Supplemental document of "*DBMS: Dynamic Borrowing Method for Frequentist Hybrid Control Designs Based on Historical-Current Data Similarity*"

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A Appendix

A.1 Bootstrapping procedure

The procedure for the dynamic historical data borrowing method using the parametric bootstrap method is outlined below:

1. Obtain estimators (s_t^2, s_c^2, and s_h^2) of the variance for each group in each trial.
2. Generate bootstrap samples using random numbers from the normal distributions $\mathcal{N}(\widehat{\mu}, s_t^2)$, $\mathcal{N}(\widehat{\mu}, s_c^2)$, and $\mathcal{N}(\widehat{\mu}, s_h^2)$, matching the sample size of each group in each trial.
3. Treat Step 2 as one set and repeat Step 2 to generate B sets of bootstrap data.
4. Calculate the mean, variance, and test statistic for each bootstrap dataset.
5. Arrange the B test statistics in descending order, and use the $\alpha/2 \times B$-th largest test statistic as the rejection threshold for hypothesis testing.

If individual-level data are available for all trials, the non-parametric bootstrap method can also be used:

1. Combine the data from all groups in all trials, and randomly sample data without replacement to match the sample size of each group in each trial to generate bootstrap samples.

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2. Treat Step 1 as one set and repeat Step 1 to generate B sets of bootstrap data.

3. Calculate the mean, variance, and test statistic for each bootstrap dataset.

4. Arrange the B test statistics in descending order, and use the $\alpha/2 \times B$-th largest test statistic as the rejection threshold for hypothesis testing.

A.2 List of methods compared in the simulation

Table 1: List of methods compared in the simulation

Method	Parameter
TTP1	$\alpha_{h1} = 0.05$
TTP2	$\alpha_{h1} = 0.10$
EQ1	$\alpha_{h2} = 0.05$
EQ2	$\alpha_{h2} = 0.10$

A.3 Adjusted significance levels and average amount of dynamic information borrowing

Table 2: Adjusted significance levels and average amount of dynamic information borrowing

Scenario	α^*_{TTP1}	α^*_{TTP2}	α^*_{EQ1}	α^*_{EQ2}	Ave DB-T	Ave DB-L1	Ave DB-L2
1	0.0217	0.0205	0.0250	0.0250	0.701	0.868	0.919
2	0.0217	0.0205	0.0250	0.0227	0.705	0.873	0.922
3	0.0217	0.0205	0.0250	0.0227	0.706	0.873	0.922
4	0.0217	0.0205	0.0209	0.0195	0.706	0.873	0.922
5	0.0217	0.0205	0.0250	0.0250	0.701	0.867	0.918
6	0.0217	0.0205	0.0250	0.0227	0.704	0.871	0.921
7	0.0217	0.0205	0.0250	0.0227	0.704	0.872	0.921
8	0.0217	0.0205	0.0209	0.0195	0.706	0.872	0.922
9	0.0217	0.0205	0.0250	0.0250	0.619	0.789	0.859
10	0.0217	0.0205	0.0250	0.0227	0.549	0.718	0.802
11	0.0217	0.0205	0.0250	0.0227	0.548	0.716	0.802
12	0.0217	0.0205	0.0209	0.0195	0.427	0.582	0.688
13	0.0217	0.0205	0.0250	0.0250	0.621	0.790	0.859
14	0.0217	0.0205	0.0250	0.0227	0.548	0.715	0.800
15	0.0217	0.0205	0.0250	0.0227	0.548	0.715	0.800
16	0.0217	0.0205	0.0209	0.0195	0.429	0.583	0.689
17	0.0217	0.0205	0.0250	0.0250	0.619	0.789	0.858
18	0.0217	0.0205	0.0250	0.0227	0.550	0.718	0.803
19	0.0217	0.0205	0.0250	0.0227	0.548	0.717	0.802
20	0.0217	0.0205	0.0209	0.0195	0.427	0.581	0.687

