96	29(395)	392	0.94
5000	27(198)	194	0.96	-6(207)	183	0.9	19(200)	194	0.93	74(197)	183	0.9

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Inácio de Carvalho: the method by Inácio de Carvalho et al. (2013).



Table S8: Estimation and inference results under the second simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.50, 0.50)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	Proposed method					Inácio de Carvalho et al. (2013)				
	Bias (SD)	SE	Cov	Time <sub>CI</sub>	Time <sub>CB</sub>	Bias (SD)	SE	Cov	Time <sub>CI</sub>	Time <sub>CB</sub>
$\rho_0 = 0.95$										
100	176.1 (1940)	1120	94.0	0.39	30	477.0 (1090)	888	97.2	24.3	216
200	29.0 (1270)	730	96.0	0.44	72	248.8 (782)	591	98.0	28.1	223
500	12.7 (821)	436	96.0	0.55	224	123.0 (516)	353	96.6	40.7	235
1000	-27.1 (572)	298	96.4	0.76	691	77.7 (375)	243	96.8	61.8	263
5000	-47.6 (258)	128	94.2	3.15	11439	44.2 (169)	113	96.6	226.5	450
$\rho_0 = 0.90$										
100	115.1 (2210)	1500	96.4	0.39	27	507.0 (1400)	1200	96.4	23.8	217
200	12.7 (1500)	1040	97.0	0.43	66	288.3 (1030)	839	96.8	28.1	223
500	-4.7 (1070)	652	96.0	0.53	246	164.4 (711)	520	95.2	40.6	238
1000	-39.1 (749)	449	96.8	0.74	679	110.2 (513)	364	96.8	60.7	260
5000	-52.8 (330)	197	94.0	2.96	11702	76.7 (230)	171	93.6	224.4	448
$\rho_0 = 0.85$										
100	173.2 (1980)	1510	98.0	0.39	30	413.0 (1340)	1170	96.0	23.2	219
200	51.3 (1410)	1050	96.6	0.43	65	250.8 (973)	824	96.8	27.7	223
500	70.0 (938)	651	95.4	0.53	245	158.3 (671)	516	94.2	40.4	237
1000	36.4 (657)	456	95.6	0.73	677	110.0 (479)	364	96.2	60.0	259
5000	15.3 (291)	200	94.2	3.20	11622	84.1 (212)	170	92.4	223.3	451
$\rho_0 = 0.80$										
100	140.0 (1570)	1330	98.4	0.39	28	296.2 (1130)	989	94.6	23.0	217
200	87.2 (1140)	916	97.0	0.44	65	191.0 (804)	701	96.0	27.8	223
500	91.3 (750)	558	95.8	0.53	240	132.1 (548)	442	94.4	39.5	235
1000	87.5 (517)	391	95.4	0.73	665	93.1 (387)	313	96.2	60.1	261
5000	72.6 (219)	169	92.4	3.43	11292	75.5 (171)	146	90.8	235.7	447

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Time<sub>CI</sub>, the averaged computational time of each iteration with second as the unit for confidence interval construction; Time<sub>CB</sub>, the averaged computational time of each iteration with second as the unit for confidence band construction.

Table S9: Estimation and inference results under the second simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.25, 0.25)^T$  and  $\mathbf{z} = (0.25, 0.75)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	$\mathbf{z} = (0.25, 0.25)^T$						$\mathbf{z} = (0.25, 0.75)^T$					
	Proposal			Inácio de Carvalho			Proposal			Inácio de Carvalho		
	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov
$\rho_0 = 0.95$												
100	332(678)	871	0.9	244(391)	428	0.98	159(1765)	1914	0.94	311(1111)	1199	1
200	160(387)	485	0.89	128(251)	267	0.98	98(1454)	1335	0.92	264(816)	893	0.98
500	134(289)	282	0.89	72(140)	160	0.98	80(781)	851	0.98	193(523)	570	0.96
1000	101(166)	171	0.9	45(114)	107	0.94	-42(564)	600	0.97	40(370)	386	0.99
5000	55(66)	67	0.82	13(47)	47	0.97	-60(282)	259	0.92	26(180)	185	0.97
$\rho_0 = 0.90$												
100	313(1225)	1353	0.91	294(789)	850	0.97	-67(2164)	2194	1	67(1426)	1556	0.99
200	113(826)	876	0.94	168(574)	603	0.99	-56(1644)	1609	0.96	153(1068)	1143	0.97
500	174(523)	549	0.94	134(367)	390	0.98	176(1136)	1115	0.96	201(698)	736	0.95
1000	120(374)	378	0.94	81(289)	271	0.93	-17(702)	760	0.97	13(502)	519	0.98
5000	59(176)	160	0.88	24(127)	125	0.95	-24(347)	331	0.92	31(243)	245	0.94
$\rho_0 = 0.85$												
100	276(1584)	1666	0.94	207(1071)	1169	0.96	-61(2012)	2047	1	-132(1373)	1487	0.97
200	35(999)	1208	0.98	131(811)	861	0.97	-47(1405)	1464	0.97	27(999)	1061	0.94
500	176(760)	753	0.94	155(541)	561	0.98	308(947)	925	0.91	151(655)	673	0.96
1000	97(597)	526	0.89	90(416)	397	0.92	41(611)	661	0.96	-12(468)	486	0.98
5000	7(247)	231	0.93	26(189)	183	0.96	25(307)	298	0.94	25(222)	226	0.93
$\rho_0 = 0.80$												
100	-47(1805)	1864	0.97	69(1210)	1350	0.96	59(1514)	1686	0.98	-240(1165)	1253	0.98
200	-100(1232)	1394	0.99	63(934)	998	0.96	-81(1131)	1185	0.97	-57(825)	867	0.94
500	92(890)	880	0.97	144(629)	647	0.98	215(705)	687	0.95	94(534)	540	0.98
1000	43(712)	619	0.9	81(478)	463	0.92	6(498)	521	0.96	-26(376)	396	0.99
5000	-38(286)	274	0.93	23(220)	214	0.98	64(222)	231	0.95	17(176)	182	0.94

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Inácio de Carvalho: the method by Inácio de Carvalho et al. (2013).

