Estimating the Best Commute:

Discussion of 6 proposed designs.

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Overview

The project aims to determine the best driving route out of 3 available. The first route called Plaza serves as a control. The other two called Rainbow and Stateline are expected to be faster than the control route. To evaluate operating characteristics three scenarios were set. Under "Null" scenario all three routes were expected to be 15 minutes long. Under "Expected" scenario assumed driving time was 13 minutes for Rainbow and Stateline and 15 minutes for Plaza. The possibility of one route being the best was explored as well. The diving time for Rainbow route was expected to be 13 minutes while Stateline driving time was expected to be 14 minutes. The control Plaza route was set to 15 minutes. During exploratory stage of the study the team estimated standard deviation for driving time to be 1.2 minutes.

A driver will drive 5 times a week and complete 33 drives, which will take 6.5 weeks. Fixed trial design with 1:1:1 allocation provided 90% power with 2.5% type 1 error allowing 2 comparisons of Rainbow and Stateline routes to the Control.

The study will utilize adaptive Bayesian design to improve operating characteristics and driving experience. All designs assumed independent dose models.

$$Y \sim N(\theta_d, \sigma^2),$$

where *d* denotes one out of three routes. The following priors were assumed for mean θ_d and variance σ^2.

$$\theta_d \sim N\left(\mu_d, \tau_d^2\right)$$

$$\sigma^2 \sim IG\left(\frac{\sigma_n}{2}, \frac{\sigma_\mu^2 \sigma_n}{2}\right)$$

There were 6 designs proposed. Operating characteristics for the designs are summarized in Table 1.

JZ design

JZ proposed fixed design with 1:1:1 allocation ratio. The design assumed deterministic accrual with no dropouts. A trial was declared successful if posterior probability of Stateline or Rainbow drive time being less than the Control drive time by 1 minute was greater than 0.7. The route to compare to the Control was picked based on the maximum posterior probability of Rainbow or Stateline having the lowest time. The prior mean μ_d was set to 15 and prior standard deviation was set τ_d^2 to 6. For variance prior σ_μ was set to 1.2 and σ_n was set to 0.1.

DIAS design

DIAS group proposed an adaptive design. The design assumed deterministic accrual with no dropouts. There were 3 interims planned at 8, 16, and 24 weeks. Pre first interim 4 drives were allocated to the Control, 4 drives were allocated to Rainbow and Stateline routes at 1:1 ratio. After 1st interim drives were allocated in blocks of 4 based on posterior probability of being the fastest route. One out of 4 routes would be always allocated to the Control. The study had stopping criteria. The study would stop for futility if posterior probability of Stateline or Rainbow drive time being less than the Control drive time by 1 minute was less than 0.1. The study would stop for success if posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.998. The route to compare to the Control was picked based on the maximum posterior probability of Rainbow or Stateline having the lowest time. The final success of a trial was determined by if posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.9836. The prior mean μ_d was set to 15 and prior standard deviation was set τ_d^2 to 5. For variance prior σ_μ was set to 5 and σ_n was set to 0.1.

The StarFish design

The StarFish group proposed an adaptive design. The design assumed continuous recruiting with 5% dropout (2 drives). After first 12 drives were completed, the study would have an interim analysis every 6 days starting at the day of the first drive. This would result in at least 4 interim analyses. Pre first interim the subjects were allocated at 2:2:2 ratio. After the 1st interim drives were allocated in blocks of 6 based on the posterior probability of being the fastest route raised to the power of 0.7. The study would stop for futility if the posterior probability of Stateline or Rainbow drive time being less than the Control drive time was less than 0.4. The study would stop for success if the posterior probability of having the lowest driving time was greater than 0.99. The study would be declared futile if at final evaluation the posterior probability of Stateline or Rainbow drive time being less than Control drive time was less than 0.4. The study would be considered successful if one out of two following criteria was true. The posterior probability of having the lowest driving time was greater than 0.99. The posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.99. The route to compare to Control was picked based on the maximum posterior probability of Rainbow or Stateline having the lowest time. The prior mean μ_d was set to 15 for Control and 13 for Rainbow and Plaza routes; and prior standard deviation was set τ_d^2 to 3 in all arms. For variance prior σ_μ was set to 10 and σ_n was set to 0.1.

