

**Web Appendix for 'Comparison of Two Correlated  
ROC Curves at a Given Specificity or Sensitivity  
Level' by Leonidas E. Bantis and Ziding Feng**

## Web-Appendix A (Simulation results)

Table 1: Comparison of sizes of  $Z$  and  $Z^*$  tests. Simulation results of 1000 replications for the scenario in which data representing diseased and healthy individuals are generated by the same bivariate normal distributions (valid null hypothesis since  $ROC_1(t) = ROC_2(t)$ ). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7$ , and  $0.8$ . Normality is also assumed for estimation. Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4, 0.6$  for the data of both the healthy and diseased individuals.

		Size results									
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	$Z$ test				$Z^*$ test				
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	
100, 100	0.2	0.6	0.051	0.054	0.056	0.046	0.048	0.053	0.054	0.048	
		0.7	0.051	0.055	0.056	0.040	0.049	0.055	0.055	0.051	
		0.8	0.050	0.058	0.044	0.018	0.049	0.060	0.057	0.051	
	0.4	0.6	0.057	0.055	0.055	0.049	0.051	0.053	0.053	0.049	
		0.7	0.049	0.052	0.048	0.032	0.047	0.052	0.049	0.046	
		0.8	0.048	0.058	0.047	0.011	0.048	0.059	0.055	0.050	
	0.6	0.6	0.052	0.052	0.057	0.041	0.051	0.052	0.055	0.045	
		0.7	0.049	0.050	0.048	0.027	0.045	0.050	0.050	0.045	
		0.8	0.047	0.050	0.036	0.010	0.046	0.054	0.050	0.045	
200, 200	0.2	0.6	0.056	0.060	0.062	0.059	0.054	0.060	0.062	0.060	
		0.7	0.057	0.057	0.060	0.051	0.053	0.057	0.059	0.061	
		0.8	0.051	0.059	0.054	0.043	0.049	0.059	0.063	0.063	
	0.4	0.6	0.052	0.066	0.065	0.056	0.051	0.065	0.065	0.058	
		0.7	0.057	0.058	0.060	0.046	0.056	0.058	0.060	0.056	
		0.8	0.057	0.060	0.054	0.035	0.055	0.060	0.061	0.061	
	0.6	0.6	0.050	0.064	0.059	0.045	0.050	0.064	0.058	0.047	
		0.7	0.055	0.059	0.055	0.039	0.055	0.059	0.055	0.052	
		0.8	0.053	0.050	0.050	0.032	0.053	0.049	0.060	0.058	
100, 200	0.2	0.6	0.049	0.049	0.045	0.052	0.046	0.048	0.043	0.051	
		0.7	0.056	0.049	0.047	0.042	0.055	0.049	0.048	0.048	
		0.8	0.057	0.040	0.040	0.024	0.056	0.043	0.046	0.050	
	0.4	0.6	0.056	0.040	0.044	0.045	0.051	0.040	0.044	0.045	
		0.7	0.056	0.042	0.041	0.040	0.054	0.044	0.041	0.046	
		0.8	0.056	0.041	0.038	0.024	0.058	0.041	0.042	0.047	
	0.6	0.6	0.054	0.035	0.043	0.042	0.051	0.035	0.044	0.042	
		0.7	0.054	0.044	0.040	0.041	0.053	0.045	0.039	0.043	
		0.8	0.052	0.042	0.032	0.023	0.056	0.043	0.046	0.050	

Table 2: Comparison of the power of  $Z$  and  $Z^*$  tests. Simulation results of 1000 replications for the normal setting (non-valid null hypothesis) under different scenarios. Normality is also assumed for estimation. Sample sizes explored are (100, 100), (200, 200), (300, 300), and (100, 300). Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for the data of both the healthy and diseased individuals. The true difference  $ROC_2(t) - ROC_1(t)$  to be detected is denoted by  $d$ .

		Power results							
		$Z$ test				$Z^*$ test			
$n_A, n_B$	$\rho$	$t = 0.540$	$t = 0.648$	$t = 0.753$	$t = 0.863$	$t = 0.540$	$t = 0.648$	$t = 0.753$	$t = 0.863$
		$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$	$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$
Assuming Normality									
50, 50	0.2	0.786	0.704	0.523	0.203	0.812	0.756	0.702	0.624
	0.4	0.872	0.796	0.585	0.216	0.897	0.863	0.800	0.6920
	0.6	0.970	0.913	0.694	0.245	0.977	0.964	0.925	0.8390
100, 100	0.2	0.975	0.963	0.918	0.713	0.978	0.971	0.951	0.900
	0.4	0.993	0.988	0.962	0.770	0.993	0.991	0.980	0.949
	0.6	1.000	0.997	0.989	0.862	1.000	0.999	0.995	0.986
200, 200	0.2	1.000	0.999	0.999	0.980	1.000	0.999	0.999	0.991
	0.4	1.000	1.000	1.000	0.994	1.000	1.000	1.000	0.999
	0.6	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Box-Cox									
50, 50	0.2	0.769	0.655	0.486	0.181	0.755	0.692	0.602	0.505
	0.4	0.861	0.745	0.543	0.192	0.866	0.788	0.690	0.564
	0.6	0.933	0.859	0.626	0.223	0.939	0.899	0.825	0.696
100, 100	0.2	0.972	0.953	0.891	0.656	0.970	0.961	0.909	0.825
	0.4	0.991	0.979	0.930	0.696	0.988	0.977	0.957	0.879
	0.6	1.000	0.996	0.979	0.782	0.998	0.993	0.984	0.946
200, 200	0.2	1.000	1.000	0.993	0.960	1.000	1.000	0.994	0.978
	0.4	1.000	1.000	1.000	0.982	0.999	0.998	0.998	0.991
	0.6	1.000	1.000	1.000	0.999	1.000	1.000	1.000	0.999

Table 3: Comparison of sizes of  $Z$  and  $Z^*$  tests. Simulation results of 1000 replications where data representing the diseased and healthy individuals are generated by the same bivariate normal distributions (valid null hypothesis). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7, \text{ and } 0.8$ . The Box-Cox approach is used for estimation. Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for the data of both the healthy and diseased individuals.

		Size results									
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	$Z$ test				$Z^*$ test				
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	
100, 100	0.2	0.6	0.054	0.055	0.058	0.037	0.047	0.054	0.057	0.039	
		0.7	0.054	0.056	0.049	0.035	0.047	0.053	0.051	0.040	
		0.8	0.052	0.057	0.049	0.025	0.047	0.049	0.045	0.045	
	0.4	0.6	0.053	0.053	0.054	0.039	0.049	0.051	0.049	0.041	
		0.7	0.048	0.055	0.047	0.035	0.044	0.052	0.047	0.040	
		0.8	0.048	0.051	0.045	0.015	0.046	0.050	0.045	0.045	
	0.6	0.6	0.060	0.057	0.054	0.038	0.054	0.051	0.051	0.044	
		0.7	0.051	0.056	0.047	0.022	0.046	0.053	0.051	0.035	
		0.8	0.045	0.050	0.031	0.012	0.045	0.049	0.046	0.039	
200, 200	0.2	0.6	0.054	0.061	0.061	0.056	0.053	0.059	0.058	0.055	
		0.7	0.054	0.059	0.056	0.054	0.051	0.058	0.058	0.060	
		0.8	0.050	0.061	0.062	0.050	0.050	0.062	0.061	0.058	
	0.4	0.6	0.050	0.064	0.063	0.056	0.047	0.064	0.062	0.054	
		0.7	0.055	0.057	0.060	0.050	0.049	0.056	0.057	0.053	
		0.8	0.060	0.060	0.058	0.041	0.053	0.062	0.057	0.052	
	0.6	0.6	0.051	0.063	0.060	0.047	0.043	0.064	0.062	0.049	
		0.7	0.052	0.059	0.055	0.042	0.045	0.057	0.056	0.053	
		0.8	0.057	0.055	0.053	0.033	0.054	0.057	0.053	0.052	
100, 200	0.2	0.6	0.053	0.047	0.047	0.047	0.052	0.047	0.050	0.052	
		0.7	0.060	0.050	0.049	0.047	0.053	0.049	0.045	0.046	
		0.8	0.056	0.045	0.044	0.027	0.056	0.045	0.046	0.044	
	0.4	0.6	0.056	0.042	0.048	0.051	0.045	0.041	0.045	0.051	
		0.7	0.059	0.043	0.040	0.047	0.055	0.044	0.044	0.054	
		0.8	0.053	0.046	0.043	0.028	0.053	0.044	0.048	0.044	
	0.6	0.6	0.055	0.038	0.042	0.047	0.043	0.037	0.045	0.050	
		0.7	0.054	0.046	0.047	0.045	0.045	0.044	0.045	0.051	
		0.8	0.053	0.043	0.047	0.023	0.052	0.045	0.041	0.040	

Table 4: Exploration of  $Z^*$  test size. Simulation results of 1000 replications where data representing the diseased and healthy individuals are generated by bivariate lognormal and bivariate gamma distributions (valid null hypothesis). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7, \text{ and } 0.8$ . The Box-Cox approach is used for estimation. Sample sizes explored are (100, 100), (200, 200) and (100, 200). Correlation is set equal to  $\rho = 0.2, 0.4$ , and 0.6 for the data of both the healthy and diseased individuals.

