Supplemental Materials of "Deep Historical Borrowing Framework to Prospectively and Simultaneously Synthesize Control Information in Confirmatory Clinical Trials with Multiple Endpoints"

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1 Additional simulation studies

In this section, we conduct additional simulation studies with historical control data in Table S-1. The empirical correlation of estimated response rate $R_{i,j}^{(c)}/n_j^{(c)}$ between two endpoints is 0.52. The constant critical values of MAP and two robust MAPs are chosen at 0.997, 0.992, and 0.986, respectively, to protect the maximum type I error rate approximately at $\alpha = 5\%$ under all three cases in Table S-2. By cross-validation, the selected DNN structure has 2 layers and 40 nodes per layer. Other parameters and settings are same with them in Section 4 of the main article.

Findings are consistent with main text Section 4. On the top of FWER control under all scenarios, our proposed DNN-based method has a higher power than alternatives under $\psi_{1,0}^{(c)} = 0.3, \psi_{2,0}^{(c)} = 0.2$ and $\psi_{1,0}^{(c)} = 0.4, \psi_{2,0}^{(c)} = 0.3$, but MAP is more powerful when $\psi_{1,0}^{(c)} = 0.5, \psi_{2,0}^{(c)} = 0.4$ (Table S-2). In terms of bias, DNN has smaller ones than MAP under prior-data conflict, and also has comparable performance with two RMAPs (Table S-3). MAP has a smaller RMSE than DNN when historical and current data are consistent at $\psi_{1,0}^{(c)} = 0.4, \psi_{2,0}^{(c)} = 0.3$, but DNN is better under prior-data conflicts (Table S-4).

j	1	2	3	4	5	6
$n_j^{(c)}$	100	100	200	200	300	300
$R_{1,j}^{(c)}$	37	38	87	88	125	134
$R_{2,j}^{(c)}$	29	25	53	67	85	92

Table S-1: Control data from $J = 6$ historical studies

				DNN			MAP			RMAP with $w = 50\%$			RMAP with $w = 80\%$		
$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\Delta_{1,0}$	$\Delta_{2,0}$	H_{12}	H_1	H_2	H_{12}	H_1	H_2	H_{12}	H_1	H_2	H_{12}	H_1	H_2
Global null hypothesis															
0.3	0.2	0	0	4.8%	1.5%	3.4%	<0.1%	<0.1%	<0.1%	0.9%	0.5%	0.4%	2.2%	1.2%	1.1%
0.4	0.3			5.1%	1.3%	3.9%	0.3%	<0.1%	0.2%	0.9%	0.2%	0.6%	1.9%	0.7%	1.1%
0.5	0.4			4.9%	0.4%	4.5%	5.0%	2.0%	3.0%	5.1%	2.5%	2.7%	5.1%	2.6%	2.5%
Single null hypothesis															
0.4	0.3	0.1	0	32.7%	30.1%	4.3%	15.7%	15.5%	0.2%	26.0%	25.5%	0.6%	33.7%	32.9%	1.2%
		0	0.1	55.2%	1.2%	54.8%	33.2%	<0.1%	33.2%	41.3%	0.2%	41.2%	44.2%	0.7%	43.8%
Alternative hypothesis															
0.3	0.2	0.1	0.1	74.9%	40.5%	58.2%	8.7%	3.4%	5.5%	32.2%	16.7%	18.6%	51.5%	28.5%	32.2%
		0.12	0.12	87.4%	55.0%	72.5%	18.3%	7.9%	11.2%	48.2%	25.6%	30.4%	68.0%	40.6%	46.2%
0.4	0.3	0.1	0.1	69.7%	31.9%	56.7%	42.5%	15.6%	31.9%	55.7%	25.5%	40.5%	62.2%	32.9%	43.7%
		0.12	0.12	82.6%	44.6%	70.3%	63.6%	29.0%	48.8%	74.6%	41.2%	56.7%	78.8%	48.6%	58.8%
0.5	0.4	0.1	0.1	62.9%	17.6%	56.3%	68.7%	46.3%	41.6%	61.1%	40.5%	34.6%	61.7%	39.7%	36.5%
		0.12	0.12	76.8%	29.2%	69.5%	82.5%	63.0%	52.8%	74.3%	52.8%	45.6%	76.1%	52.9%	49.3%

