Correction to: Optimal Decision Criteria for the Study Design and Sample Size of a Biomarker-Driven Phase III Trial

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In the original article in the section “Application to the Motivating Example”, Greenberg’s trial data have been deleted from the historical data. Tables 3, 4, and 5 along with corresponding text in the manuscript have been updated using Risner’s trial data as the single historical data set. Greenberg’s trial was a crossover study; the values of σ^2 calculated from this study was the within-subjects variance, not the between-subjects variance. Thus, it was not appropriate to calculate the between-subjects variance and derive the predictive distribution including Greenberg’s trial data.

Updated Tables 3, 4, and 5 are below, along with updated manuscript text.

Application to the Motivating Example

Here, we show what decisions are made when we apply the proposed method to the motivating example described above. Table 3 shows the result of clinical trial that evaluated the change from baseline in ADAS-cog compared to placebo in a randomized study. Note that a negative number indicates the improvement from the observed ADAS-cog at baseline. The estimates of variance of treatment effect in each ApoE4 status were calculated using the sample size in each arm and the result to derive a predictive distribution of treatment effect.

Using the value presented in Table 3, we calculated the standard deviation of response in each arm and each population as $\sigma=4.94$ and we set the between-trial standard deviation as $\tau=0.25$, a small between-trial variance of response ($\sigma/\tau=20$), and $\tau=0.99$, a large between-trial variance

Table 3. Result of Clinical Trial in the Motivating Example.

Historical Data	ApoE4 Status	Sample Size ^a		Result	Estimates of Variance of Treatment Effect
		Arm E	Arm P		
Risner et al. ¹¹	Positive	36	35	1.49 [− 0.81, 3.80]	1.34
	Negative	42	43	− 2.94 [− 5.06, − 0.81]	1.15

^aArm E and Arm P denote an Experimental Arm and a Placebo Arm, respectively. The Experimental Arms are Rosiglitazone and Donepezil in Risner et al.,¹¹ respectively.

The original article can be found online at <https://doi.org/10.1007/s43441-020-00119-1>.

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Table 4. Predictive Distribution of Treatment Effects in Each Population.

Populations	$\tau=0.25$	$\tau=0.99$
ApoE4-positive	N (1.49, 1.59)	N (1.49, 5.28)
ApoE4-negative	N (− 2.94, 1.40)	N (− 2.94, 5.09)
Full	N (− 0.06, 0.84)	N (− 0.06, 2.85)

Table 5. The Optimal Sample Size, PoS, and eNPV in the Motivating Example.

τ	Designs	Optimal Sample Size (total)	PoS	eNPV
0.25	Traditional	N/A	N/A	N/A
	Enriched	80	0.74	1538
	Stratified	310	0.77	1658
	Adaptive enrichment	180	0.80	1721
0.99	Traditional	N/A	N/A	N/A
	Enriched	130	0.71	606
	Stratified	370	0.70	1161
	Adaptive enrichment	190	0.70	1430

N/A Indicates that the PoS of the design did not exceed 0.70 in the Maximum Sample Size.

($\sigma/\tau=5$). The predictive distributions of treatment effects in ApoE4-positive, ApoE4-negative, and full populations are derived by using formula (1) and above values, and presented in Table 4. Note that the prevalence of the ApoE4-positive population λ and ApoE4-negative population $(1-\lambda)$ are set as 0.65 and 0.35, respectively.²⁷

To calculate the eNPV, we also need to set the parameters related to the study design, the development cost, and the revenue. The values of each parameter used to calculate the eNPV are presented in Table A3 of Appendix 4. Table 5 shows the optimal sample size, PoS, and eNPV in each design.

The eNPV was higher in the order of the adaptive enrichment design, stratified design, enriched design, and traditional design, regardless of the value of τ . Therefore, the adaptive enrichment design is the optimal design in the motivating example and we decided to use the adaptive enrichment design in the phase III confirmatory study.

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