		Size results (Box-Cox)								
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	Bivariate Gammas				Bivariate Lognormals			
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$
100, 100	0.2	0.6	0.042	0.051	0.047	0.054	0.054	0.055	0.058	0.043
		0.7	0.045	0.042	0.049	0.049	0.060	0.057	0.055	0.043
		0.8	0.045	0.049	0.039	0.043	0.060	0.055	0.043	0.035
	0.4	0.6	0.030	0.039	0.046	0.045	0.057	0.056	0.058	0.050
		0.7	0.041	0.042	0.049	0.044	0.055	0.052	0.047	0.039
		0.8	0.039	0.050	0.048	0.046	0.054	0.054	0.048	0.035
	0.6	0.6	0.025	0.050	0.051	0.042	0.059	0.054	0.059	0.046
		0.7	0.036	0.051	0.058	0.048	0.054	0.053	0.051	0.038
		0.8	0.047	0.049	0.041	0.036	0.052	0.051	0.039	0.033
200, 200	0.2	0.6	0.048	0.059	0.057	0.054	0.069	0.079	0.082	0.068
		0.7	0.047	0.051	0.049	0.047	0.062	0.071	0.071	0.058
		0.8	0.044	0.049	0.048	0.039	0.066	0.065	0.067	0.055
	0.4	0.6	0.038	0.050	0.055	0.049	0.055	0.068	0.071	0.060
		0.7	0.045	0.040	0.033	0.033	0.058	0.062	0.060	0.051
		0.8	0.044	0.054	0.047	0.043	0.062	0.062	0.059	0.053
	0.6	0.6	0.036	0.045	0.051	0.051	0.054	0.065	0.062	0.046
		0.7	0.033	0.042	0.044	0.041	0.057	0.057	0.058	0.044
		0.8	0.036	0.040	0.044	0.043	0.057	0.053	0.057	0.051
100, 200	0.2	0.6	0.039	0.040	0.052	0.053	0.065	0.056	0.050	0.051
		0.7	0.039	0.049	0.048	0.045	0.061	0.054	0.052	0.051
		0.8	0.044	0.049	0.048	0.045	0.068	0.053	0.048	0.050
	0.4	0.6	0.034	0.041	0.037	0.054	0.058	0.054	0.047	0.050
		0.7	0.041	0.049	0.045	0.040	0.055	0.052	0.044	0.052
		0.8	0.045	0.042	0.038	0.032	0.055	0.043	0.047	0.047
	0.6	0.6	0.038	0.044	0.051	0.053	0.049	0.041	0.044	0.044
		0.7	0.029	0.041	0.042	0.045	0.052	0.051	0.042	0.042
		0.8	0.037	0.041	0.038	0.042	0.051	0.041	0.046	0.040

Table 5: Power simulation results of 1000 replications for the non-normal settings (non-valid null hypothesis) under different scenarios. The kernel-based method is considered for estimation. Sample sizes explored are (100, 100), (200, 200), (300, 300), and (100, 300). Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for data of both the healthy and diseased individuals. The true difference  $ROC_2(t) - ROC_1(t)$  to be detected is denoted by  $d$ .

Power results									
$n_A, n_B$	$\rho$	Bivariate Gammas				Bivariate Lognormals			
		$t = 0.540$ $d = 0.20$	$t = 0.648$ $d = 0.15$	$t = 0.753$ $d = 0.10$	$t = 0.863$ $d = 0.05$	$t = 0.3790$ $d = 0.20$	$t = 0.5350$ $d = 0.15$	$t = 0.6890$ $d = 0.10$	$t = 0.847$ $d = 0.05$
Box-Cox approach									
50, 50	0.2	0.503	0.462	0.347	0.217	0.733	0.642	0.503	0.337
	0.4	0.600	0.544	0.419	0.273	0.842	0.755	0.607	0.397
	0.6	0.758	0.687	0.532	0.333	0.953	0.893	0.756	0.526
100, 100	0.2	0.806	0.739	0.610	0.430	0.942	0.905	0.820	0.637
	0.4	0.892	0.833	0.688	0.493	0.986	0.967	0.894	0.726
	0.6	0.973	0.949	0.842	0.621	1.000	0.994	0.975	0.855
200, 200	0.2	0.977	0.965	0.885	0.718	0.996	0.992	0.969	0.890
	0.4	0.999	0.991	0.944	0.801	1.000	1.000	0.993	0.949
	0.6	1.000	0.999	0.990	0.897	1.000	1.000	1.000	0.993
Kernel-based approach									
50, 50	0.2	0.4180	0.3930	0.3000	0.1790	0.6250	0.5200	0.3340	0.1620
	0.4	0.5190	0.4620	0.3690	0.2270	0.7200	0.5810	0.4000	0.1930
	0.6	0.6310	0.5710	0.4390	0.2770	0.8480	0.7250	0.5310	0.2610
100, 100	0.2	0.7240	0.6850	0.5620	0.3690	0.9010	0.7960	0.5910	0.3050
	0.4	0.8060	0.7900	0.6440	0.4210	0.9500	0.8790	0.6950	0.3670
	0.6	0.9270	0.8970	0.7720	0.5140	0.9910	0.9570	0.8320	0.5160
200, 200	0.2	0.9340	0.9320	0.8490	0.6340	0.9950	0.9720	0.8730	0.5470
	0.4	0.9790	0.9770	0.9170	0.7300	0.9990	0.9910	0.9260	0.6400
	0.6	0.9970	0.9930	0.9700	0.8260	1.0000	1.0000	0.9770	0.7920

Table 6: Exploration of  $Z^*$  test size. Simulation results of 1000 replications where data representing diseased and healthy individuals are generated by bivariate lognormal and bivariate gamma distributions (valid null hypothesis since  $ROC_1(t) = ROC_2(t)$ ). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7$ , and  $0.8$ . The kernel-based approach is used for estimation. Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for the data of both the healthy and diseased individuals.

		Size results (Kernel-based $Z^*$ statistic)								
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	Bivariate Gammas				Bivariate Lognormals			
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$
100, 100	0.2	0.6	0.034	0.036	0.040	0.049	0.044	0.045	0.053	0.057
		0.7	0.033	0.039	0.032	0.046	0.042	0.052	0.057	0.057
		0.8	0.047	0.049	0.051	0.051	0.039	0.049	0.057	0.060
	0.4	0.6	0.035	0.031	0.037	0.045	0.048	0.055	0.054	0.053
		0.7	0.039	0.035	0.041	0.039	0.048	0.058	0.049	0.054
		0.8	0.040	0.038	0.043	0.048	0.048	0.052	0.046	0.051
	0.6	0.6	0.036	0.0440	0.0430	0.0310	0.0480	0.062	0.055	0.043
		0.7	0.042	0.0450	0.0460	0.0570	0.0530	0.061	0.048	0.045
		0.8	0.043	0.0440	0.0410	0.0440	0.0490	0.047	0.047	0.043
200, 200	0.2	0.6	0.054	0.052	0.050	0.042	0.051	0.055	0.055	0.063
		0.7	0.049	0.046	0.045	0.051	0.051	0.056	0.057	0.071
		0.8	0.044	0.045	0.043	0.050	0.053	0.050	0.072	0.067
	0.4	0.6	0.046	0.045	0.046	0.044	0.048	0.052	0.058	0.060
		0.7	0.043	0.037	0.039	0.040	0.050	0.054	0.058	0.070
		0.8	0.035	0.053	0.038	0.043	0.046	0.054	0.070	0.068
	0.6	0.6	0.045	0.044	0.041	0.047	0.045	0.053	0.068	0.059
		0.7	0.043	0.042	0.043	0.051	0.045	0.051	0.064	0.067
		0.8	0.033	0.039	0.048	0.060	0.046	0.054	0.068	0.065
100, 200	0.2	0.6	0.051	0.049	0.055	0.058	0.050	0.045	0.046	0.056
		0.7	0.049	0.049	0.044	0.052	0.056	0.043	0.052	0.058
		0.8	0.051	0.045	0.050	0.054	0.053	0.048	0.057	0.062
	0.4	0.6	0.046	0.043	0.042	0.049	0.047	0.040	0.048	0.054
		0.7	0.044	0.042	0.040	0.050	0.055	0.046	0.051	0.057
		0.8	0.045	0.040	0.049	0.038	0.052	0.042	0.054	0.061
	0.6	0.6	0.039	0.042	0.053	0.053	0.056	0.044	0.052	0.052
		0.7	0.044	0.038	0.043	0.049	0.058	0.051	0.049	0.050
		0.8	0.041	0.035	0.037	0.041	0.058	0.051	0.051	0.055



Table 7: Size simulation results with respect to the  $AUC$  of 1000 replications where data representing the diseased and healthy individuals are generated by bivariate lognormal and bivariate gamma distributions (valid null hypothesis  $ROC_1(t) = ROC_2(t)$ ). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7$ , and  $0.8$ . The Box-Cox, kernel-based and DeLong's methods are compared. Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for the data of both the healthy and diseased individuals.