Table 3: Percentage of borrowing historical data for TTP and EQ

Scenario	$TTP1$	$TTP2$	$EQ1$	$EQ2$
1	94.4	89.3	0.0	0.2
2	94.8	89.9	0.6	17.5
3	94.8	89.9	0.5	17.4
4	94.8	89.8	36.6	59.9
5	94.3	89.2	0.0	0.2
6	94.7	89.6	0.5	17.5
7	94.8	89.7	0.5	17.4
8	94.8	89.8	36.9	60.1
9	88.5	81.1	0.0	0.2
10	82.6	73.4	0.3	10.9
11	82.6	73.2	0.3	10.7
12	70.5	58.8	14.5	26.8
13	88.4	81.0	0.0	0.2
14	82.4	73.2	0.3	10.7
15	82.5	73.1	0.3	10.8
16	70.4	58.9	14.8	27.3
17	88.5	80.9	0.0	0.1
18	82.7	73.5	0.3	10.8
19	82.6	73.4	0.3	10.7
20	70.4	58.6	14.5	27.0

The percentage of borrowing historical data for TTP presented that the p-value for the decision to borrow historical data is smaller for larger sample sizes, indicating a lower percentage of borrowing historical data. On the other hand, the percentage of borrowing historical data for EQ presented that the smaller the sample size, the wider the confidence interval, indicating that the smaller the sample size, the lower the percentage of borrowing historical data.

A.4 Supplemental simulation

We performed the supplemental simulations according to Table 4. The number of simulations in each scenario was 10,000. The number of bootstrap sets was 5,000 due to the computing cost.

Table 4: Parameter setting for supplemental simulation

Scenario	n_t	n_c	n_h	μ_t	μ_c	μ_h	$\sigma_t = \sigma_c = \sigma_h$
S1	50	25	25	0	0	-1	5
S2	50	50	50	0	0	-1	5
S3	100	50	50	0	0	-1	5
S4	100	100	100	0	0	-1	5
S5	50	25	25	2	0	0	8
S6	50	50	50	2	0	0	8
S7	100	50	50	2	0	0	8
S8	100	100	100	2	0	0	8
S9	50	25	25	2	0	1	8
S10	50	50	50	2	0	1	8
S11	100	50	50	2	0	1	8
S12	100	100	100	2	0	1	8
S13	50	25	25	2	0	-1	8
S14	50	50	50	2	0	-1	8
S15	100	50	50	2	0	-1	8
S16	100	100	100	2	0	-1	8
S17	50	25	25	2	-1	0	8
S18	50	50	50	2	-1	0	8
S19	100	50	50	2	-1	0	8
S20	100	100	100	2	-1	0	8

Table 5: Adjusted significance levels and average amount of dynamic information borrowing in supplemental simulation

Scenario	α^*_{TTP1}	α^*_{TTP2}	α^*_{EQ1}	α^*_{EQ2}	Ave DB-T	Ave DB-L1	Ave DB-L2
S1	0.0217	0.0205	0.0250	0.0250	0.617	0.787	0.856
S2	0.0217	0.0205	0.0250	0.0227	0.545	0.714	0.800
S3	0.0217	0.0205	0.0250	0.0227	0.548	0.717	0.803
S4	0.0217	0.0205	0.0209	0.0195	0.428	0.583	0.687
S5	0.0217	0.0205	0.0250	0.0250	0.700	0.870	0.920
S6	0.0217	0.0205	0.0250	0.0227	0.706	0.874	0.922
S7	0.0217	0.0205	0.0250	0.0227	0.705	0.873	0.923
S8	0.0217	0.0205	0.0209	0.0195	0.702	0.868	0.919
S9	0.0217	0.0205	0.0250	0.0250	0.670	0.838	0.896
S10	0.0217	0.0205	0.0250	0.0227	0.639	0.809	0.875
S11	0.0217	0.0205	0.0250	0.0227	0.638	0.807	0.874
S12	0.0217	0.0205	0.0209	0.0195	0.577	0.746	0.825
S13	0.0217	0.0205	0.0250	0.0250	0.669	0.837	0.895
S14	0.0217	0.0205	0.0250	0.0227	0.637	0.809	0.875
S15	0.0217	0.0205	0.0250	0.0227	0.642	0.810	0.875
S16	0.0217	0.0205	0.0209	0.0195	0.581	0.753	0.831
S17	0.0217	0.0205	0.0250	0.0250	0.665	0.834	0.894
S18	0.0217	0.0205	0.0250	0.0227	0.643	0.816	0.880
S19	0.0217	0.0205	0.0250	0.0227	0.638	0.805	0.871
S20	0.0217	0.0205	0.0209	0.0195	0.585	0.754	0.831