Table S10: Estimation and inference results under the first simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.75, 0.25)^T$  and  $\mathbf{z} = (0.75, 0.75)^T$  by our proposed method and an existing Bayesian method (Inácio de Carvalho et al. 2013) are estimated and presented. Results were summarized over 100 Monte Carlo iterations.

$n_1 = n_0$	$\mathbf{z} = (0.75, 0.25)^T$						$\mathbf{z} = (0.75, 0.75)^T$					
	Proposal			Inácio de Carvalho			Proposal			Inácio de Carvalho		
	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov	Bias (SD)	SE	Cov
$\rho_0 = 0.95$												
100	477(1341)	1419	0.96	-69(2408)	2186	0.93	288(640)	759	0.99	-3(1383)	1573	0.99
200	170(749)	926	0.98	-108(1549)	1810	0.97	176(397)	535	1	197(894)	1216	0.99
500	111(523)	511	0.94	24(1229)	1158	0.92	82(294)	318	0.97	110(734)	757	0.97
1000	68(336)	347	0.96	-92(783)	819	0.96	61(207)	225	0.95	6(468)	537	0.98
5000	-4(142)	142	0.95	0(353)	373	0.97	15(86)	104	1	19(194)	254	0.99
$\rho_0 = 0.90$												
100	328(1682)	1772	0.98	-99(1943)	2068	0.98	197(1125)	1244	0.98	-299(1390)	1610	0.99
200	178(1171)	1369	0.97	192(1402)	1609	1	177(731)	944	1	82(880)	1125	0.98
500	38(826)	838	0.96	42(1031)	1053	0.96	79(574)	584	0.95	48(706)	715	0.94
1000	11(536)	588	0.96	-19(648)	725	0.97	80(393)	419	0.97	-19(441)	514	0.98
5000	-39(242)	255	0.94	32(287)	325	0.98	20(166)	196	0.99	10(192)	239	0.99
$\rho_0 = 0.85$												
100	175(2007)	1905	0.98	-269(1605)	1661	0.94	-4(1346)	1430	0.97	-369(1100)	1278	0.98
200	188(1306)	1498	0.98	73(902)	1152	0.98	111(862)	1089	0.97	-5(674)	829	0.97
500	38(992)	952	0.93	78(679)	714	0.96	38(687)	685	0.95	5(522)	529	0.95
1000	44(644)	680	0.96	-26(463)	513	0.96	67(458)	491	0.96	-30(324)	381	0.98
5000	-17(287)	302	0.97	-6(194)	224	0.97	15(195)	230	1	2(145)	176	0.99
$\rho_0 = 0.80$												
100	-195(1903)	1871	0.94	-233(1254)	1271	0.95	-186(1366)	1414	0.98	-343(795)	927	0.99
200	148(1215)	1413	0.96	-12(585)	793	0.98	34(854)	1055	0.98	-51(473)	569	0.97
500	-30(883)	927	0.97	-30(484)	469	0.94	-4(681)	669	0.96	-17(351)	359	0.94
1000	143(588)	656	0.98	-47(304)	335	0.96	46(440)	478	0.97	-32(220)	259	0.96
5000	-11(282)	293	0.96	-47(128)	147	0.97	7(191)	223	0.99	-1(100)	119	0.99

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval; Inácio de Carvalho: the method by Inácio de Carvalho et al. (2013).

Table S11: Evaluation of the proposed method with monotonicity restoration under the first and second simulation setting. Specificity  $\phi_0(\mathbf{z})$  under controlled sensitivity level  $\rho_0$  at the covariate selection  $\mathbf{z} = (0.50, 0.50)^T$  by our proposed method with monotonization are estimated and presented. Results were summarized over 5000 Monte Carlo iterations.

$n_1 = n_0$	Setting 1				Setting 2			
	Bias	SD	SE	Cov	Bias	SD	SE	Cov
$\rho_0 = 0.95$								
100	291	1055	1129	95.0	219	1039	1067	93.9
200	142	706	779	96.1	119	665	733	95.1
500	48	434	470	95.8	7	404	432	96.3
1000	35	305	323	95.1	-28	283	297	95.9
5000	5	136	139	95.1	-48	125	128	93.8
$\rho_0 = 0.90$								
100	226	1073	1185	97.0	212	1374	1494	97.3
200	121	748	807	95.8	105	954	1041	96.8
500	41	457	492	95.9	-14	623	641	95.4
1000	30	329	343	95.0	-41	432	448	95.1
5000	4	147	150	95.1	-57	193	196	94.4
$\rho_0 = 0.85$								
100	167	1018	1113	97.6	188	1375	1515	98.0
200	91	707	766	96.8	111	966	1048	96.8
500	33	440	473	96.0	35	623	651	95.4
1000	25	320	328	94.6	23	440	454	95.3
5000	1	142	144	94.6	10	195	199	95.1
$\rho_0 = 0.80$								
100	119	911	995	97.6	146	1176	1330	98.3
200	72	642	686	96.6	124	835	912	97.1
500	22	398	424	96.1	75	537	562	95.5
1000	18	286	296	95.1	71	380	392	95.0
5000	-1	128	130	94.9	-1	128	130	94.9

Bias,  $(\hat{\phi} - \phi_0) \times 10^4$ ; SD, standard deviation  $\times 10^4$ ; SE, standard error estimated using bootstrap-based variance estimation  $\times 10^4$ ; Cov (%), coverage rates of 95% confidence interval.