AUC size results								
		Bivariate Gammas				Bivariate Lognormals		
$n_A, n_B$	$\rho$	$AUC$	<i>Box - Cox</i>	<i>Kernel</i>	<i>DeLong</i>	<i>Box - Cox</i>	<i>Kernel</i>	<i>DeLong</i>
100, 100	0.2	0.6	0.051	0.040	0.042	0.056	0.051	0.055
		0.7	0.049	0.048	0.043	0.057	0.053	0.052
		0.8	0.059	0.055	0.044	0.054	0.054	0.055
	0.4	0.6	0.040	0.037	0.044	0.058	0.059	0.058
		0.7	0.042	0.042	0.043	0.055	0.055	0.056
		0.8	0.041	0.043	0.043	0.055	0.055	0.051
	0.6	0.6	0.052	0.045	0.048	0.052	0.062	0.061
		0.7	0.047	0.045	0.044	0.057	0.059	0.058
		0.8	0.047	0.050	0.045	0.053	0.055	0.045
200, 200	0.2	0.6	0.057	0.059	0.054	0.058	0.063	0.059
		0.7	0.057	0.050	0.053	0.059	0.053	0.057
		0.8	0.046	0.041	0.044	0.063	0.056	0.049
	0.4	0.6	0.053	0.050	0.046	0.062	0.059	0.057
		0.7	0.040	0.038	0.038	0.060	0.049	0.050
		0.8	0.048	0.048	0.049	0.061	0.053	0.053
	0.6	0.6	0.047	0.045	0.040	0.065	0.056	0.062
		0.7	0.044	0.044	0.042	0.059	0.051	0.056
		0.8	0.041	0.036	0.038	0.057	0.056	0.050
100, 200	0.2	0.6	0.045	0.042	0.039	0.045	0.051	0.052
		0.7	0.049	0.047	0.045	0.051	0.049	0.044
		0.8	0.051	0.052	0.052	0.046	0.048	0.047
	0.4	0.6	0.044	0.042	0.043	0.047	0.044	0.047
		0.7	0.043	0.040	0.045	0.051	0.045	0.043
		0.8	0.043	0.047	0.054	0.049	0.051	0.046
	0.6	0.6	0.039	0.044	0.046	0.041	0.043	0.043
		0.7	0.031	0.030	0.031	0.043	0.044	0.045
		0.8	0.039	0.039	0.045	0.048	0.054	0.046

Table 8: Power simulation results with respect to the  $AUC$  of 1000 replications where data representing diseased and healthy individuals are generated by bivariate lognormal and bivariate gamma distributions (non-valid null hypothesis). The Box-Cox, kernel-based and DeLong's methods are compared. Sample sizes explored are  $(50, 50)$ ,  $(100, 100)$ , and  $(200, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for data of both the healthy and diseased individuals.

AUC power results							
		Bivariate Gammas			Bivariate Lognormals		
$n_A, n_B$	$\rho$	<i>Box - Cox</i>	<i>Kernel</i>	<i>DeLong</i>	<i>Box - Cox</i>	<i>Kernel</i>	<i>DeLong</i>
50, 50	0.2	0.511	0.469	0.480	0.762	0.663	0.721
	0.4	0.610	0.569	0.575	0.857	0.754	0.830
	0.6	0.768	0.737	0.736	0.949	0.894	0.952
100, 100	0.2	0.809	0.776	0.771	0.953	0.909	0.949
	0.4	0.896	0.882	0.875	0.988	0.964	0.987
	0.6	0.972	0.969	0.969	0.994	0.994	0.998
200, 200	0.2	0.979	0.968	0.972	0.999	0.998	0.999
	0.4	0.998	0.995	0.993	1.000	1.000	1.000
	0.6	1.000	1.000	1.000	1.000	1.000	1.000

## Web-Appendix B (technical details)

# 1 Appendix

## 1.1 Derivation of the partial derivatives for the delta method

$$\begin{aligned}
\frac{\partial ROC_1(t)}{\partial \mu_{1A}} &= -\frac{\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-0.5 \left(\frac{\mu_{1A} - \mu_{1B} - \Phi^{-1}(t)\sigma_{1A}}{\sigma_{1B}}\right)^2\right) \\
\frac{\partial ROC_1(t)}{\partial \mu_{1B}} &= \frac{\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-0.5 \left(\frac{\mu_{1A} - \mu_{1B} - \Phi^{-1}(t)\sigma_{1A}}{\sigma_{1B}}\right)^2\right) \\
\frac{\partial ROC_1(t)}{\partial \sigma_{1A}} &= \frac{\Phi^{-1}(t)}{\sqrt{2\pi}\sigma_{1B}} \exp\left(-0.5 \left(\frac{\mu_{1A} - \mu_{1B} - \Phi^{-1}(t)\sigma_{1A}}{\sigma_{1B}}\right)^2\right) \\
\frac{\partial ROC_1(t)}{\partial \sigma_{1B}} &= \frac{\sqrt{2}}{2\sqrt{\pi}} \exp\left(-0.5 \left(\frac{\mu_{1A} - \mu_{1B} - \Phi^{-1}(t)\sigma_{1A}}{\sigma_{1B}}\right)^2\right) \left(\frac{\mu_{1A} - \mu_{1B} - \sigma_{1A}\Phi^{-1}(t)}{\sigma_{1B}^2}\right)
\end{aligned}$$

and the expressions are similar for  $\frac{\partial ROC_2(t)}{\partial \mu_{2A}}$ ,  $\frac{\partial ROC_2(t)}{\partial \mu_{2B}}$ ,  $\frac{\partial ROC_2(t)}{\partial \sigma_{2A}}$  and  $\frac{\partial ROC_2(t)}{\partial \sigma_{2B}}$ .

$$\begin{aligned}
\frac{\partial \Phi^{-1}(R\hat{O}C_1(t))}{\partial \mu_{1A}} &= -\frac{1}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(R\hat{O}C_1(t))}{\partial \mu_{1B}} &= \frac{1}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(R\hat{O}C_1(t))}{\partial \sigma_{1A}} &= \frac{\Phi^{-1}(t)}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(R\hat{O}C_1(t))}{\partial \sigma_{1B}} &= \frac{\mu_{1A} - \mu_{1B} - \Phi^{-1}(t)\sigma_{1A}}{\sigma_{1B}^2}.
\end{aligned}$$

(1)

Similarly for the expressions that correspond to  $\Phi^{-1}(R\hat{O}C_2(t))$ .

## 1.2 Derivation of the partial derivatives for the delta method in the presence of covariates

$$\begin{aligned}
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \beta_0^{(1A)}} &= -\frac{1}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \beta_j^{(1A)}} &= -\frac{z_j^{(1A)}}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \beta_0^{(1B)}} &= \frac{1}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \beta_j^{(1A)}} &= \frac{z_j^{(1B)}}{\sigma_{1B}} \\
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \sigma_{1A}} &= -\frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}^2} \\
\frac{\partial \Phi^{-1}(ROC_{1,Z}(t))}{\partial \sigma_{1B}} &= -\frac{(\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_{ji}^{(1B)}) - (\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)})}{\sigma_{1B}^2} + \frac{\Phi^{-1}(t)}{\sigma_{1A}^2}.
\end{aligned}$$

where  $j = 1, \dots, p$ . The expressions for  $ROC_2(t)$  are similar.

### 1.3 Partial derivatives for the delta method (AUC)

$$\begin{aligned}
\frac{\partial \Phi^{-1}(AUC_1)}{\partial \mu_{1A}} &= \frac{-1}{\sigma_{1B} \sqrt{1 + (\sigma_{1A}/\sigma_{1B})^2}} \\
\frac{\partial \Phi^{-1}(AUC_1)}{\partial \mu_{1B}} &= \frac{1}{\sigma_{1B} \sqrt{1 + (\sigma_{1A}/\sigma_{1B})^2}} \\
\frac{\partial \Phi^{-1}(AUC_1)}{\partial \sigma_{1A}} &= \frac{\sigma_{1A}(\mu_{1A} - \mu_{1B})}{\sigma_{1B}^3 (1 + (\sigma_{1A}/\sigma_{1B})^2)^{3/2}} \\
\frac{\partial \Phi^{-1}(AUC_1)}{\partial \sigma_{1B}} &= \frac{(\mu_{1A} - \mu_{1B})}{\sigma_{1B}^2 (1 + (\sigma_{1A}/\sigma_{1B})^2)^{3/2}}
\end{aligned}$$

### 1.4 Partial derivatives for the delta method in the presence of covariates (AUC)

$$\begin{aligned}
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \beta_0^{(1A)}} &= \frac{-1}{\sigma_{1B} \sqrt{1 + \left(\frac{\sigma_{1A}}{\sigma_{1B}}\right)^2}} \\
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \beta_j^{(1A)}} &= \frac{-z_j^{(1A)}}{\sigma_{1B} \sqrt{1 + \left(\frac{\sigma_{1A}}{\sigma_{1B}}\right)^2}} \\
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \beta_0^{(1B)}} &= \frac{1}{\sigma_{1B} \sqrt{1 + \left(\frac{\sigma_{1A}}{\sigma_{1B}}\right)^2}} \\
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \beta_j^{(1B)}} &= \frac{z_j^{(1B)}}{\sigma_{1B} \sqrt{1 + \left(\frac{\sigma_{1A}}{\sigma_{1B}}\right)^2}} \\
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \sigma_{1A}} &= -\frac{\sigma_{1A}}{\sigma_{1B}^3 \left(\frac{\sigma_{1A}^2}{\sigma_{1B}^2} + 1\right)^{3/2}} \\
\frac{\partial \Phi^{-1}(AUC_{1,Z})}{\partial \sigma_{1B}} &= \frac{\sigma_{1A}^2}{\sigma_{1B}^4 \left(\frac{\sigma_{1A}^2}{\sigma_{1B}^2} + 1\right)^{3/2}} - \frac{1}{\sigma_{1B}^2 \left(\frac{\sigma_{1A}^2}{\sigma_{1B}^2} + 1\right)^{1/2}}
\end{aligned}$$

The expressions are similar for  $\Phi^{-1}(AUC_{2,Z})$ .