Lauren's and Elena's design

Lauren's and Elena's design had an arm dropping feature. The design assumed continuous recruiting with no dropouts. After first 15 drives were completed, the study would have one and only interim analysis. If the posterior probability of having the smallest driving time is less than 0.5 Rainbow or Stateline arm would be dropped. The study would be considered futile and stopped if one out of two following criteria is true. The posterior probability of Stateline or Rainbow drive time being less than Control drive time was less than 0.4. The posterior probability of having the smallest driving time is less than 0.4. The study would be declared futile if at final evaluation if the posterior probability of Stateline or Rainbow drive time being less than Control drive time was less than 0.4. The study would be declared successful if the posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.98. The route to compare to Control was picked based on the maximum posterior probability of Rainbow or Stateline having the lowest time. The prior mean μ_d was set to 15 for Control and 13 for Rainbow and Plaza routes; and prior standard deviation was set τ_d^2 to 3 in all arms. For variance prior σ_μ was set to 10 and σ_n was set to 0.1.

Dr. Byron Gajewski's design

Dr. Byron Gajewski proposed two similar designs. One had fixed allocation to the Control and another had no fixed allocation. The designs assumed deterministic accrual with no dropouts. There were 5 interims planned at 10, 15, 20, 25, and 30 subjects. Under fixed allocation among first 10 subjects 4 were allocated to the Control and remaining 6 were divided equally between Rainbow and Stateline. All remaining subjects were allocated at the blocks of 10 with 4 subjects allocated to the Control and the rest were allocated based on the posterior probability of being the fastest route weighted by the following information formula:

$$V_d = \left(\frac{P_d \;\; Var(\theta^{Q_d})}{n_d + 1}\right)^{1/2}$$

Allocation ratio in each arm was calculated as $V_j/(V_1 + V_2)$, and it would randomize next route to the more beneficial arm. Under no fixed allocation to the Control all three arms would be considered for response adaptive randomization and allocation ratio in each arm was calculated as $V_d/(V_1 + V_2 + V_3)$. Both designs had the same success and futility criteria and priors. The study would stop for futility if posterior probability of Stateline or Rainbow drive time being less than Control drive time by 0.5 minute was less than 0.15. The study would stop for success if posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.99925. The route to compare to the Control was picked based on the maximum posterior probability of Rainbow or Stateline having the lowest time. The final success of a trial was determined by the posterior probability of Stateline or Rainbow drive time being less than Control drive time was greater than 0.99. The prior mean μ_d was set to 10 and prior standard deviation was set τ_d^2 to 10. For variance prior σ_μ was set to 1.2 and σ_n was set to 0.01.

Discussion

All designs provided control over the target Type 1 error of 2.5% (Table 1). Most of the designs achieved 90% power under both “Expected” and “Best” scenario. Only designs proposed by DIAS group and Dr. Gajewski showed reduced number of drives required to achieve target power. However, No Fixed Control design by Dr. Gajewski had less desirable characteristics compared to Fixed Control design. Fixed control design and DIAS design provided similar rates of early sample savings, but DIAS design showed slightly improved power under both “Expected” and “Best” scenarios. DIAS design required only 3 interims compared to 5 interims under Fixed Control. This could be considered as an advantage as less resources would be required to complete the study. Overall, DIAS design provided the most optimal combination of operating characteristics and demonstrated opportunity for best driving experience and study execution.

Table 1. Operating characteristics.

Team	**Hypothesis**	**Mean subjects**	**Proportion of successful trials**

DIAS	Null	23.55	0.024
	Expected	23.59	0.980
	Best	25.11	0.944
TheStarFish	Null	29.48	0.024
	Expected	32.89	0.949
	Best	31.93	0.897
Lauren&Elena	Null	30.13	0.020
	Expected	33	0.987
	Best	32.98	0.937
JZ	Null	33	0.015
	Expected	33	0.979
	Best	33	0.926
Fixed Control by Gajewski	Null	25.55	0.020
	Expected	22.53	0.978
	Best	24.11	0.935
No Fixed Control by Gajewski	Null	25.67	0.026
	Expected	24.34	0.902
	Best	25.39	0.886