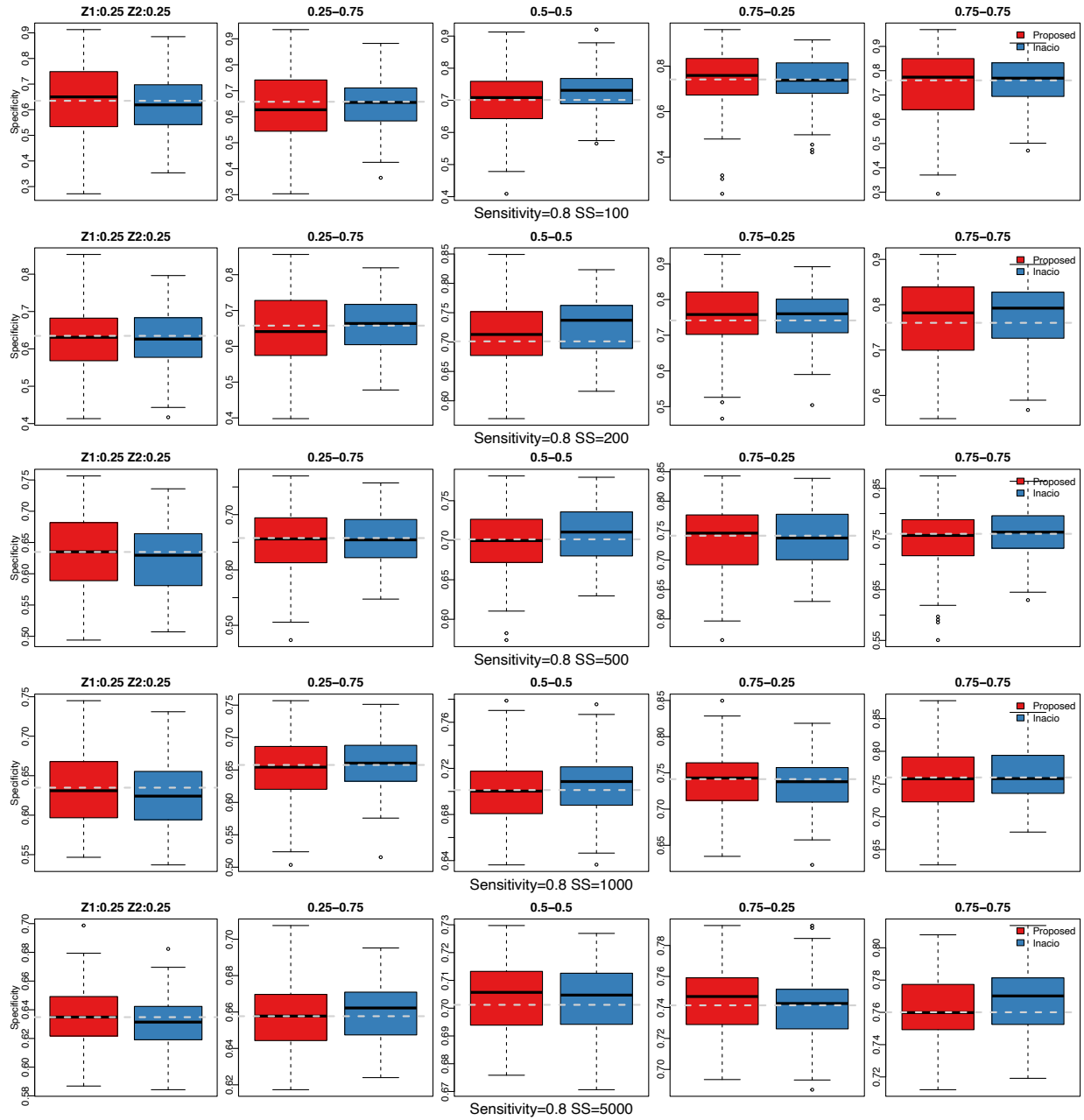


Figure S1: Simulation results in the first simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.8. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