## 1.5 Derivation of the information matrix for the binormal-bivariate setting

Fisher's information matrix in this case is of the form:

$$I = - \begin{pmatrix} \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1A}^2} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1A} \partial \mu_{2A}} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A}^2} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A} \partial \sigma_{2A}} & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A} \partial cov_A} & 0 \\ 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1B}^2} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1B} \partial \mu_{2B}} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B}^2} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B} \partial \sigma_{2B}} & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B} \partial cov_B} \\ \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2A} \partial \mu_{1A}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2A}^2} & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A} \partial \sigma_{1A}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A}^2} & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A} \partial cov_A} & 0 \\ 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2B} \partial \mu_{1B}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2B}^2} & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2B} \partial \sigma_{1B}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2B}^2} & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2B} \partial cov_B} \\ 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_A \partial \sigma_{1A}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_A \partial \sigma_{2A}} & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_A^2} & 0 \\ 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_B \partial \sigma_{1B}} & 0 & 0 & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_B \partial \sigma_{2B}} & 0 & \frac{\partial^2 l(\mathbf{p})}{\partial cov_B^2} \end{pmatrix}.$$

We present all the derivations required:

$$\begin{aligned} \frac{\partial^2 \log L}{\partial \mu_{1A}^2} &= \frac{n_A}{\sigma_{1A}^2 \left( \frac{cov_A^2}{\sigma_{1A}^2 \sigma_{2A}^2} - 1 \right)} \\ \frac{\partial^2 \log L}{\partial \sigma_{1A}^2} &= \frac{1}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^3} \sum_{i=1}^{n_A} (A_{1i} - A_{2i} - A_{3i} - A_{4i} + A_{5i}) \end{aligned}$$

where

$$\begin{aligned} A_{1i} &= \sigma_{1A}^4 \sigma_{2A}^6 + cov_A^3 (2 \mu_{1A} \mu_{2A} \sigma_{2A}^2 + 2 W_{1Ai} W_{2Ai} \sigma_{2A}^2 - 2 W_{1Ai} \mu_{2A} \sigma_{2A}^2 - 2 W_{2Ai} \mu_{1A} \sigma_{2A}^2) \\ A_{2i} &= \sigma_{1A}^2 (3 W_{1Ai}^2 \sigma_{2A}^6 - 6 W_{1Ai} \mu_{1A} \sigma_{2A}^6 + 3 \mu_{1A}^2 \sigma_{2A}^6) \\ A_{3i} &= cov_A^2 (\sigma_{1A}^2 (3 W_{2Ai}^2 \sigma_{2A}^2 - 6 W_{2Ai} \mu_{2A} \sigma_{2A}^2 + 3 \mu_{2A}^2 \sigma_{2A}^2) + W_{1Ai}^2 \sigma_{2A}^4 + \mu_{1A}^2 \sigma_{2A}^4 - 2 W_{1Ai} \mu_{1A} \sigma_{2A}^4) \\ A_{4i} &= cov_A^4 (W_{2Ai}^2 - 2 W_{2Ai} \mu_{2A} + \mu_{2A}^2 + \sigma_{2A}^2) \\ A_{5i} &= cov_A \sigma_{1A}^2 (6 \mu_{1A} \mu_{2A} \sigma_{2A}^4 + 6 W_{1Ai} W_{2Ai} \sigma_{2A}^4 - 6 W_{1Ai} \mu_{2A} \sigma_{2A}^4 - 6 W_{2Ai} \mu_{1A} \sigma_{2A}^4) \end{aligned}$$

$$\frac{\partial^2 \log L}{\partial cov_A^2} = - \frac{1}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^3} \sum_{i=1}^{n_A} (B_{1i} - B_{2i} + B_{3i} - B_{4i})$$

$$\begin{aligned} B_{1i} &= cov_A^2 ((3 W_{2Ai}^2 - 6 W_{2Ai} \mu_{2A} + 3 \mu_{2A}^2) \sigma_{1A}^2 + (3 W_{1Ai}^2 - 6 W_{1Ai} \mu_{1A} + 3 \mu_{1A}^2) \sigma_{2A}^2) \\ B_{2i} &= cov_A^3 (2 W_{1Ai} W_{2Ai} - 2 W_{1Ai} \mu_{2A} - 2 W_{2Ai} \mu_{1A} + 2 \mu_{1A} \mu_{2A}) \\ B_{3i} &= cov_A^4 + \sigma_{2A}^4 (\sigma_{1A}^2 (W_{1Ai}^2 - 2 W_{1Ai} \mu_{1A} + \mu_{1A}^2) - \sigma_{1A}^4) + \sigma_{1A}^4 \sigma_{2A}^2 (W_{2Ai}^2 - 2 W_{2Ai} \mu_{2A} + \mu_{2A}^2) \\ B_{4i} &= cov_A \sigma_{1A}^2 \sigma_{2A}^2 (6 W_{1Ai} W_{2Ai} - 6 W_{1Ai} \mu_{2A} - 6 W_{2Ai} \mu_{1A} + 6 \mu_{1A} \mu_{2A}) \end{aligned}$$

$$\begin{aligned} \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \sigma_{1A}} &= \frac{2 \sigma_{1A} \sigma_{2A}^2 \sum_{i=1}^{n_A} (W_{2Ai} cov_A - cov_A \mu_{2A} - W_{1Ai} \sigma_{2A}^2 + \mu_{1A} \sigma_{2A}^2)}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^2} = 0 \\ \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \mu_{2A}} &= \frac{n_A cov_A}{\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2} \\ \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \sigma_{2A}} &= - \frac{\sigma_{2A} \sum_{i=1}^{n_A} (2 cov_A^2 (W_{1Ai} - \mu_{1A}) - 2 cov_A \sigma_{1A}^2 (W_{2Ai} - \mu_{2A}))}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^2} = 0 \\ \frac{\partial^2 \log L}{\partial \mu_{1A} \partial cov_A} &= - \sum_{i=1}^{n_A} \frac{cov_A^2 (W_{2Ai} - \mu_{2A}) - \sigma_{2A}^2 (cov_A (2 W_{1Ai} - 2 \mu_{1A}) - \sigma_{1A}^2 (W_{2Ai} - \mu_{2A}))}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^2} = 0 \\ \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \mu_{2A}} &= - \frac{\sigma_{1A} \sum_{i=1}^{n_A} (2 cov_A^2 (W_{2Ai} - \mu_{2A}) - 2 cov_A \sigma_{2A}^2 (W_{1Ai} - \mu_{1A}))}{(\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2)^2} = 0 \end{aligned}$$

$$\begin{aligned} \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \sigma_{2A}} &= \sum_{i=1}^{n_A} (\sigma_{1A}^3 (2 \text{cov}_A (C_{1i}) + 2 \text{cov}_A^2) - \text{cov}_A^2 \sigma_{1A} (4 W_{1A}^2 - 8 W_{1A} \mu_{1A} + 4 \mu_{1A}^2)) \sigma_{2A}^3 \\ &+ \sum_{i=1}^{n_A} (\sigma_{1A} (2 \text{cov}_A^3 (C_{1i}) - 2 \text{cov}_A^4) - \text{cov}_A^2 \sigma_{1A}^3 (4 W_{2A}^2 - 8 W_{2A} \mu_{2A} + 4 \mu_{2A}^2)) \sigma_{2A} \end{aligned}$$

where

$$C_{1i} = 2 W_{1A} W_{2A} - 2 W_{1A} \mu_{2A} - 2 W_{2A} \mu_{1A} + 2 \mu_{1A} \mu_{2A}$$

$$\frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \text{cov}_A} = \sum_{i=1}^{n_A} \frac{\sigma_{1A} (\text{cov}_A^3 D_{1i} + D_{2i} - \text{cov}_A^2 \sigma_{2A}^2 D_{3i}) - \sigma_{1A}^3 (\sigma_{2A}^4 D_{4i} + \text{cov}_A D_{5i})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^3}$$

$$\begin{aligned} D_{1i} &= 2 W_{2Ai}^2 - 4 W_{2Ai} \mu_{2A} + 2 \mu_{2A}^2 + 2 \sigma_{2A}^2 \\ D_{2i} &= \text{cov}_A \sigma_{2A}^4 (4 W_{1Ai}^2 - 8 W_{1Ai} \mu_{1A} + 4 \mu_{1A}^2) \\ D_{3i} &= 6 W_{1Ai} W_{2Ai} - 6 W_{1Ai} \mu_{2A} - 6 W_{2Ai} \mu_{1A} + 6 \mu_{1A} \mu_{2A} \\ D_{4i} &= 2 W_{1Ai} W_{2Ai} - 2 W_{1Ai} \mu_{2A} - 2 W_{2Ai} \mu_{1A} + 2 \mu_{1A} \mu_{2A} \\ D_{5i} &= 2 \sigma_{2A}^4 - \sigma_{2A}^2 (2 W_{2Ai}^2 - 4 W_{2Ai} \mu_{2A} + 2 \mu_{2A}^2) \end{aligned}$$