Table 6: Percentage of borrowing historical data for TTP and EQ in supplemental simulation

Scenario	$TTP1$	$TTP2$	$EQ1$	$EQ2$
S1	88.1	80.9	0.0	0.1
S2	82.5	73.2	0.2	10.8
S3	82.8	73.3	0.2	10.8
S4	70.4	58.9	14.5	27.4
S5	94.3	89.2	0.0	0.3
S6	94.2	89.3	0.5	17.1
S7	94.8	89.7	0.7	17.6
S8	95.1	90.2	36.7	60.7
S9	91.9	85.8	0.0	0.1
S10	90.5	83.7	0.5	14.2
S11	89.5	82.2	0.5	14.1
S12	85.3	76.5	24.9	43.1
S13	91.7	86.2	0.0	0.2
S14	90.2	83.0	0.4	14.3
S15	90.2	83.5	0.4	14.8
S16	85.0	76.8	25.1	44.0
S17	92.0	86.5	0.0	0.2
S18	89.6	82.2	0.5	14.4
S19	90.2	82.9	0.4	14.8
S20	85.2	76.8	26.3	44.4

A.5 Simulation of full borrowing and without borrowing

Table 7: Type 1 error rates

Scenario	Full	Without
1	2.69	2.70
2	2.62	2.59
3	2.59	2.61
4	2.54	2.51
S1	7.40	2.73
S2	8.51	2.62
S3	10.58	2.59
S4	12.68	2.52

Table 8: Powers

Scenario	Full	Without
5	51.8	37.7
6	63.7	51.7
7	80.7	63.6
8	90.4	80.8
9	32.8	37.8
10	41.3	51.7
11	56.3	63.6
12	68.7	80.4
13	70.7	37.7
14	82.3	51.8
15	94.2	63.6
16	98.3	80.7
17	70.5	68.7
18	82.0	85.0
19	94.3	93.4
20	98.3	98.9
S5	51.9	37.9
S6	63.5	51.6
S7	80.7	63.9
S8	90.7	80.6
S9	32.6	37.9
S10	41.2	51.8
S11	56.4	64.0
S12	68.6	80.7
S13	70.6	37.8
S14	82.1	51.6
S15	94.1	63.8
S16	98.3	80.7
S17	70.8	68.9
S18	82.0	84.9
S19	94.1	93.2
S20	98.3	98.9

A.6 Supplemental simulation of Bayesian method

We conducted information borrowing from historical data using a commensurate prior as a supplemental simulation. The number of simulations was set to 1,000 due to the computational time required. The commensurate prior assumes a prior distribution for the difference (δ) between the means of the current control group and the historical control group. The prior distribution is assumed to follow a normal distribution ($N(\delta|0, 1/\tau)$), where τ is assumed to follow either a half-Cauchy distribution ($C^+(0, 2)$) or a half-normal distribution $N^+(0, 0.5)$ (Hobbs et al. (2011, 2012)). The simulation was conducted using the commensurate.cont function from the psBayesborrow package in R. The simulation results (Table 9 and Table 10) are presented below.