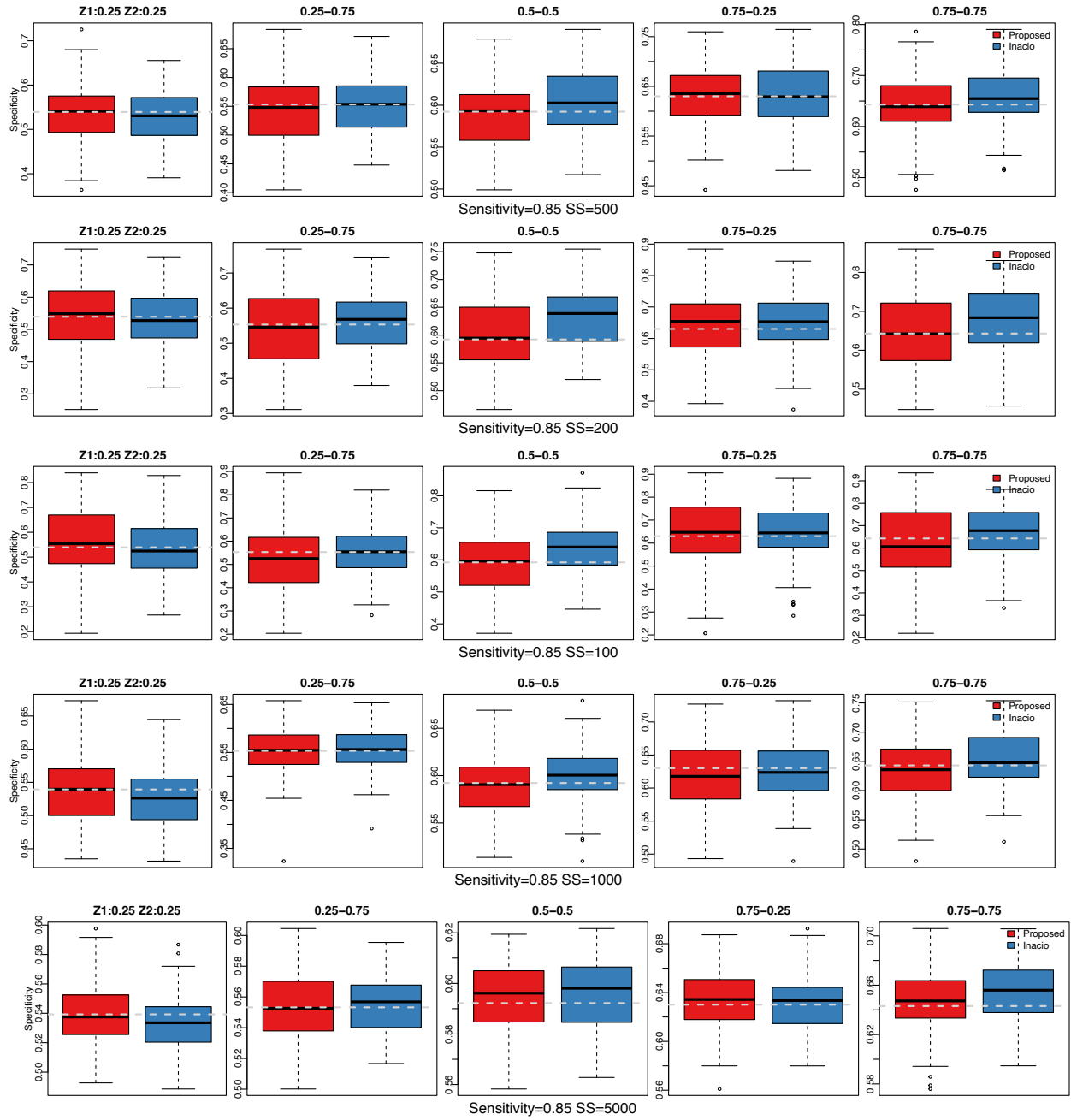


Figure S2: Simulation results in the first simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.85. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