Table S-2: Type I error rate and power of DNN-based approach, MAP and RMAP

				DNN		MAP		RMAP with $w = 50\%$		RMAP with $w = 80\%$	
$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\Delta_{1,0}$	$\Delta_{2,0}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$
Global null hypothesis											
0.3	0.2	0	0	0.029	0.026	0.048	0.042	0.020	0.023	0.010	0.013
0.4	0.3			0.007	0.005	0.014	-0.005	0.010	-0.003	0.007	-0.001
0.5	0.4			-0.014	-0.017	-0.042	-0.046	-0.024	-0.019	-0.012	-0.008
Single null hypothesis											
0.4	0.3	0.1	0	0.007	0.005	0.014	-0.005	0.011	-0.003	0.007	-0.001
		0	0.1	0.007	0.004	0.014	-0.006	0.011	-0.004	0.007	-0.002
Alternative hypothesis											
0.3	0.2	0.1	0.1	0.029	0.026	0.049	0.042	0.020	0.023	0.010	0.013
		0.12	0.12	0.029	0.025	0.044	0.044	0.019	0.024	0.010	0.014
0.4	0.3	0.1	0.1	0.007	0.005	0.014	-0.005	0.011	-0.003	0.007	-0.001
		0.12	0.12	0.007	0.005	0.014	-0.005	0.011	-0.003	0.007	-0.001
0.5	0.4	0.1	0.1	-0.014	-0.017	-0.043	-0.044	-0.024	-0.019	-0.012	-0.008
		0.12	0.12	-0.014	-0.017	-0.043	-0.044	-0.024	-0.019	-0.013	-0.008

Table S-3: Bias of posterior means $\psi_{1,0}^{(c)}$ and $\psi_{2,0}^{(c)}$ in DNN, MAP and RMAP

				DNN		MAP		RMAP with $w = 50\%$		RMAP with $w = 80\%$	
$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\Delta_{1,0}$	$\Delta_{2,0}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$	$\psi_{1,0}^{(c)}$	$\psi_{2,0}^{(c)}$
Global null hypothesis											
0.3	0.2	0	0	0.042	0.036	0.061	0.050	0.050	0.044	0.043	0.039
0.4	0.3			0.031	0.029	0.021	0.015	0.026	0.021	0.031	0.027
0.5	0.4			0.035	0.036	0.051	0.058	0.047	0.051	0.044	0.045
Single null hypothesis											
0.4	0.3	0.1	0	0.031	0.029	0.022	0.016	0.026	0.021	0.031	0.027
		0	0.1	0.031	0.029	0.022	0.016	0.026	0.021	0.031	0.027
Alternative hypothesis											
0.3	0.2	0.1	0.1	0.042	0.036	0.063	0.051	0.050	0.044	0.043	0.038
		0.12	0.12	0.042	0.036	0.061	0.052	0.050	0.044	0.043	0.039
0.4	0.3	0.1	0.1	0.031	0.029	0.021	0.016	0.026	0.021	0.031	0.027
		0.12	0.12	0.031	0.029	0.022	0.016	0.026	0.021	0.031	0.027
0.5	0.4	0.1	0.1	0.035	0.036	0.050	0.059	0.047	0.051	0.044	0.045
		0.12	0.12	0.035	0.036	0.050	0.060	0.047	0.052	0.044	0.046

Table S-4: RMSE of posterior means $\psi_{1,0}^{(c)}$ and $\psi_{2,0}^{(c)}$ in DNN, MAP and RMAP