RESEARCH DISSERTATION REPORT

ON

"MULTI-TREATMENT RESPONSE ADAPTIVE ALLOCATION DESIGN"

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ABSTRACT

This project proposes a Multi-Treatment Response Adaptive Allocation Rule, analyses it's Allocation Proportions in presence of a superior treatment and discusses about testing procedures related to the same. We have also compared the performance of our proposed rule with appropriate competitor rules. This project contains thorough descriptions with algorithms, coding references from R, visualizations and precise inference.

KEYWORDS

Response Adaptive Allocation Rule, Allocation Rule, Adaptive Allocation, Superior Treatment, Multi-Treatment Allocation, Multi-Treatment Response Adaptive Allocation, Mean Proportion of Allocation, Consistency of Allocation Rule, Computation of Allocation Rule

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I. Introduction:

What is "Multi-treatment Response Adaptive Allocation Design" ?

Suppose, patients are entering into the clinical trial one-by-one sequentially with some common disease/cause for treatment, and they are treated with any one of some competing treatments, treatment $A_1, A_2, ..., A_K$. The main aspects of a clinical trial are :

(a) To derive the information regarding the effectiveness of the treatments for comparison purpose;

(b) The patients should be provided the best possible treatment to cure the disease;

(c) The trial should not be unneccessarily prolonged i.e. the period of trial should not be larger than neccessary.

In a prolonged trial, there may have larger number of patients given to the inferior treatment. The basic problem is to provide the treatment assignment rule which gives a good rule compromise between the above requirements. Keeping these points into consideration, the **response adaptive allocation designs** are used with an ethical motivation that larger number of patients are treated by the better treatment i.e. during the trial the collected responses are used to update/adapt the future allocations so that the allocation becomes skewed/tilted in favour of the better treatment. Now, as in our case, we are treating with multiple treatments together at a time, so we can say that, our **response adaptive allocation design** is a **"Multi-treatment Response Adaptive Allocation Design"**.

II. Procedure:

A. What is "Multi-treatment Response Adaptive Allocation Design" Procedure ?

Suppose, we are treating with n patients. Now, these K treatments are applied randomly to the patients. So, we can define the random treatment assignments by δ_k, $k = 1(1)K$ by

$\delta_k = 1,\ if\ a\ randomly\ entering\ patient\ be\ assigned\ to\ treatment\ k$
$= 0,\ if\ a\ randomly\ entering\ patient\ be\ assigned\ to\ treatment\ k'\ (\neq k).$

Now, let R_k be the probability that a randomly entering patient be assigned to treatment k, k=1(1)K i.e.
$R_k = P(\delta_k = 1),\ for\ all\ k = 1(1)K.$

Now, in our case, we are assuming that, higher the response better the treatment. Next, also let X_k denote the response of a patient with treatment A_k, for all k=1(1)K.

Now, if the response obtained from patients with the treatment A_k are higher than the response obtained from patients with the treatments except A_k, then obviously a randomly entering patient will be assigned to treatment k i.e. in notation we can write that, if
$X_k > max\{X_{k'},\ k' = 1(1)K,\ k' \neq k\}$, then $\delta_k = 1$.
So, we can write that,
$R_k = P(X_k > max\{X_{k'},\ k' = 1(1)K,\ k' \neq k\})$ .....(i)

Now, as the response of a patient with treatment A_k, for all k=1(1)K, is generally unknown to us, so it is a random variable and obviously it has a probability distribution. Now, if all the treatments are equivalent, then obviously any treatment among our k treatments can be allotted to a randomly entering patient with equal probability, i.e. then $R_k = \frac{1}{K},\ for\ all\ k = 1(1)K$.

But in general, we don't know whether the treatments are equivalent or not. So, we have to assume separate probability distributions for each of the random variables X_k, for all k=1(1)K.

Now, let μ_k= suitable measure of central tendency for X_k and σ_k = suitable measure of dispersion for X_k(if any). Now, to identify the assumed distributional assumptions completely, first we have to estimate the parameters μ_k and σ_k(if any) for all k=1(1)K.