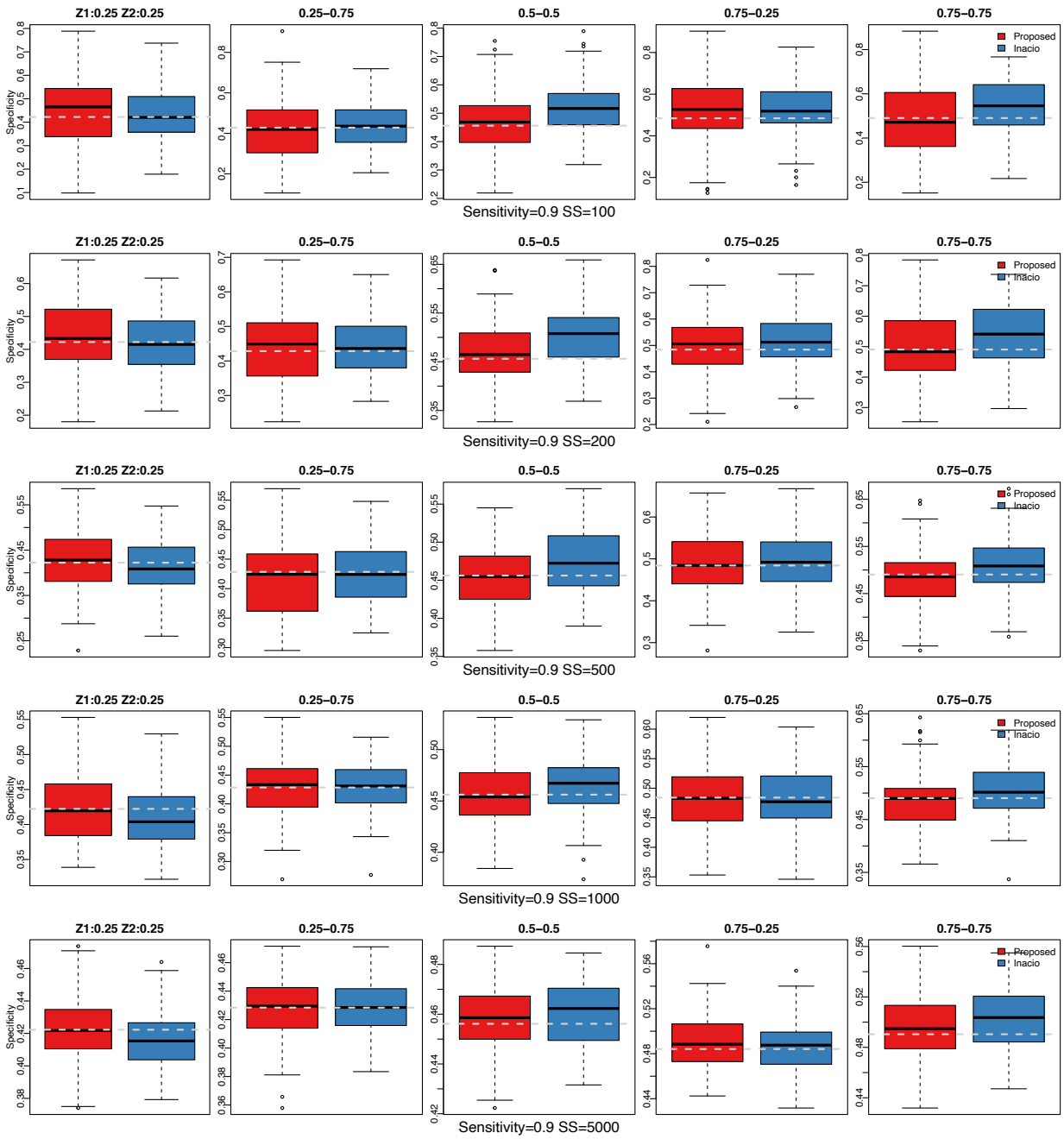


Figure S3: Simulation results in the first simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.90. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

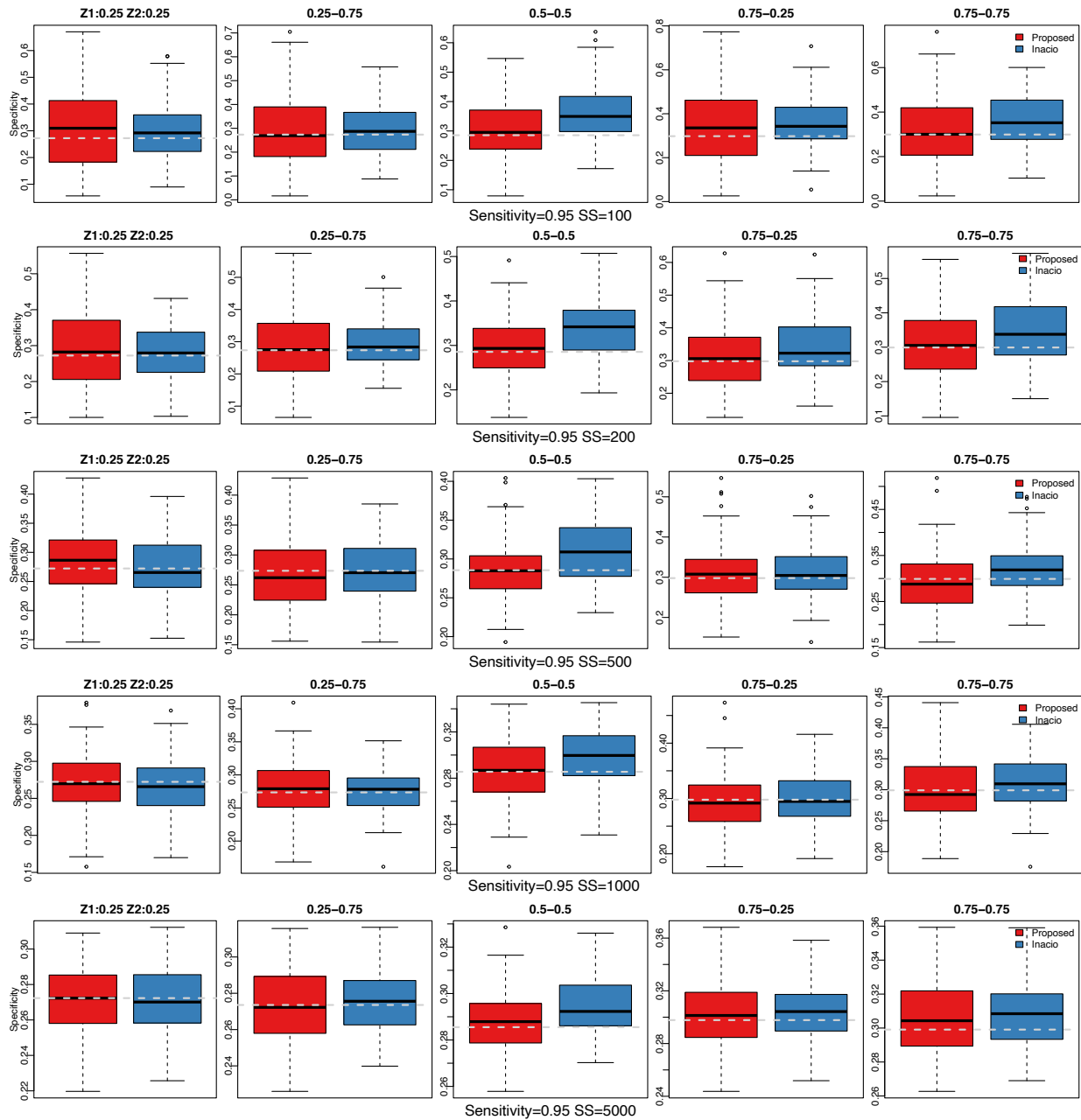


Figure S4: Simulation results in the first simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.95. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.