Table 9: Type-1 error rates of commensurate prior method

Scenario	half-Cauchy	half-normal
1	1.5	2.0
2	2.3	2.1
3	2.2	2.1
4	2.9	2.7
S1	3.3	6.4
S2	3.4	6.3
S3	4.0	7.0
S4	3.9	5.8

Table 10: Powers of commensurate prior method

Scenario	half-Cauchy	half-normal
5	40.5	47.5
6	52.7	57.9
7	69.8	77.4
8	84.6	87.7
9	29.9	29.2
10	43.8	39.7
11	61.2	58.2
12	78.4	71.9
13	48.2	62.2
14	58.2	72.7
15	73.7	87.2
16	85.6	94.1
17	67.3	65.4
18	81.1	80.4
19	91.7	93.6
20	98.3	98.6
S5	17.9	21.3
S6	24.7	27.3
S7	35.4	38.5
S8	43.8	49.8
S9	26.6	33.2
S10	31.2	40.7
S11	38.7	54.3
S12	53.5	66.6
S13	22.2	31.9
S14	29.2	39.1
S15	40.2	56.8
S16	50.0	66.0
S17	30.2	32.3
S18	42.2	41.0
S19	59.4	59.4
S20	74.9	73.0

References

1. Hobbs BP, Carlin BP, Mandrekar SJ, Sargent DJ. Hierarchical commensurate and power prior models for adaptive incorporation of historical information in clinical trials. Biometrics 2011; 67:1047-1056.

2. Hobbs BP, Sargent DJ, Carlin BP. Commensurate priors for incorporating historical information in clinical trials using general and generalized linear models. Bayesian Analysis 2012;

7:639-674.

We also conducted a supplemental simulation for another information borrowing method using a Bayesian approach, the modified power prior (Chen et al. (2011) and Neal (2003)). The modified power prior constructs the prior distribution for the mean of the current control group (μ_c) as follows:

$$\pi(\mu_c, a|\overline{x}_h, s_h^2, n_h) \propto \frac{L(\mu_c|\overline{x}_h, s_h^2, n_h)\pi(\mu_c)\pi(a)}{\int L(\mu_c|\overline{x}_h, s_h^2, n_h)\pi(\mu_c)\pi(a)d\mu_c} \tag{1}$$

where $\pi(a)$ was assumed to follow a Beta(1,1) distribution. The simulation was conducted using the power.two.grp.random.a0 function from the BayesPPD package in R. The simulation results (Table 11 and Table 12) are presented below.

Table 11: Type-1 error rates of modified power prior method

Scenario	
1	1.3
2	1.4
3	1.2
4	0.9
S1	3.7
S2	4.1
S3	3.0
S4	5.6

Table 12: Powers of modified power prior method

Scenario	
5	47.3
6	57.1
7	75.1
8	84.4
9	32.5
10	42.8
11	57.9
12	64.7
13	56.2
14	67.9
15	85.3
16	92.1
17	70.7
18	83.8
19	95.4
20	97.8
S5	19.8
S6	24.9
S7	33.4
S8	40.9
S9	13.4
S10	16.1
S11	21.8
S12	27.1
S13	24.0
S14	32.1
S15	42.1
S16	52.7
S17	34.9
S18	41.2
S19	54.0
S20	67.8

References

1. Chen, Ming-Hui, et al. "Bayesian design of noninferiority trials for medical devices using historical data." Biometrics 67.3 (2011): 1163-1170.

2. Neal, Radford M. Slice sampling. Ann. Statist. 31 (2003), no. 3, 705–767

A.7 Supplemental simulation with a large discrepancy between the current and historical data

We conducted a supplemental simulation to examine the average dynamic borrowing amount when there is a large discrepancy between the current data and the historical data. The simulation settings are shown in Tables 13, 15, and 17, and the results are presented in Tables 14, 16, and 18. When the discrepancy is large, the amount of information borrowed becomes zero.