Note that all remaining nonzero derivatives are completely analogous to the above results and can be derived by substituting the parameters of the corresponding group. We also derive:

$$\frac{\partial^2 \log L}{\partial \mu_{1A} \partial \mu_{1B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \sigma_{1B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \mu_{2B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \sigma_{2B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1A} \partial \text{cov}_B} = 0$$

$$\frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \mu_{1B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \sigma_{1B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \mu_{2B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \sigma_{2B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1A} \partial \text{cov}_B} = 0$$

$$\frac{\partial^2 \log L}{\partial \mu_{1B} \partial \mu_{2A}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1B} \partial \sigma_{2A}} = 0, \frac{\partial^2 \log L}{\partial \mu_{1B} \partial \text{cov}_A} = 0,$$

$$\frac{\partial^2 \log L}{\partial \sigma_{1B} \partial \mu_{2A}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1B} \partial \sigma_{2A}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{1B} \partial \text{cov}_A} = 0,$$

$$\frac{\partial^2 \log L}{\partial \mu_{2A} \partial \mu_{2B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{2A} \partial \sigma_{2B}} = 0, \frac{\partial^2 \log L}{\partial \mu_{2A} \partial \text{cov}_B} = 0,$$

$$\frac{\partial^2 \log L}{\partial \sigma_{2A} \partial \mu_{2B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{2A} \partial \sigma_{2B}} = 0, \frac{\partial^2 \log L}{\partial \sigma_{2A} \partial \text{cov}_B} = 0,$$

$$\frac{\partial^2 \log L}{\partial \mu_{2B} \partial \text{cov}_A} = 0, \frac{\partial^2 \log L}{\partial \sigma_{2B} \partial \text{cov}_A} = 0, \frac{\partial^2 \log L}{\partial \text{cov}_A \partial \text{cov}_B} = 0.$$



The derivatives included in the upper left  $10 \times 10$  part of the above matrix are completely analogous to the ones derived in the previous subsection. Counting the matrix columns from left to right, note also that given the derivatives of the 11th column, the derivatives of the 12th column can be straightforwardly obtained by simple substitution of the corresponding parameters involved. Regarding the derivatives of the 11th column, we derive:

$$\begin{aligned}\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1A}^{(\lambda_1)} \partial \lambda_1} &= \sum_{i=1}^{n_A} \frac{\sigma_{2A}^{(\lambda_2)^2} (W_{1Ai}^{\lambda_1} \lambda_1 \log(W_{1Ai}) - W_{1Ai}^{\lambda_1} + 1)}{\lambda_1^2 \left( \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - \text{cov}_A^{(\lambda_1, 2)^2} \right)} \\ \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A}^{(\lambda_1)} \partial \lambda_1} &= \sum_{i=1}^{n_A} \frac{2 \sigma_{1A}^{(\lambda_1)} \sigma_{2A}^{(\lambda_2)^2} (K_{1i}) (K_{2i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - \text{cov}_A^{(\lambda_1, 2)^2} \right)^2}\end{aligned}$$

where,

$$\begin{aligned}K_{1i} &= W_{1Ai}^{\lambda_1} \lambda_1 \log(W_{1Ai}) - W_{1Ai}^{\lambda_1} + 1 \\ K_{2i} &= \text{cov}_A^{(\lambda_1, 2)} \lambda_1 (1 - W_{2Ai}^{\lambda_2} \lambda_2) - \lambda_2 \sigma_{2A}^{(\lambda_2)^2} (1 + W_{1Ai}^{\lambda_1}) + (\lambda_1 \lambda_2) (\text{cov}_A^{(\lambda_1, 2)} \mu_{2A}^{(\lambda_2)} - \mu_{1A}^{(\lambda_1)} \sigma_{2A}^{(\lambda_2)^2})\end{aligned}$$

$$\begin{aligned}\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1B}^{(\lambda_1)} \partial \lambda_1} &= \sum_{i=1}^{n_B} \frac{\sigma_{2B}^{(\lambda_1)^2} (W_{1Bi}^{\lambda_1} \lambda_1 \log(W_{1Bi}) - W_{1Bi}^{\lambda_1} + 1)}{\lambda_1^2 \left( \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - \text{cov}_B^{(\lambda_1, 2)^2} \right)} \\ \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B}^{(\lambda_1)} \partial \lambda_1} &= \sum_{i=1}^{n_B} \frac{2 \sigma_{1B}^{(\lambda_1)} \sigma_{2B}^{(\lambda_1)^2} (K'_{1i}) (K'_{2i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - \text{cov}_B^{(\lambda_1, 2)^2} \right)^2}\end{aligned}$$

where,

$$\begin{aligned}K'_{1i} &= W_{1Bi}^{\lambda_1} \lambda_1 \log(W_{1Bi}) - W_{1Bi}^{\lambda_1} + 1 \\ K'_{2i} &= \text{cov}_B^{(\lambda_1, 2)} \lambda_1 (1 - W_{2Bi}^{\lambda_2} \lambda_2) - \lambda_2 \sigma_{2B}^{(\lambda_1)^2} (1 + W_{1Bi}^{\lambda_1}) + (\lambda_1 \lambda_2) (\text{cov}_B^{(\lambda_1, 2)} \mu_{2B}^{(\lambda_2)} - \mu_{1B}^{(\lambda_1)} \sigma_{2B}^{(\lambda_1)^2})\end{aligned}$$

$$\begin{aligned}\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2A}^{(\lambda_2)} \partial \lambda_1} &= \sum_{i=1}^{n_A} - \frac{\text{cov}_A^{(\lambda_1, 2)} (W_{1Ai}^{\lambda_1} \lambda_1 \log(W_{1Ai}) - W_{1Ai}^{\lambda_1} + 1)}{\lambda_1^2 \left( \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - \text{cov}_A^{(\lambda_1, 2)^2} \right)} \\ \frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A}^{(\lambda_2)} \partial \lambda_1} &= \sum_{i=1}^{n_A} - \frac{2 \text{cov}_A^{(\lambda_1, 2)} \sigma_{2A}^{(\lambda_2)} (K_{1i}) (L_{1i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - \text{cov}_A^{(\lambda_1, 2)^2} \right)^2}\end{aligned}$$

where

$$L_{1i} = \text{cov}_A^{(\lambda_1, 2)} \lambda_2 (1 - W_{1Ai}^{\lambda_2}) - \lambda_1 \sigma_{1A}^{(\lambda_1)^2} (1 + W_{2Ai}^{\lambda_2})^{\lambda_2} + \lambda_1 \lambda_2 (\text{cov}_A^{(\lambda_1, 2)} \mu_{1A}^{(\lambda_1)} - \mu_{2A}^{(\lambda_2)} \sigma_{1A}^{(\lambda_1)^2})$$



$$\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2B}^{(\lambda_2)} \partial \lambda_1} = \sum_{i=1}^{n_B} \frac{\text{cov}_B^{(\lambda_{1,2})} (W_{1Bi}^{\lambda_1} \lambda_1 \log(W_{1Bi}) - W_{1Bi}^{\lambda_1} + 1)}{\lambda_1^2 \left( \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - \text{cov}_B^{(\lambda_{1,2})^2} \right)}$$

$$\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2B}^{(\lambda_2)} \partial \lambda_1} = \sum_{i=1}^{n_B} \frac{2 \text{cov}_B^{(\lambda_{1,2})} \sigma_{2B}^{(\lambda_1)} (K'_{1i}) (L'_{1i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - \text{cov}_B^{(\lambda_{1,2})^2} \right)^2}$$

where

$$L'_{1i} = \text{cov}_B^{(\lambda_{1,2})} \lambda_2 (1 - W_{1Bi}^2) - \lambda_1 \sigma_{1B}^{(\lambda_1)^2} (1 + W_{2Bi})^{\lambda_2} + \lambda_1 \lambda_2 (\text{cov}_B^{(\lambda_{1,2})} \mu_{1B}^{(\lambda_1)} - \mu_{2B}^{(\lambda_2)} \sigma_{1B}^{(\lambda_1)^2})$$

$$\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_A^{(\lambda_{1,2})} \partial \lambda_1} = \sum_{i=1}^{n_A} \frac{(K_{1i}) (M_{1i} + M_{2i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - \text{cov}_A^{(\lambda_{1,2})^2} \right)^2}$$

where

$$M_{1i} = \text{cov}_A^{(\lambda_{1,2})^2} (1 - W_{2Ai}^{\lambda_2}) - 2 \text{cov}_A^{(\lambda_{1,2})} \lambda_2 \sigma_{2A}^{(\lambda_2)^2} (1 - W_{1Ai}^{\lambda_1}) + \lambda_1 \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} + 2W_{1Ai}^{\lambda_1}$$