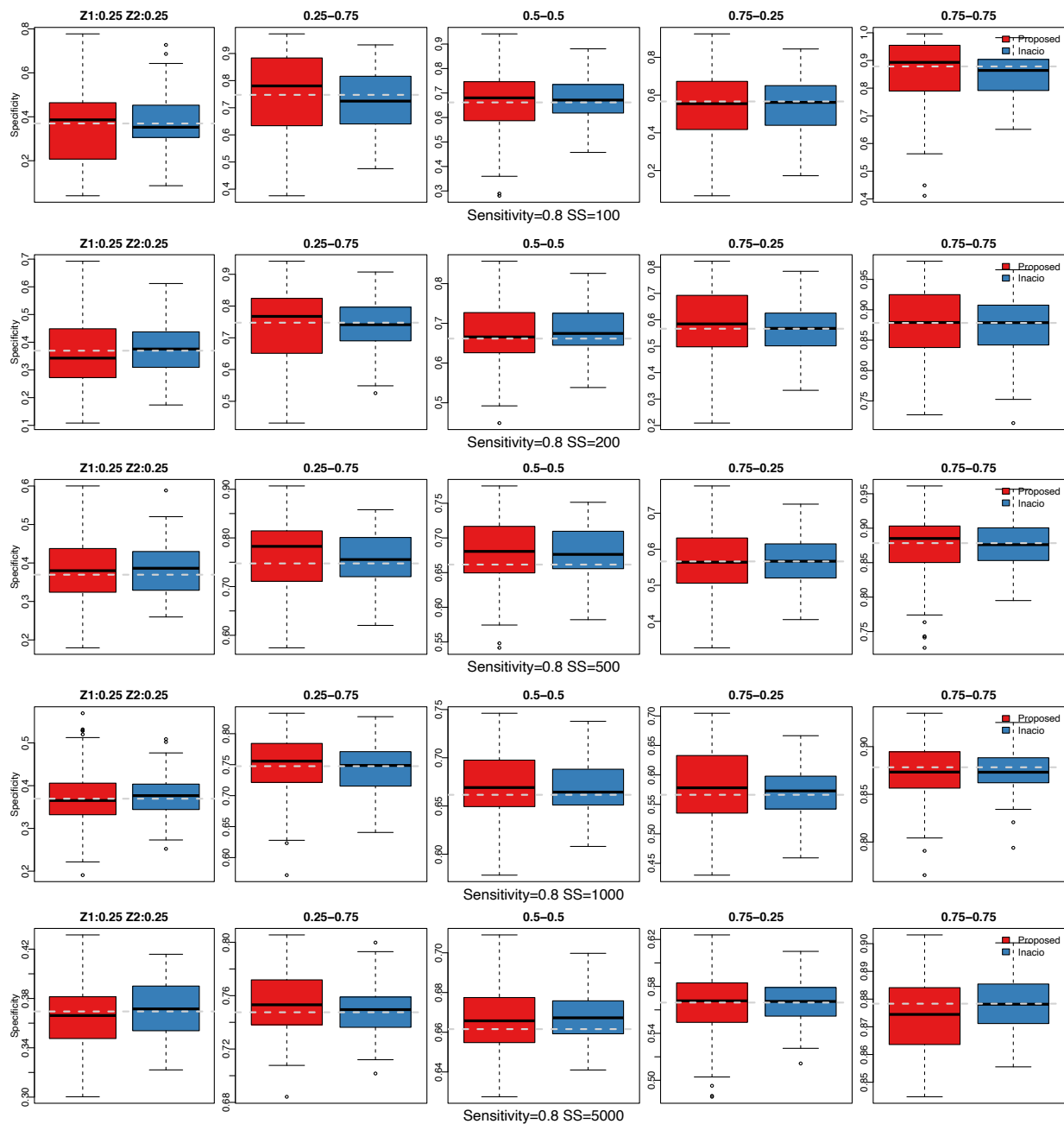


Figure S5: Simulation results in the second simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.80. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

