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Supplementary material to "Two-stage Biomarker Panel Study and Estimation Allowing Early Termination for Futility"

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k	n	Fixed Sample $\hat\beta$	Koopmeiners & Vogel $\hat\beta$	Two-Stage Design with $m=n/2$ $\hat\beta_{all}$	$\hat\beta_{s2}$	$\hat\beta_{cond}$
				$\gamma_0 = 0.55$		
2	1600	(0.50, 1.01)	(0.50, 1.01)	(0.50, 1.01)	(0.51, 1.01)	(0.51, 1.01)
	800	(0.51, 1.01)	(0.51, 1.01)	(0.50, 1.02)	(0.51, 1.03)	(0.51, 1.03)
	400	(0.52, 1.01)	(0.52, 1.02)	(0.51, 1.03)	(0.52, 1.06)	(0.51, 1.03)
	200	(0.56, 1.09)	(0.57, 1.09)	(0.54, 1.06)	(0.54, 1.11)	(0.53, 1.08)
4	1600	(0.40, 0.51, 0.49, 0.50)	(0.40, 0.51, 0.49, 0.50)	(0.40, 0.51, 0.51, 0.51)	(0.40, 0.51, 0.51, 0.51)	(0.40, 0.51, 0.51, 0.51)
	800	(0.40, 0.53, 0.51, 0.53)	(0.41, 0.53, 0.51, 0.54)	(0.41, 0.51, 0.51, 0.51)	(0.42, 0.52, 0.52, 0.52)	(0.42, 0.51, 0.51, 0.52)
	400	(0.46, 0.54, 0.50, 0.54)	(0.47, 0.54, 0.51, 0.54)	(0.42, 0.52, 0.52, 0.52)	(0.44, 0.53, 0.55, 0.54)	(0.44, 0.54, 0.55, 0.54)
	200	(0.39, 0.55, 0.55, 0.54)	(0.39, 0.56, 0.53, 0.55)	(0.43, 0.54, 0.54, 0.54)	(0.47, 0.61, 0.59, 0.60)	(0.46, 0.60, 0.59, 0.61)
				$\gamma_0 = 0.59$		
2	1600	(0.50, 1.01)	(0.50, 1.01)	(0.51, 1.01)	(0.51, 1.01)	(0.51, 1.01)
	800	(0.51, 1.01)	(0.51, 1.01)	(0.51, 1.03)	(0.51, 1.03)	(0.51, 1.03)
	400	(0.52, 1.03)	(0.52, 1.04)	(0.52, 1.04)	(0.54, 1.06)	(0.53, 1.06)
	200	(0.53, 1.09)	(0.54, 1.08)	(0.54, 1.10)	(0.54, 1.14)	(0.54, 1.12)
4	1600	(0.40, 0.51, 0.49, 0.50)	(0.40, 0.51, 0.49, 0.50)	(0.40, 0.51, 0.51, 0.51)	(0.41, 0.51, 0.51, 0.52)	(0.41, 0.51, 0.51, 0.51)
	800	(0.40, 0.53, 0.51, 0.53)	(0.40, 0.54, 0.51, 0.53)	(0.41, 0.51, 0.51, 0.51)	(0.42, 0.52, 0.52, 0.52)	(0.42, 0.52, 0.51, 0.52)
	400	(0.46, 0.54, 0.50, 0.54)	(0.47, 0.54, 0.51, 0.54)	(0.42, 0.52, 0.52, 0.51)	(0.43, 0.53, 0.54, 0.54)	(0.44, 0.54, 0.54, 0.54)
	200	(0.39, 0.55, 0.55, 0.54)	(0.40, 0.52, 0.56, 0.55)	(0.43, 0.54, 0.54, 0.54)	(0.47, 0.59, 0.58, 0.60)	(0.47, 0.59, 0.58, 0.59)
				$\gamma_0 = 0.65$		
2	1600	(0.50, 1.01)	(0.50, 1.01)	(0.51, 1.02)	(0.51, 1.01)	(0.51, 1.01)
	800	(0.51, 1.01)	(0.52, 1.00)	(0.51, 1.02)	(0.51, 1.03)	(0.51, 1.03)
	400	(0.52, 1.01)	(0.51, 0.98)	(0.52, 1.04)	(0.52, 1.06)	(0.52, 1.07)
	200	(0.56, 1.09)	(0.53, 1.12)	(0.54, 1.06)	(0.56, 1.11)	(0.56, 1.12)
4	1600	(0.40, 0.51, 0.49, 0.50)	(0.41, 0.51, 0.49, 0.50)	(0.40, 0.51, 0.51, 0.51)	(0.41, 0.51, 0.51, 0.52)	(0.41, 0.51, 0.51, 0.51)
	800	(0.40, 0.53, 0.51, 0.53)	(0.40, 0.54, 0.50, 0.53)	(0.41, 0.51, 0.51, 0.51)	(0.42, 0.52, 0.52, 0.52)	(0.42, 0.52, 0.51, 0.52)