$$M_{2i} = \lambda_1 \lambda_2 \mu_{2A}^{(\lambda_2)} (\text{cov}_A^{(\lambda_{1,2})^2} + \sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2}) - \lambda_1 \sigma_{2A}^{(\lambda_2)^2} (W_{2Ai}^{\lambda_2} \sigma_{1A}^{(\lambda_1)^2} + 2 \text{cov}_A^{(\lambda_{1,2})} \lambda_2 \mu_{1A}^{(\lambda_1)})$$

$$\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_B^{(\lambda_{1,2})} \partial \lambda_1} = \sum_{i=1}^{n_B} \frac{(K_{1i}) (M_{1i} + M_{2i})}{\lambda_1^3 \lambda_2 \left( \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - \text{cov}_B^{(\lambda_{1,2})^2} \right)^2}$$

where

$$M'_{1i} = \text{cov}_B^{(\lambda_{1,2})^2} (1 - W_{2Bi}^{\lambda_2}) - 2 \text{cov}_B^{(\lambda_{1,2})} \lambda_2 \sigma_{2B}^{(\lambda_1)^2} (1 - W_{1Bi}^{\lambda_1}) + \lambda_1 \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} + 2W_{1Bi}^{\lambda_1}$$

$$M'_{2i} = \lambda_1 \lambda_2 \mu_{2B}^{(\lambda_2)} (\text{cov}_B^{(\lambda_{1,2})^2} + \sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2}) - \lambda_1 \sigma_{2B}^{(\lambda_1)^2} (W_{2Bi}^{\lambda_2} \sigma_{1B}^{(\lambda_1)^2} + 2 \text{cov}_B^{(\lambda_{1,2})} \lambda_2 \mu_{1B}^{(\lambda_1)})$$

$$\frac{\partial^2 l(\mathbf{p})}{\partial \lambda_1^2} = \sum_{i=1}^{n_A} \frac{\frac{2N_{1i}^2 - N_{2i}}{\sigma_{1A}^{(\lambda_1)^2}} + \frac{N_{3i}}{\sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2}}}{\frac{2 \text{cov}_A^{(\lambda_{1,2})^2}}{\sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2}} - 2} + \sum_{i=1}^{n_B} \frac{\frac{2N'_{1i}{}^2 - N'_{2i}}{\sigma_{1B}^{(\lambda_1)^2}} + \frac{N'_{3i}}{\sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2}}}{\frac{2 \text{cov}_B^{(\lambda_{1,2})^2}}{\sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2}} - 2}$$

where,

$$\begin{aligned}
N_{1i} &= \frac{W_{1Ai}^{\lambda_1} - 1}{\lambda_1^2} - \frac{W_{1Ai}^{\lambda_1} \log(W_{1Ai})}{\lambda_1} \\
N_{2i} &= \left( 2\mu_{1A}^{(\lambda_1)} - \frac{2(W_{1Ai}^{\lambda_1} - 1)}{\lambda_1} \right) \left( \frac{2W_{1Ai}^{\lambda_1} - 2}{\lambda_1^3} - \frac{2W_{1Ai}^{\lambda_1} \log(W_{1Ai})}{\lambda_1^2} + \frac{W_{1Ai}^{\lambda_1} \log(W_{1Ai})^2}{\lambda_1} \right) \\
N_{3i} &= 2\text{cov}_A^{(\lambda_1, 2)} \left( \mu_{2A}^{(\lambda_2)} - \frac{W_{2Ai}^{\lambda_2} - 1}{\lambda_2} \right) \left( \frac{2W_{1Ai}^{\lambda_1} - 2}{\lambda_1^3} - \frac{2W_{1Ai}^{\lambda_1} \log(W_{1Ai})}{\lambda_1^2} + \frac{W_{1Ai}^{\lambda_1} \log(W_{1Ai})^2}{\lambda_1} \right) \\
N'_{1i} &= \frac{W_{1Bi}^{\lambda_1} - 1}{\lambda_1^2} - \frac{W_{1Bi}^{\lambda_1} \log(W_{1Bi})}{\lambda_1} \\
N'_{2i} &= \left( 2\mu_{1B}^{(\lambda_1)} - \frac{2(W_{1Bi}^{\lambda_1} - 1)}{\lambda_1} \right) \left( \frac{2W_{1Bi}^{\lambda_1} - 2}{\lambda_1^3} - \frac{2W_{1Bi}^{\lambda_1} \log(W_{1Bi})}{\lambda_1^2} + \frac{W_{1Bi}^{\lambda_1} \log(W_{1Bi})^2}{\lambda_1} \right) \\
N'_{3i} &= 2\text{cov}_B^{(\lambda_1, 2)} \left( \mu_{2B}^{(\lambda_2)} - \frac{W_{2Bi}^{\lambda_2} - 1}{\lambda_2} \right) \left( \frac{2W_{1Bi}^{\lambda_1} - 2}{\lambda_1^3} - \frac{2W_{1Bi}^{\lambda_1} \log(W_{1Bi})}{\lambda_1^2} + \frac{W_{1Bi}^{\lambda_1} \log(W_{1Bi})^2}{\lambda_1} \right)
\end{aligned}$$

$$\begin{aligned}
\frac{\partial^2 l(\mathbf{p})}{\partial \lambda_1 \partial \lambda_2} &= \sum_{i=1}^{n_A} \frac{2\text{cov}_A^{(\lambda_1, 2)} \left( W_{1Ai}^{\lambda_1} \lambda_1 \log(W_{1Ai}) - W_{1Ai}^{\lambda_1} + 1 \right) \left( W_{2Ai}^{\lambda_2} \lambda_2 \log(W_{2Ai}) - W_{2Ai}^{\lambda_2} + 1 \right)}{\lambda_1^2 \lambda_2^2 \left( 2\sigma_{1A}^{(\lambda_1)^2} \sigma_{2A}^{(\lambda_2)^2} - 2\text{cov}_A^{(\lambda_1, 2)^2} \right)} \\
&+ \sum_{i=1}^{n_B} \frac{2\text{cov}_B^{(\lambda_1, 2)} \left( W_{1Bi}^{\lambda_1} \lambda_1 \log(W_{1Bi}) - W_{1Bi}^{\lambda_1} + 1 \right) \left( W_{2Bi}^{\lambda_2} \lambda_2 \log(W_{2Bi}) - W_{2Bi}^{\lambda_2} + 1 \right)}{\lambda_1^2 \lambda_2^2 \left( 2\sigma_{1B}^{(\lambda_1)^2} \sigma_{2B}^{(\lambda_1)^2} - 2\text{cov}_B^{(\lambda_1, 2)^2} \right)}.
\end{aligned}$$

Derivatives included in the last column of Fisher's information matrix:  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1A}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1B}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2A}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A}^{(\lambda_1)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_A^{(\lambda_1, 2)} \partial \lambda_2}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_B^{(\lambda_1, 2)} \partial \lambda_2}$ , are respectively completely analogous to  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1A}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1A}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{1B}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{1B}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2A}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2A}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \mu_{2B}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \sigma_{2B}^{(\lambda_1)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_A^{(\lambda_1, 2)} \partial \lambda_1}$ ,  $\frac{\partial^2 l(\mathbf{p})}{\partial \text{cov}_B^{(\lambda_1, 2)} \partial \lambda_1}$  and can be obtained by simple substitution of  $W_{1A}$ ,  $W_{1B}$ ,  $\lambda_1$ ,  $\mu_{1A}$  and  $\mu_{1B}$  with  $W_{2A}$ ,  $W_{2B}$ ,  $\lambda_2$ ,  $\mu_{2A}$ ,  $\mu_{2B}$ , respectively.

## 1.7 Normality with covariates

Here, we restate and derive all derivatives of matrix  $M_A$ . All derivatives contained in matrix  $M_B$  are completely analogous to the ones that follow.

$$M_A = \begin{pmatrix} \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)^2}} & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \partial \beta_j^{(1A)}} & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \partial \beta_p^{(2A)}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \partial \sigma_{1A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \partial \sigma_{2A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \partial cov_A} \\ \vdots & \cdots & \vdots & \cdots & \vdots & \vdots & \vdots & \vdots \\ \vdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)^2}} & \cdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)} \partial \sigma_{1A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)} \partial \sigma_{2A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)} \partial cov_A} \\ \vdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)} \partial \beta_{j'}^{(1A)}} & \cdots & \cdots & \cdots & \cdots & \cdots \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_p^{(2A)} \partial \beta_0^{(1A)}} & \cdots & \cdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_p^{(2A)^2}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_p^{(2A)} \partial \sigma_{1A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_p^{(2A)} \partial \sigma_{2A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_p^{(2A)} \partial cov_A} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial \beta_0^{(1A)}} & \cdots & \cdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial \beta_p^{(2A)}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A}^2} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial \sigma_{2A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial cov_A} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A} \partial \beta_0^{(1A)}} & \cdots & \cdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A} \partial \beta_p^{(2A)}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A} \partial \sigma_{1A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A}^2} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A} \partial cov_A} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial cov_A \partial \beta_0^{(1A)}} & \cdots & \cdots & \cdots & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial cov_A \partial \beta_p^{(2A)}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial cov_A \partial \sigma_{1A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial cov_A \partial \sigma_{2A}} & \frac{\partial^2 l(\mathbf{p}_Z)}{\partial cov_A^2} \end{pmatrix} \quad ((p+4) \times (p+4)).$$