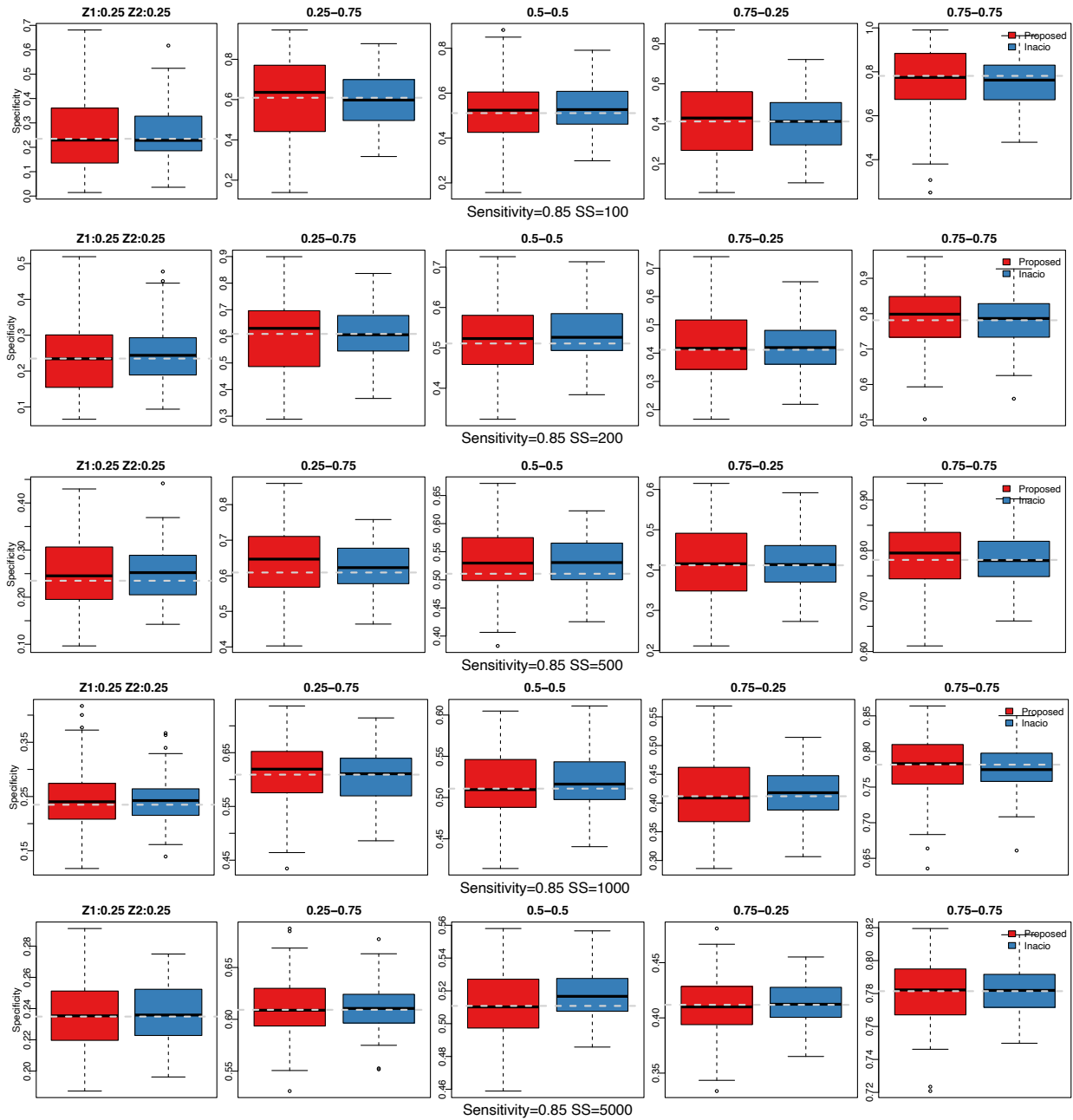


Figure S6: Simulation results in the second simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.85. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