Now, suppose initially $n_0$patients are allocated to each treatment arm for generating the initial estimates of the parameters of interest $\mu_k's$ and also of the nuisance parameters, like variability parameters, $\sigma_k's$, if any, for all k=1(1)K.

Let, $\hat{\mu}_{kj}$denote estimate of μ_k based on $\mathfrak{F}_j = \{\delta_i, X_{ki},\ i = 1(1)j,\ k = 1(1)K\}$, where $\{\mathfrak{F}_j = \delta_i, X_{ki},\ i = 1(1)j,\ k = 1(1)K\}$ denotes the information upto the j^{th} stage of sampling i.e treatment allocations upto the j^{th} stage along with the treatment responses upto that stage with treatment k for all k=1(1)K.

Now, the $(j+1)^{th}$ patient will be allocated to treatment (1) based on a response-adaptive allocation probability,

$R_{1,j+1} = P(\delta_{1,j+1} = 1) = \hat{P}_j(X_1 > max\{X_2, ..., X_K\})$, where $j = Kn_0,\ Kn_0+1,\ .....,\ n-1$,

$\delta_{1,j+1}$ denotes "a randomly entering patient at the $(j+1)^{th}$ stage, be assigned to treatment (1)" and $R_{1,j+1}$ denotes "the probability that a randomly entering patient at the $(j+1)^{th}$ stage, be assigned to treatment (1)".

Thus, in general, response-adaptive allocation probability for $(j+1)^{th}$ patient to treatment arm k is :

$R_{k,j+1} = P(\delta_{k,j+1} = 1) = \hat{P}_j(X_k > max\{X_k's,\ k' = 1(1)K,\ k' \neq k\})$,

for all $j = Kn_0,\ Kn_0+1,\ .....,\ n-1$ and also for all $k = 1(1)K$.

B. Checking Ethical Efficiency of "Multi-treatment Response Adaptive Allocation Design" Procedure:

Here, suppose that the random variables $X_k's$ are independent and exponentially distributed random variables with mean θ_k for all k=1(1)K, i.e. $X_k \sim Exp(mean = \theta_k)$ for all k=1(1)K.

Now, let for the sake of simplicity, we will treat with three treatments here, i.e. here our K=3.

Also assume that, these three treatments be denoted as : $A_1 = A,\ A_2 = B\ and\ A_3 = C$.

Hence, we get that, $X_A \sim Exp(mean = \theta_A),\ X_B \sim Exp(mean = \theta_B)\ and\ X_C \sim Exp(mean = \theta_C)$ independently.

Now, first we have to find the maximum likelihood estimates of $\theta_A, \theta_B\ and\ \theta_C$ respectively. For this, we are considering the likelihood of $\theta_A, \theta_B\ and\ \theta_C$ based on first n stages of sampling :

$L(\theta_A, \theta_B, \theta_C) \propto \prod_{i=1}^{n} \{f_{X_{Ai}}(x_{Ai})\}^{\delta_{Ai}}\}\{f_{X_{Bi}}(x_{Bi})\}^{\delta_{Bi}}\}\{f_{X_{Ci}}(x_{Ci})\}^{\delta_{Ci}}\}$, where $\delta_{Ai} + \delta_{Bi} + \delta_{Ci} = 1$

and $f_{X_{ki}}(x_{ki}) = \frac{1}{\theta_k} e^{-\frac{x_{ki}}{\theta_k}},\ for\ k = A, B, C\ and\ for\ i = 1(1)n$

i.e., $L(\theta_A, \theta_B, \theta_C) = c'. \prod_{i=1}^{n} \{f_{X_{Ai}}(x_{Ai})\}^{\delta_{Ai}}\}\{f_{X_{Bi}}(x_{Bi})\}^{\delta_{Bi}}\}\{f_{X_{Ci}}(x_{Ci})\}^{\delta_{Ci}}\}$, where $c = Proportionality\ constant$

i.e., $l = ln\ L(\theta_A, \theta_B, \theta_C) = ln\ c' + \sum_{i=1}^{n} \{\delta_{Ai} ln\ f_{X_{Ai}}(x_{Ai}) + \delta_{Bi} ln\ f_{X_{Bi}}(x_{Bi}) + \delta_{Ci} ln\ f_{X_{Ci}}(x_{Ci})\}$