$$\begin{aligned} \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)^2}} &= -\frac{n_A}{\sigma_{1A}^2 - \frac{cov_A^2}{\sigma_{2A}^2}} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \beta_j^{(1A)}} &= -\sum_{i=1}^{n_A} \frac{Z_{ji}^{(1A)}}{\sigma_{1A}^2 - \frac{cov_A^2}{\sigma_{2A}^2}} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \beta_j^{(2A)}} &= \sum_{i=1}^{n_A} \frac{Z_{ji}^{(2A)} cov_A}{\sigma_{1A}^2 \sigma_{2A}^2 - cov_A^2} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \sigma_{1A}} &= 0 \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} \sigma_{2A}} &= 0 \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_0^{(1A)} cov_A} &= 0 \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)^2}} &= -\sum_{i=1}^{n_A} \frac{Z_{ji}^{(1A)}}{\sigma_{1A}^2 - \frac{cov_A^2}{\sigma_{2A}^2}} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(2A)^2}} &= -\sum_{i=1}^{n_A} \frac{Z_{ji}^{(2A)}}{\sigma_{2A}^2 - \frac{cov_A^2}{\sigma_{1A}^2}} \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(1A)} \beta_{j'}^{(1A)}} &= -\sum_{i=1}^{n_A} \frac{Z_j^{(1A)} Z_{j'}^{(1A)}}{\sigma_{1A}^2 - \frac{cov_A^2}{\sigma_{2A}^2}}, j \neq j' \\ \frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_j^{(2A)} \beta_{j'}^{(2A)}} &= -\sum_{i=1}^{n_A} \frac{Z_j^{(2A)} Z_{j'}^{(2A)}}{\sigma_{2A}^2 - \frac{cov_A^2}{\sigma_{1A}^2}}, j \neq j' \end{aligned}$$

$$\begin{aligned}
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(1A)} \sigma_{1A}} &= \sigma_{1A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(1A)} \text{cov}_A \sigma_{2A}^2 (W_{2Ai} - \beta_0^{(2A)} - \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sigma_{1A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(1A)} \sigma_{2A}^4 (W_{1Ai} - \beta_0^{(1A)} - \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(2A)} \sigma_{2A}} &= \sigma_{2A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(2A)} \text{cov}_A \sigma_{1A}^2 (W_{1Ai} - \beta_0^{(1A)} - \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sigma_{2A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(2A)} \sigma_{1A}^4 (W_{2Ai} - \beta_0^{(2A)} - \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(1A)} \sigma_{2A}} &= \sigma_{2A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(1A)} \text{cov}_A \sigma_{1A}^2 (W_{2Ai} - \beta_0^{(2A)} - \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sigma_{2A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(1A)} \text{cov}_A^2 (W_{1Ai} - \beta_0^{(1A)} - \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(2A)} \sigma_{1A}} &= \sigma_{1A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(2A)} \text{cov}_A \sigma_{2A}^2 (W_{1Ai} - \beta_0^{(1A)} - \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sigma_{1A} \sum_{i=1}^{n_A} \frac{2Z_{ki}^{(2A)} \text{cov}_A^2 (W_{2Ai} - \beta_0^{(2A)} - \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(1A)} \text{cov}_A} &= - \sum_{i=1}^{n_A} \sigma_{2A}^2 \frac{2Z_{ki}^{(1A)} \text{cov}_A (\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)} - W_{1Ai})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sum_{i=1}^{n_A} \frac{Z_{ki}^{(1A)} \sigma_{1A}^2 \sigma_{2A}^2 (\beta_0^{(2A)} + \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)} - W_{2Ai})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sum_{i=1}^{n_A} \frac{Z_{ki}^{(1A)} \text{cov}_A^2 (\beta_0^{(2A)} + \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)} - W_{2Ai})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \beta_k^{(2A)} \text{cov}_A} &= - \sum_{i=1}^{n_A} \sigma_{1A}^2 \frac{2Z_{ki}^{(2A)} \text{cov}_A (\beta_0^{(2A)} + \sum_{j=1}^p \beta_j^{(2A)} Z_{ji}^{(2A)} - W_{2Ai})}{(\sigma_{2A}^2 \sigma_{1A}^2 - \text{cov}_A^2)^2} \\
&- \sum_{i=1}^{n_A} \frac{Z_{ki}^{(2A)} \sigma_{2A}^2 \sigma_{1A}^2 (\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)} - W_{1Ai})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2} \\
&- \sum_{i=1}^{n_A} \frac{Z_{ki}^{(2A)} \text{cov}_A^2 (\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_{ji}^{(1A)} - W_{1Ai})}{(\sigma_{1A}^2 \sigma_{2A}^2 - \text{cov}_A^2)^2}
\end{aligned}$$

and the remaining derivatives  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A}^2}$ ,  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A}^2}$ ,  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial \sigma_{2A}}$ ,  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{1A} \partial \text{cov}_A}$ ,  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \sigma_{2A} \partial \text{cov}_A}$  and  $\frac{\partial^2 l(\mathbf{p}_Z)}{\partial \text{cov}_A^2}$  are analogous to their counterparts presented in section (1.5).

## 1.8 Partial derivatives for the construction of the $Z$ test in the setting where covariates are present

$$\begin{aligned}
\frac{\partial ROC_{1,Z}(t)}{\partial \beta_0^{(1A)}} &= -\frac{\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
\frac{\partial ROC_{1,Z}(t)}{\partial \beta_j^{(1A)}} &= -\frac{z_j^{(1A)}\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
\frac{\partial ROC_{1,Z}(t)}{\partial \beta_0^{(1B)}} &= \frac{\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
\frac{\partial ROC_{1,Z}(t)}{\partial \beta_j^{(1B)}} &= \frac{z_j^{(1B)}\sqrt{2}}{2\sqrt{\pi}\sigma_{1B}} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
\frac{\partial ROC_{1,Z}(t)}{\partial \sigma_{1A}} &= \frac{-\sigma_{1B}\Phi^{-1}(t)}{\sqrt{2\pi}\sigma_{1A}^2} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
\frac{\partial ROC_{1,Z}(t)}{\partial \sigma_{1B}} &= \frac{1}{3\pi\sqrt{2}} \exp\left(-\frac{1}{2}\left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}} - \frac{\sigma_{1B}\Phi^{-1}(t)}{\sigma_{1A}}\right)^2\right) \\
&\quad \times \left(\frac{\beta_0^{(1A)} + \sum_{j=1}^p \beta_j^{(1A)} Z_j^{(1A)} - (\beta_0^{(1B)} + \sum_{j=1}^p \beta_j^{(1B)} Z_j^{(1B)})}{\sigma_{1B}^2} + \frac{\Phi^{-1}(t)}{\sigma_{1A}}\right)
\end{aligned}$$

## 2 Figure: Box-Cox-based ROC curves for the prostate cancer data

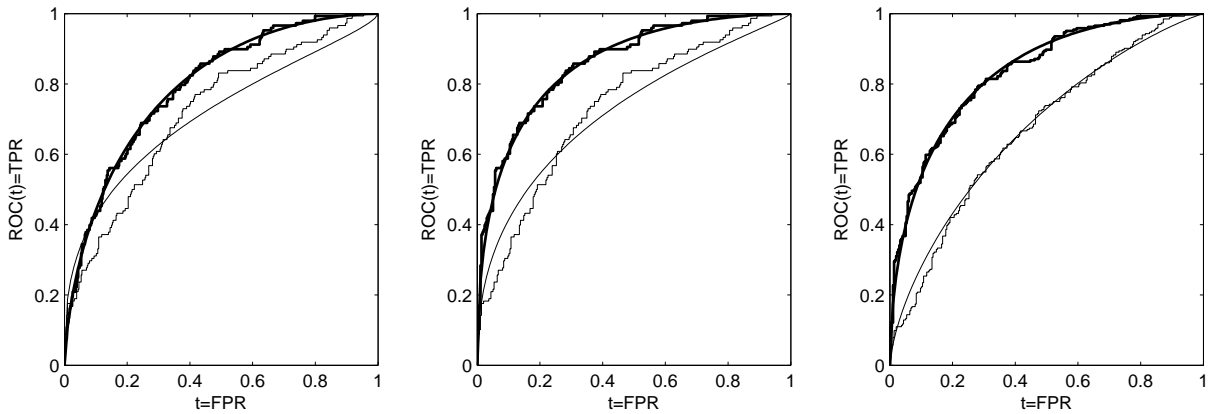


Figure 1: ROC estimates obtained from empirical-based and Box-Cox approaches for PSA alone (thin line) and the combined biomarker values (thick line). Left to right (i.e., scenarios (1) to (3)) for the empirical-based approach: ( $AUC_{PSA} = 0.7185$ ,  $AUC_C = 0.7933$ ), ( $AUC_{PSA} = 0.7347$ ,  $AUC_C = 0.8620$ ), ( $AUC_{PSA} = 0.6682$ ,  $AUC_C = 0.8342$ ). Left to right (i.e., scenarios (1) to (3)) for the Box-Cox approach: ( $AUC_{PSA} = 0.7118$ ,  $AUC_C = 0.7946$ ), ( $AUC_{PSA} = 0.7242$ ,  $AUC_C = 0.8597$ ), ( $AUC_{PSA} = 0.6728$ ,  $AUC_C = 0.8345$ ).