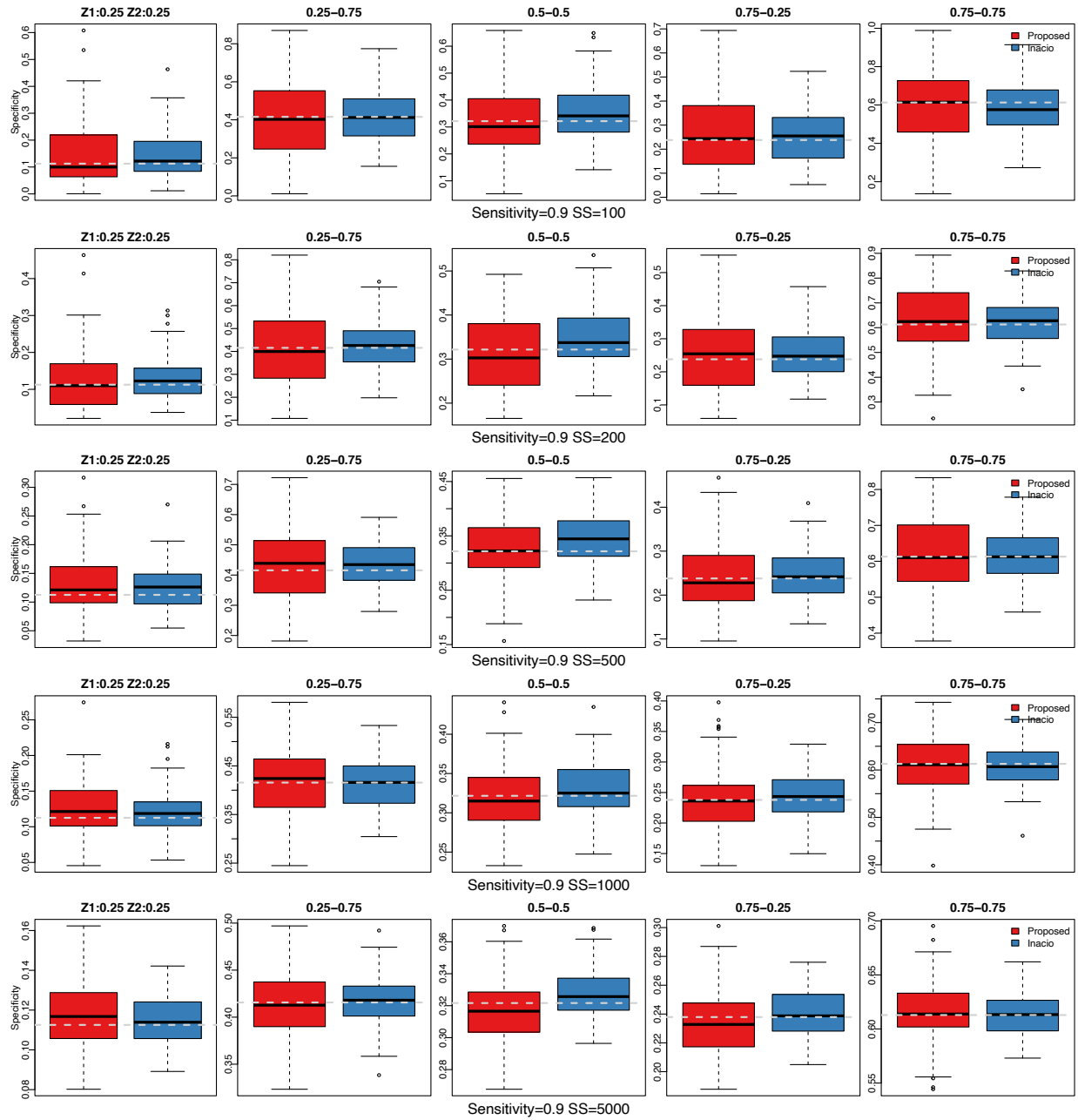


Figure S7: Simulation results in the second simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.90. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.

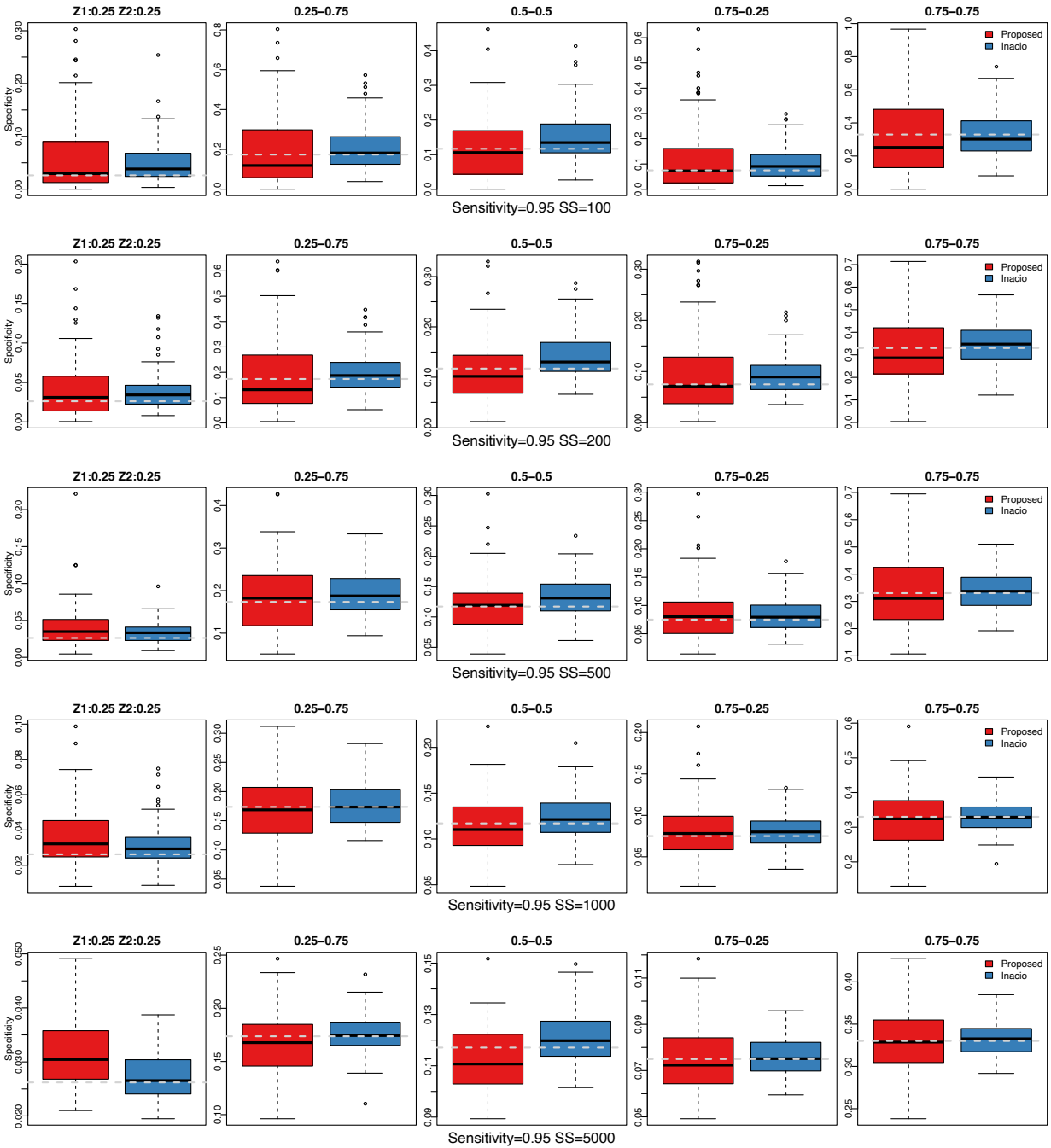


Figure S8: Simulation results in the second simulation setting of the proposed method (red box), the Inácio de Carvalho et al. (2013) (blue), and true value (black). From top panel to the bottom panel, the sample sizes are 100, 200, 500, 1000, and 5000. The Sensitivity level is fixed at 0.95. The title of each figure shows the covariate combination for  $Z_1$  and  $Z_2$ . All results are summarized over 100 Monte Carlo datasets.