i.e., $l = c + \sum_{i=1}^{n} \{\delta_{Ai} ln\ f_{X_{Ai}}(x_{Ai}) + \delta_{Bi} ln\ f_{X_{Bi}}(x_{Bi}) + \delta_{Ci} ln\ f_{X_{Ci}}(x_{Ci})\}$

i.e., $l = c + \sum_{i=1}^{n} [\delta_{Ai}\{-ln\ \theta_A - \frac{x_{Ai}}{\theta_A}\} + \delta_{Bi}\{-ln\ \theta_B - \frac{x_{Bi}}{\theta_B}\} + \delta_{Ci}\{-ln\ \theta_C - \frac{x_{Ci}}{\theta_C}\}]$

i.e., $l = c - N_{An} ln\ \theta_A - \frac{\sum_{i=1}^{n} \delta_{Ai} x_{Ai}}{\theta_A} - N_{Bn} ln\ \theta_B - \frac{\sum_{i=1}^{n} \delta_{Bi} x_{Bi}}{\theta_B} - N_{Cn} ln\ \theta_C - \frac{\sum_{i=1}^{n} \delta_{Ci} x_{Ci}}{\theta_C}$,

where $N_{kn} = \sum_{i=1}^{n} \delta_{ki} = \#$ patients allocated to treatment k out of first n patients = a random variable as $\delta_{ki}'s$ are also random variables .....($\star$)

Now, by setting $\frac{\delta l}{\delta \theta_k} = 0$,

we get that, $-\frac{N_{kn}}{\theta_k} + \frac{\sum_{i=1}^{n} \delta_{ki} x_{ki}}{\theta_k^2} = 0$ i.e. $\theta_k = \frac{\sum_{i=1}^{n} \delta_{ki} x_{ki}}{N_{kn}} = \hat{\theta}_{k,n}^{MLE}$, say , k=A,B,C.

Next, by applying the same procedure described in **Part-A**, we have now allotted the treatments to all the n patients by **multi-treatment response**

adaptive allocation procedure.

Now, suppose somehow we can observe that the treatment A is superior compared to the other two treatments. Now, to check the ethical efficiency of the **multi-treatment response adaptive allocation procedure**, we have to check whether in our treatment allocations to n patients, proportion of allocations to the treatment A is larger than the other two. If it happens, then we can claim that : Our **multi-treatment response adaptive allocation procedure** is ethically efficient.

C. "Checking Statistical Efficiency of "Multi-treatment Response Adaptive Allocation Design" Procedure:

Here, suppose that the random variables $X_k's$ are independent and exponentially distributed random variables with mean θ_k for all k=1(1)K,

i.e. $X_k \sim Exp(mean = \theta_k)$ for all k=1(1)K.

Now, let for the sake of simplicity, we will treat with three treatments here, i.e. here our K=3.

Also assume that, these three treatments be denoted as : $A_1 = A,\ A_2 = B\ and\ A_3 = C$.

Hence, we get that, $X_A \sim Exp(mean = \theta_A),\ X_B \sim Exp(mean = \theta_B)\ and\ X_C \sim Exp(mean = \theta_C)$ independently.

Now, first we have to find the maximum likelihood estimates of $\theta_A, \theta_B\ and\ \theta_C$ respectively. For this, we are considering the likelihood of $\theta_A, \theta_B\ and\ \theta_C$ based on first n stages of sampling :

$L(\theta_A, \theta_B, \theta_C) \propto \prod_{i=1}^{n} \{f_{X_{Ai}}(x_{Ai})\}^{\delta_{Ai}}\}\{f_{X_{Bi}}(x_{Bi})\}^{\delta_{Bi}}\}\{f_{X_{Ci}}(x_{Ci})\}^{\delta_{Ci}}\}$, where $\delta_{Ai} + \delta_{Bi} + \delta_{Ci} = 1$

and $f_{X_{ki}}(x_{ki}) = \frac{1}{\theta_k} e^{-\frac{x_{ki}}{\theta_k}},\ for\ k = A, B, C\ and\ for\ i = 1(1)n$