	400	(0.46, 0.54, 0.50, 0.54)	(0.45, 0.54, 0.51, 0.55)	(0.42, 0.52, 0.52, 0.52)	(0.43, 0.53, 0.54, 0.53)	(0.42, 0.54, 0.54, 0.52)
	200	(0.39, 0.55, 0.55, 0.54)	(0.44, 0.52, 0.55, 0.54)	(0.43, 0.55, 0.53, 0.53)	(0.47, 0.60, 0.58, 0.59)	(0.46, 0.57, 0.58, 0.60)
				$\gamma_0 = 0.70$		
2	1600	(0.50, 1.01)	(0.52, 1.03)	(0.50, 1.01)	(0.51, 1.01)	(0.51, 1.01)
	800	(0.51, 1.01)	(0.50, 1.04)	(0.50, 1.02)	(0.51, 1.03)	(0.51, 1.03)
	400	(0.52, 1.01)	(0.49, 1.05)	(0.52, 1.05)	(0.52, 1.06)	(0.53, 1.08)
	200	(0.56, 1.09)	(0.54, 1.11)	(0.54, 1.07)	(0.56, 1.11)	(0.56, 1.10)
4	1600	(0.40, 0.51, 0.49, 0.50)	(0.42, 0.51, 0.51, 0.48)	(0.41, 0.53, 0.53, 0.53)	(0.40, 0.51, 0.51, 0.51)	(0.41, 0.51, 0.51, 0.51)
	800	(0.40, 0.53, 0.51, 0.53)	(0.41, 0.51, 0.53, 0.53)	(0.43, 0.52, 0.52, 0.52)	(0.42, 0.52, 0.52, 0.52)	(0.42, 0.52, 0.52, 0.52)
	400	(0.46, 0.54, 0.50, 0.54)	(0.47, 0.56, 0.51, 0.53)	(0.43, 0.53, 0.54, 0.53)	(0.44, 0.53, 0.55, 0.54)	(0.44, 0.53, 0.56, 0.55)
	200	(0.39, 0.55, 0.55, 0.54)	(0.41, 0.54, 0.55, 0.54)	(0.44, 0.53, 0.54, 0.55)	(0.47, 0.61, 0.59, 0.60)	(0.47, 0.60, 0.59, 0.58)

Table 1. Simulation results on $\hat\beta$comparing performance between fixed sample design, Koopmeiners & Vogel approach and the proposed two-stage design with $m = n/2$. True β is $(0.5, 1)^T$ for $k = 2$ and $(0.4, 0.5, 0.5, 0.5)^T$ for $k = 4$.

		Fixed Sample		Koopmeiners & Vogel			Two-Stage Design with $m = 0.33n$				
k	n	$\hat{ROC}(0.2)$(se)	# samples	$\hat{ROC}(0.2)$(se)	%($C=1$).	# samples	$\hat{ROC}_{all}(0.2)(se)$	$\hat{ROC}_{s2}(0.2)(se)$	$\hat{ROC}_{cond}(0.2)$(se)	%($C=1$)	# samples
					$\gamma_0 = 0.55$						
2	1600	0.590 (0.041)	1600	0.589 (0.035)	81.4	1451	0.590 (0.028)	0.590 (0.034)	0.590 (0.027)	100.0	1600
	800	0.589 (0.057)	800	0.588 (0.050)	75.2	701	0.592 (0.038)	0.591 (0.045)	0.592(0.037)	99.8	799
	400	0.586 (0.081)	400	0.584 (0.070)	71.2	342	0.589 (0.052)	0.587 (0.062)	0.588 (0.049)	100.0	400
	200	0.582 (0.114)	200	0.577 (0.101)	69.1	169	0.584 (0.072)	0.576 (0.088)	0.581 (0.069)	100.0	200
4	1600	0.587 (0.040)	1600	0.585 (0.035)	83.4	1467	0.587 (0.027)	0.586 (0.033)	0.586 (0.026)	100.0	1600
	800	0.584 (0.058)	800	0.580 (0.050)	78.9	716	0.588 (0.037)	0.585 (0.046)	0.585 (0.036)	100.0	800
	400	0.578 (0.081)	400	0.570 (0.073)	76.7	353	0.575 (0.051)	0.570 (0.063)	0.569 (0.050)	100.0	400
	200	0.566 (0.117)	200	0.551 (0.106)	77.3	177	0.569 (0.075)	0.559 (0.090)	0.559 (0.072)	100.0	200
					$\gamma_0 = 0.59$						
2	1600	0.590 (0.041)	1600	0.589 (0.035)	46.9	1175	0.591 (0.027)	0.591 (0.034)	0.590 (0.027)	99.2	1594