Table 13: Parameter setting for supplemental simulation

Scenario	n_t	n_c	n_h	μ_t	μ_c	μ_h	$\sigma_t = \sigma_c = \sigma_h$
S1	50	25	25	2	0	**5**	5
S2	50	50	50	2	0	**5**	5
S3	100	50	50	2	0	**5**	5
S4	100	100	100	2	0	**5**	5
S5	50	25	25	2	0	**-5**	5
S6	50	50	50	2	0	**-5**	5
S7	100	50	50	2	0	**-5**	5
S8	100	100	100	2	0	**-5**	5
S9	50	25	25	2	**-5**	0	5
S10	50	50	50	2	**-5**	0	5
S11	100	50	50	2	**-5**	0	5
S12	100	100	100	2	**-5**	0	5

Table 14: Average amount of dynamic information borrowing in the parameter setting in Table 13

Scenario	Ave DB-T	Ave DB-L1	Ave DB-L2
1	0.034	0.041	0.081
2	0.002	0.001	0.004
3	0.002	0.001	0.004
4	0.000	0.000	0.000
5	0.034	0.042	0.082
6	0.002	0.001	0.004
7	0.002	0.001	0.004
8	0.000	0.000	0.000
9	0.034	0.042	0.081
10	0.002	0.001	0.004
11	0.002	0.001	0.003
12	0.000	0.000	0.000

Table 15: Parameter setting for supplemental simulation

Scenario	n_t	n_c	n_h	μ_t	μ_c	μ_h	$\sigma_t = \sigma_c = \sigma_h$
S1	50	25	25	2	0	**10**	5
S2	50	50	50	2	0	**10**	5
S3	100	50	50	2	0	**10**	5
S4	100	100	100	2	0	**10**	5
S5	50	25	25	2	0	**-10**	5
S6	50	50	50	2	0	**-10**	5
S7	100	50	50	2	0	**-10**	5
S8	100	100	100	2	0	**-10**	5
S9	50	25	25	2	**-10**	0	5
S10	50	50	50	2	**-10**	0	5
S11	100	50	50	2	**-10**	0	5
S12	100	100	100	2	**-10**	0	5

Table 16: Average amount of dynamic information borrowing in the parameter setting in Table 15

Scenario	Ave DB-T	Ave DB-L1	Ave DB-L2
1	0.000	0.000	0.000
2	0.000	0.000	0.000
3	0.000	0.000	0.000
4	0.000	0.000	0.000
5	0.000	0.000	0.000
6	0.000	0.000	0.000
7	0.000	0.000	0.000
8	0.000	0.000	0.000
9	0.000	0.000	0.000
10	0.000	0.000	0.000
11	0.000	0.000	0.000
12	0.000	0.000	0.000

Table 17: Parameter setting for supplemental simulation

Scenario	n_t	n_c	n_h	μ_t	μ_c	μ_h	$\sigma_t = \sigma_c = \sigma_h$
S1	50	25	25	2	0	**50**	5
S2	50	50	50	2	0	**50**	5
S3	100	50	50	2	0	**50**	5
S4	100	100	100	2	0	**50**	5
S5	50	25	25	2	0	**-50**	5
S6	50	50	50	2	0	**-50**	5
S7	100	50	50	2	0	**-50**	5
S8	100	100	100	2	0	**-50**	5
S9	50	25	25	2	**-50**	0	5
S10	50	50	50	2	**-50**	0	5
S11	100	50	50	2	**-50**	0	5
S12	100	100	100	2	**-50**	0	5

Table 18: Average amount of dynamic information borrowing in Table 17

Scenario	Ave DB-T	Ave DB-L1	Ave DB-L2
1	0.000	0.000	0.000
2	0.000	0.000	0.000
3	0.000	0.000	0.000
4	0.000	0.000	0.000
5	0.000	0.000	0.000
6	0.000	0.000	0.000
7	0.000	0.000	0.000
8	0.000	0.000	0.000
9	0.000	0.000	0.000
10	0.000	0.000	0.000
11	0.000	0.000	0.000
12	0.000	0.000	0.000