i.e., $L(\theta_A, \theta_B, \theta_C) = c'. \prod_{i=1}^{n} \{f_{X_{Ai}}(x_{Ai})\}^{\delta_{Ai}}\}\{f_{X_{Bi}}(x_{Bi})\}^{\delta_{Bi}}\}\{f_{X_{Ci}}(x_{Ci})\}^{\delta_{Ci}}\}$, where $c = Proportionality\ constant$

i.e., $l = ln\ L(\theta_A, \theta_B, \theta_C) = ln\ c' + \sum_{i=1}^{n} \{\delta_{Ai} ln\ f_{X_{Ai}}(x_{Ai}) + \delta_{Bi} ln\ f_{X_{Bi}}(x_{Bi}) + \delta_{Ci} ln\ f_{X_{Ci}}(x_{Ci})\}$

i.e., $l = c + \sum_{i=1}^{n} \{\delta_{Ai} ln\ f_{X_{Ai}}(x_{Ai}) + \delta_{Bi} ln\ f_{X_{Bi}}(x_{Bi}) + \delta_{Ci} ln\ f_{X_{Ci}}(x_{Ci})\}$

i.e., $l = c + \sum_{i=1}^{n} [\delta_{Ai} \{-ln\ \theta_A - \frac{x_{Ai}}{\theta_A}\} + \delta_{Bi} \{-ln\ \theta_B - \frac{x_{Bi}}{\theta_B}\} + \delta_{Ci} \{-ln\ \theta_C - \frac{x_{Ci}}{\theta_C}\}]$

i.e., $l = c - N_{An} ln\ \theta_A - \frac{\sum_{i=1}^{n} \delta_{Ai} x_{Ai}}{\theta_A} - N_{Bn} ln\ \theta_B - \frac{\sum_{i=1}^{n} \delta_{Bi} x_{Bi}}{\theta_B} - N_{Cn} ln\ \theta_C - \frac{\sum_{i=1}^{n} \delta_{Ci} x_{Ci}}{\theta_C}$,

where $N_{kn} = \sum_{i=1}^{n} \delta_{ki}$ = # patients allocated to treatment k out of first n patients = a random variable as $\delta_{ki}'s$ are also random variables .....($\star$)

Now, by setting $\frac{\delta l}{\delta \theta_k} = 0$, we get that, $-\frac{N_{kn}}{\theta_k} + \frac{\sum_{i=1}^{n} \delta_{ki} x_{ki}}{\theta_k^2} = 0$ i.e. $\theta_k = \frac{\sum_{i=1}^{n} \delta_{ki} x_{ki}}{N_{kn}} = \hat{\theta}_{k,n}^{MLE}$, say , k=A,B,C.

Now, $\frac{\delta^2 l}{\delta\theta_k^2} = \frac{N_{kn}}{\theta_k^2} - 2.\frac{\sum_{i=1}^{n}\delta_{ki}x_{ki}}{\theta_k^3}$, where k=A,B,C and $\frac{\delta^2 l}{\delta\theta_{k'}\delta\theta_k} = 0$ for k'=A,B,C & k' $\neq$ k where k=A,B,C.

Now, for testing purpose with $\theta_k,\ k = A, B, C$ (see later), we have to find the asymptotic distribution of the $\hat{\theta}_{k,n}^{MLE}$ for all k=A,B,C. So, we can proceed as follows.