	800	0.589 (0.057)	800	0.588 (0.050)	48.6	594	0.592 (0.038)	0.591 (0.045)	0.591 (0.037)	99.6	798
	400	0.586 (0.081)	400	0.584 (0.070)	52.9	306	0.589 (0.051)	0.586 (0.062)	0.588 (0.049)	99.6	399
	200	0.582 (0.114)	200	0.578 (0.100)	56.5	157	0.584 (0.072)	0.576 (0.088)	0.580 (0.069)	100.0	200
4	1600	0.587 (0.040)	1600	0.585 (0.035)	49.4	1195	0.587 (0.027)	0.586 (0.033)	0.586 (0.027)	98.7	1590
	800	0.584 (0.058)	800	0.580 (0.050)	54.4	617	0.588 (0.037)	0.585 (0.046)	0.585 (0.036)	99.8	799
	400	0.578 (0.081)	400	0.571 (0.073)	60.2	320	0.576 (0.051)	0.570 (0.063)	0.569 (0.050)	99.0	398
	200	0.566 (0.117)	200	0.551 (0.106)	65.8	166	0.569 (0.075)	0.560 (0.090)	0.559 (0.072)	99.8	199
					$\gamma_0 = 0.65$						
2	1600	0.590 (0.041)	1600	0.588 (0.036)	12.8	902	0.593 (0.027)	0.590 (0.034)	0.590 (0.028)	91.5	1532
	800	0.589 (0.057)	800	0.589 (0.050)	22.4	489	0.593 (0.037)	0.591 (0.045)	0.591 (0.038)	98.0	792
	400	0.586 (0.081)	400	0.584 (0.070)	31.9	264	0.590 (0.051)	0.586 (0.062)	0.588 (0.050)	97.9	396
	200	0.582 (0.114)	200	0.577 (0.100)	42.7	143	0.584 (0.072)	0.576 (0.088)	0.580 (0.070)	99.7	199
4	1600	0.587 (0.040)	1600	0.586 (0.035)	15.0	920	0.590 (0.027)	0.586 (0.033)	0.585 (0.028)	89.2	1514
	800	0.584 (0.058)	800	0.580 (0.050)	26.5	506	0.590 (0.037)	0.585 (0.046)	0.585 (0.037)	95.3	781
	400	0.578 (0.081)	400	0.571 (0.072)	38.9	278	0.577 (0.051)	0.569 (0.063)	0.569 (0.051)	95.6	391
	200	0.566 (0.117)	200	0.552 (0.106)	51.7	152	0.570 (0.074)	0.560 (0.090)	0.559 (0.072)	98.8	199
					$\gamma_0 = 0.70$						
2	1600	0.590 (0.041)	1600	0.587 (0.036)	1.3	810	0.598 (0.027)	0.589 (0.034)	0.589 (0.031)	60.3	1282
	800	0.589 (0.057)	800	0.590 (0.050)	6.4	425	0.597 (0.036)	0.591 (0.045)	0.591 (0.039)	86.4	746
	400	0.586 (0.081)	400	0.583 (0.070)	15.8	232	0.591 (0.051)	0.585 (0.062)	0.587 (0.051)	93.8	388
	200	0.582 (0.114)	200	0.578 (0.100)	27.7	128	0.586 (0.071)	0.577 (0.089)	0.581 (0.070)	98.0	198
4	1600	0.587 (0.040)	1600	0.585 (0.039)	1.5	812	0.596 (0.026)	0.585 (0.032)	0.585 (0.029)	56.4	1251
	800	0.584 (0.058)	800	0.581 (0.051)	8.3	433	0.594 (0.035)	0.585 (0.046)	0.585 (0.038)	80.7	723
	400	0.578 (0.081)	400	0.574 (0.070)	20.9	242	0.580 (0.050)	0.569 (0.064)	0.569 (0.053)	89.2	378
	200	0.566 (0.117)	200	0.553 (0.105)	36.6	137	0.573 (0.073)	0.561 (0.090)	0.559 (0.073)	96.5	197

Table 2. Simulation results on $\hat{ROC}(0.2)$ comparing performance between fixed sample design, Koopmeiners & Vogel approach and the proposed two-stage design with $m = 0.33n$. True $ROC(0.2)$ is 0.591 for $k = 2$ and 0.590 for $k = 4$.