## Web-Appendix C (Additional Simulation results)

Table 9: Comparison of sizes of BTI and BTII confidence intervals by Qin et al. (2006). Simulation results of 1000 replications for the scenario in which data representing diseased and healthy individuals are generated by the same bivariate normal distributions (valid null hypothesis since  $ROC_1(t) = ROC_2(t)$ ). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7$ , and  $0.8$ . Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4, 0.6$  for the data of both the healthy and diseased individuals.

		Size results									
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	BTI				BTII				
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	
100, 100	0.2	0.6	0.032	0.064	0.052	0.049	0.031	0.042	0.038	0.035	
		0.7	0.046	0.045	0.042	0.030	0.029	0.038	0.027	0.018	
		0.8	0.029	0.031	0.031	0.017	0.021	0.025	0.023	0.008	
	0.4	0.6	0.048	0.059	0.040	0.040	0.034	0.047	0.029	0.024	
		0.7	0.045	0.046	0.039	0.031	0.030	0.033	0.025	0.017	
		0.8	0.030	0.035	0.025	0.021	0.020	0.022	0.020	0.008	
	0.6	0.6	0.039	0.052	0.035	0.031	0.023	0.036	0.025	0.020	
		0.7	0.035	0.044	0.041	0.027	0.026	0.027	0.017	0.012	
		0.8	0.032	0.027	0.026	0.013	0.023	0.017	0.015	0.004	
200, 200	0.2	0.6	0.060	0.047	0.057	0.041	0.048	0.039	0.052	0.036	
		0.7	0.054	0.052	0.048	0.042	0.046	0.040	0.040	0.033	
		0.8	0.051	0.049	0.043	0.031	0.043	0.040	0.033	0.020	
	0.4	0.6	0.0470	0.043	0.044	0.032	0.037	0.043	0.039	0.025	
		0.7	0.0470	0.046	0.047	0.034	0.039	0.043	0.036	0.030	
		0.8	0.0470	0.054	0.035	0.025	0.029	0.044	0.027	0.018	
	0.6	0.6	0.0360	0.046	0.052	0.028	0.026	0.034	0.035	0.027	
		0.7	0.0450	0.043	0.041	0.035	0.032	0.037	0.030	0.025	
		0.8	0.0390	0.046	0.036	0.023	0.037	0.031	0.026	0.012	
100, 200	0.2	0.6	0.043	0.051	0.052	0.054	0.039	0.036	0.038	0.037	
		0.7	0.043	0.046	0.038	0.036	0.031	0.036	0.035	0.023	
		0.8	0.051	0.032	0.033	0.026	0.037	0.030	0.029	0.013	
	0.4	0.6	0.040	0.034	0.044	0.043	0.033	0.025	0.034	0.028	
		0.7	0.038	0.042	0.039	0.034	0.030	0.031	0.032	0.021	
		0.8	0.048	0.030	0.032	0.027	0.034	0.021	0.023	0.015	
	0.6	0.6	0.035	0.030	0.040	0.032	0.027	0.021	0.028	0.018	
		0.7	0.043	0.039	0.039	0.025	0.028	0.020	0.022	0.013	
		0.8	0.054	0.026	0.036	0.016	0.039	0.016	0.019	0.006	

Table 10: Comparison of sizes of BTI and BTII confidence intervals by Qin et al. (2006). Simulation results of 1000 replications for the scenario in which data representing diseased and healthy individuals are generated by the same bivariate gamma distributions (valid null hypothesis since  $ROC_1(t) = ROC_2(t)$ ). The data are generated such that  $AUC_1 = AUC_2 = 0.6, 0.7$ , and  $0.8$ . Sample sizes explored are  $(100, 100)$ ,  $(200, 200)$  and  $(100, 200)$ . Correlation is set equal to  $\rho = 0.2, 0.4, 0.6$  for the data of both the healthy and diseased individuals.

		Size results									
$n_A, n_B$	$\rho$	$AUC_1 = AUC_2$	BTI				BTII				
			$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	$t = 0.2$	$t = 0.4$	$t = 0.6$	$t = 0.8$	
100, 100	0.2	0.6	0.038	0.040	0.038	0.042	0.027	0.032	0.028	0.032	
		0.7	0.043	0.042	0.044	0.035	0.035	0.029	0.027	0.028	
		0.8	0.042	0.045	0.035	0.022	0.030	0.033	0.025	0.010	
	0.4	0.6	0.033	0.041	0.040	0.041	0.019	0.024	0.028	0.029	
		0.7	0.039	0.040	0.041	0.037	0.021	0.022	0.026	0.022	
		0.8	0.043	0.031	0.033	0.017	0.031	0.021	0.020	0.010	
	0.6	0.6	0.033	0.049	0.036	0.036	0.022	0.034	0.022	0.023	
		0.7	0.037	0.035	0.032	0.026	0.023	0.026	0.017	0.012	
		0.8	0.029	0.036	0.030	0.008	0.017	0.023	0.012	0.002	
200, 200	0.2	0.6	0.057	0.039	0.037	0.045	0.051	0.0310	0.036	0.035	
		0.7	0.049	0.035	0.036	0.039	0.042	0.0350	0.034	0.029	
		0.8	0.048	0.042	0.037	0.028	0.032	0.0410	0.032	0.017	
	0.4	0.6	0.042	0.041	0.047	0.040	0.028	0.0310	0.035	0.028	
		0.7	0.034	0.033	0.036	0.028	0.026	0.0280	0.020	0.022	
		0.8	0.037	0.046	0.034	0.026	0.028	0.0400	0.027	0.014	
	0.6	0.6	0.028	0.042	0.038	0.041	0.023	0.029	0.032	0.027	
		0.7	0.037	0.039	0.035	0.046	0.023	0.028	0.023	0.029	
		0.8	0.027	0.036	0.051	0.026	0.023	0.024	0.039	0.022	
100, 200	0.2	0.6	0.043	0.049	0.048	0.052	0.034	0.036	0.043	0.041	
		0.7	0.048	0.041	0.048	0.040	0.040	0.036	0.034	0.025	
		0.8	0.049	0.037	0.036	0.021	0.035	0.030	0.030	0.014	
	0.4	0.6	0.041	0.047	0.035	0.034	0.034	0.028	0.027	0.017	
		0.7	0.038	0.045	0.039	0.037	0.024	0.033	0.026	0.026	
		0.8	0.042	0.039	0.022	0.021	0.027	0.020	0.021	0.010	
	0.6	0.6	0.034	0.040	0.046	0.039	0.024	0.029	0.037	0.026	
		0.7	0.039	0.034	0.029	0.026	0.026	0.022	0.021	0.015	
		0.8	0.037	0.033	0.036	0.016	0.022	0.023	0.015	0.007	



Table 11: Power simulation results of 1000 replications for the normal setting (non-valid null hypothesis) under different scenarios. The BTI and BTII methods are considered. Sample sizes explored are (50, 50), (100, 100), and (200, 200). Correlation is set equal to  $\rho = 0.2, 0.4$ , and  $0.6$  for data of both the healthy and diseased individuals. The true difference  $ROC_2(t) - ROC_1(t)$  to be detected is denoted by  $d$ .

Power results									
Normals									
BTI					BTII				
$n_A, n_B$	$\rho$	$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$	$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$
50, 50	0.2	0.518	0.415	0.285	0.100	0.504	0.421	0.256	0.085
	0.4	0.574	0.454	0.294	0.097	0.568	0.436	0.269	0.087
	0.6	0.636	0.504	0.319	0.105	0.644	0.490	0.292	0.083
100, 100	0.2	0.826	0.754	0.622	0.306	0.848	0.774	0.632	0.302
	0.4	0.860	0.802	0.653	0.319	0.891	0.812	0.665	0.301
	0.6	0.923	0.833	0.695	0.338	0.944	0.870	0.725	0.329
200, 200	0.2	0.984	0.966	0.906	0.646	0.987	0.972	0.925	0.689
	0.4	0.995	0.972	0.930	0.667	0.997	0.984	0.936	0.703
	0.6	1.000	0.989	0.952	0.705	1.000	0.996	0.962	0.749
Gammass									
BTI					BTII				
$n_A, n_B$	$\rho$	$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$	$d = 0.20$	$d = 0.15$	$d = 0.10$	$d = 0.05$
50, 50	0.2	0.329	0.271	0.186	0.080	0.303	0.264	0.174	0.064
	0.4	0.341	0.294	0.204	0.083	0.324	0.265	0.182	0.076
	0.6	0.423	0.338	0.221	0.099	0.399	0.316	0.199	0.071
100, 100	0.2	0.562	0.518	0.376	0.194	0.560	0.509	0.372	0.176
	0.4	0.619	0.535	0.405	0.228	0.617	0.537	0.408	0.221
	0.6	0.743	0.623	0.445	0.217	0.754	0.624	0.445	0.194
200, 200	0.2	0.841	0.778	0.648	0.403	0.851	0.781	0.662	0.419
	0.4	0.892	0.851	0.747	0.477	0.893	0.861	0.755	0.480
	0.6	0.947	0.910	0.797	0.512	0.956	0.919	0.816	0.518