$$
\begin{aligned}
-\tfrac{1}{n}\tfrac{\delta^2 l}{\delta\theta_k^2} &= -\tfrac{1}{n}\big[\tfrac{\sum_{i=1}^{n}\delta_{ki}}{\theta_k^2} - 2.\tfrac{\sum_{i=1}^{n}\delta_{ki}x_{ki}}{\theta_k^3}\big] \\
&= +\tfrac{1}{n}\textstyle\sum_{i=1}^{n}\big[-\tfrac{\delta_{ki}}{\theta_k^2} + 2.\tfrac{\delta_{ki}x_{ki}}{\theta_k^3}\big] \\
&\to E\big[-\tfrac{\delta_k}{\theta_k^2} + 2.\tfrac{\delta_k X_k}{\theta_k^3}\big] \\
&= -\tfrac{E(\delta_k)}{\theta_k^2} + 2.\tfrac{E(\delta_k X_k)}{\theta_k^3} \\
&= -\tfrac{R_k}{\theta_k^2} + 2.\tfrac{EE[\delta_k X_k|\delta_k]}{\theta_k^3} \\
&= -\tfrac{R_k}{\theta_k^2} + 2.\tfrac{E[\delta_k.E(X_k|\delta_k)]}{\theta_k^3} \\
&= -\tfrac{R_k}{\theta_k^2} + 2.\tfrac{E[\delta_k\theta_k]}{\theta_k^3} \\
&= -\tfrac{R_k}{\theta_k^2} + \tfrac{2}{\theta_k^2}R_k \\
&= \tfrac{R_k}{\theta_k^2} \\
&= \gamma_{kk}, \text{ say where k=A,B,C.}
\end{aligned}
$$

Hence, using **Martingle** CLT, we can write that, the asymptotic distribution of $\hat{\theta}_{k,n}^{MLE},\ k = A, B, C$ is as below :

$$\sqrt{n}(\hat{\theta}_{A,n} - \theta_A, \hat{\theta}_{B,n} - \theta_B, \hat{\theta}_{C,n} - \theta_C) \xrightarrow[n\to\infty]{D} N(\underline{0}, \Gamma^{-1}) \qquad .....(\star\star)$$

where, $\Gamma = \begin{pmatrix} \gamma_{AA} & 0 & 0 \\ 0 & \gamma_{BB} & 0 \\ 0 & 0 & \gamma_{CC} \end{pmatrix}$ i.e. $\Gamma^{-1} = \begin{pmatrix} \frac{1}{\gamma_{AA}} & 0 & 0 \\ 0 & \frac{1}{\gamma_{BB}} & 0 \\ 0 & 0 & \frac{1}{\gamma_{CC}} \end{pmatrix}$.

Next, by applying the same procedure described in **Part-1**, we have now allotted the treatments to all the n patients by **multi-treatment response adaptive allocation procedure**. Now, suppose somehow we are expecting that the treatment A is better than the other two treatments B and C. So, now we have to test this statement by forming the hypothesis as :

H_0 : A, B and C are equivalent

vs H_1 : A is better than B and C;

i.e., $H_0 : \theta_A = \theta_B = \theta_C = \theta(say)$

vs $H_1 : \theta_A \geq \theta_B,\ \theta_A \geq \theta_C$ with strict inequality for at least one case;

i.e., $H_0 : \theta_A - \theta_B = 0,\ \theta_A - \theta_C = 0$

vs $H_1 : \theta_A - \theta_B \geq 0,\ \theta_A - \theta_C \geq 0$ with strict inequality for at least one case.

Now, from $(\star\star)$ we get that,

$$\sqrt{n}\{(\hat{\theta}_{An}-\hat{\theta}_{Bn})-(\theta_A-\theta_B),\ (\hat{\theta}_{An}-\hat{\theta}_{Cn})-(\theta_A-\theta_C)\} \xrightarrow[n\to\infty]{D} N_2[\begin{pmatrix}0\\0\end{pmatrix}, \begin{pmatrix}\frac{1}{\gamma_{AA}}+\frac{1}{\gamma_{BB}} & \frac{1}{\gamma_{AA}}\\ \frac{1}{\gamma_{AA}} & \frac{1}{\gamma_{AA}}+\frac{1}{\gamma_{CC}}\end{pmatrix}].$$

Now, under H_0 we get that,

$$\sqrt{n}(\hat{\theta}_{An}-\hat{\theta}_{Bn},\ \hat{\theta}_{An}-\hat{\theta}_{Cn}) \xrightarrow[n\to\infty]{D} N_2[\begin{pmatrix}0\\0\end{pmatrix}, \frac{1}{\gamma}\begin{pmatrix}2 & 1\\1 & 2\end{pmatrix}] \qquad .....(\star\star\star)$$

where $\gamma_{AA} = \gamma_{BB} = \gamma_{CC} = \gamma$ under H_0 and $\gamma = \frac{\frac{1}{3}}{\theta^2}$ as under H_0 : $R_A = R_B = R_C = \frac{1}{3}$.

Now, this distribution still involves an unknown quantity θ, which has to be estimated by the maximum likelihood method under H_0. So let, $\hat{\theta}_n$ be the MLE of θ under H_0 based on 1st n responses. Now, this $\hat{\theta}_n$ is as follows :

So, the log-likelihood of $\theta_A, \theta_B \ and\ \theta_C$ based on first n stages of sampling is (from $(\star)$) :

$$l = c - N_{An} ln\ \theta_A - \frac{\sum_{i=1}^{n}\delta_{Ai}x_{Ai}}{\theta_A} - N_{Bn} ln\ \theta_B - \frac{\sum_{i=1}^{n}\delta_{Bi}x_{Bi}}{\theta_B} - N_{Cn} ln\ \theta_C - \frac{\sum_{i=1}^{n}\delta_{Ci}x_{Ci}}{\theta_C}.$$

Hence, the log-likelihood of $\theta_A, \theta_B \ and\ \theta_C$ based on first n stages of sampling under H_0 is (from $(\star)$) :

$$l_{H_0} = c - N_{An} ln\ \theta - N_{Bn} ln\ \theta - N_{Cn} ln\ \theta - \frac{\sum_{i=1}^{n}\delta_{Ai}x_{Ai}}{\theta} - \frac{\sum_{i=1}^{n}\delta_{Bi}x_{Bi}}{\theta} - \frac{\sum_{i=1}^{n}\delta_{Ci}x_{Ci}}{\theta};$$

i.e., $l_{H_0} = c - (N_{An} + N_{Bn} + N_{Cn})ln\theta - \frac{1}{\theta}(\sum_{i=1}^{n}\delta_{Ai}x_{Ai} + \sum_{i=1}^{n}\delta_{Bi}x_{Bi}) + \sum_{i=1}^{n}\delta_{Ci}x_{Ci})$.

So, by equating $\frac{\delta l_{H_0}}{\delta\theta} = 0$, we get that,

$$-\frac{n}{\theta} + \frac{1}{\theta^2}(\sum_{i=1}^{n}\delta_{Ai}x_{Ai} + \sum_{i=1}^{n}\delta_{Bi}x_{Bi}) + \sum_{i=1}^{n}\delta_{Ci}x_{Ci}) = 0$$

i.e. $\theta = \frac{1}{n}(\sum_{i=1}^{n}\delta_{Ai}x_{Ai} + \sum_{i=1}^{n}\delta_{Bi}x_{Bi}) + \sum_{i=1}^{n}\delta_{Ci}x_{Ci}) = \frac{N_{An}\hat{\theta}_{An}+N_{Bn}\hat{\theta}_{Bn}+N_{Cn}\hat{\theta}_{Cn}}{n} = \hat{\theta}_n$.

Hence, from $(\star\star\star)$ we get that,

$$\sqrt{n}[\sqrt{\frac{\hat{\gamma}_n}{2}}(\hat{\theta}_{An} - \hat{\theta}_{Bn}),\ \sqrt{\frac{\hat{\gamma}_n}{2}}(\hat{\theta}_{An} - \hat{\theta}_{Cn})] \xrightarrow[H_0]{D} N_2[\begin{pmatrix}0\\0\end{pmatrix}, \begin{pmatrix}1 & \frac{1}{2}\\ \frac{1}{2} & 1\end{pmatrix}],$$

where $\hat{\gamma}_n = \frac{1}{3\hat{\theta}_n^2}$ i.e. $\frac{\hat{\gamma}_n}{2} = \frac{1}{6\hat{\theta}_n^2}$;

i.e., $[\sqrt{n}.\frac{(\hat{\theta}_{An}-\hat{\theta}_{Bn})}{\sqrt{6}\hat{\theta}_n},\ \sqrt{n}.\frac{(\hat{\theta}_{An}-\hat{\theta}_{Bn})}{\sqrt{6}\hat{\theta}_n}] \xrightarrow[H_0]{D} N_2[\begin{pmatrix}0\\0\end{pmatrix}, \begin{pmatrix}1 & \frac{1}{2}\\ \frac{1}{2} & 1\end{pmatrix}]$.

Now, let us define that $D_{1,n} = \sqrt{n}.\frac{(\hat{\theta}_{An}-\hat{\theta}_{Bn})}{\sqrt{6}\hat{\theta}_n}$ and $D_{2,n} = \sqrt{n}.\frac{(\hat{\theta}_{An}-\hat{\theta}_{Cn})}{\sqrt{6}\hat{\theta}_n}$ .....(ii)

Now, if maximum of $D_{1,n}$ and $D_{2,n}$ tends to be very large, then we should favour H_1, else H_0.

Hence, we can take our test statistic as $max\{D_{1,n}, D_{2,n}\}$ whose distribution is unknown-parameter-free under H_0.

So, our critical region will be $\rightarrow$ CR(H_0 vs H_1) : $max\{D_{1,n}, D_{2,n}\} > c$ or $D_n > c$ where $D_n = max\{D_{1,n}, D_{2,n}\}$ where c can be determined from size condition.

Now, as suppose somehow we were expecting that the treatment A is better than the other two treatments B and C, so now to check the statistical efficiency of the **multi-treatment response adaptive allocation procedure**, we have to check whether in this test procedure, the null hypothesis is getting rejected (because, then we can claim that : Treatment A is better than the other two treatment). If it happens, then we can claim that : Our **multi-treatment response adaptive allocation procedure** is statistically efficient.

III. Objective:

As the name has **'multi-treatment'** in itself, we can consider our objective to be searching for the best treatment amongst all. Now, there can be multiple perspectives of calling a treatment the **best one**.

(i) By Ethical Efficiency : The treatment which gets the maximum proportion of allocation from this adaptive procedure can be considered to be the best.

(i) By Statistical Efficiency : Consider the test discussed previously in **Part-C** based on differences of parameters of distributions corresponding to the several treatments. Now, the power of the test will reflect the efficiency of detecting significant difference in the parameters i.e. efficiency of selecting the best / superior treatment. Hence, the power of the test comes handy here.

Now, as said earlier, suppose somehow we were expecting that the treatment A is better than the other two treatments B and C. So, for our proposed rule of adaptive allocation defined at (i), we shall consider competitor allocation rules. Comparing with these competitors, we shall check how good our proposed rule of allocation is in detecting the superior treatment.

We have considered two competitors as defined below:

Competitor-1 : $R_{1,j+1} = P(\delta_{j+1} = 1) = \frac{\hat{\mu}_{1,j}}{\sum_{i=1}^{k} \hat{\mu}_{i,j}},\ j = kn_0,\ kn_0{+}1,\ .....,\ n-1;$

Competitor-2 : $R_{1,j+1} = P(\delta_{j+1} = 1) = \frac{1}{k},\ j = kn_0,\ kn_0 + 1,\ .....,\ n-1;$

So, summing up, we shall check the mean of proportion allocations & power of tests corresponding to all three of the aforesaid allocation rules and hence, we shall conclude which rule could trace treatment-A to be the best one appropriately.

IV. Simulation & Computational Procedures:

In this section, we shall check :

- **Computation of each of the allocation rules algorithmically;**
- **The tests corresponding to each of the allocation rules;**
- **Computation of mean proportions of allocation of the treatments & power corresponding to the tests;**
- **Comparison amongst the allocation rules using Tables & Visualizations**

Computation of the allocation rules :

Proposed allocation rule :

Response adaptive allocation probability ($\hat{R}_{k,j+1}$) for $(j+1)^{th}$ patient to treatment arm k for all $j = kn_0,\ kn_0+1,\ .....,\ n-1$ & for all k=1(1)K (Notations defined previously) is computed as follows :

- Simulate from distributions using estimated parameters corresponding to each treatment arm (K=3, i.e. A,B,C say).
- Check the number of cases where simulated value corresponding to treatment A will be more than that of treatment B & C. Repeat the same for treatments B and C as well.
- Calculate the proportions of the above cases to generate $\hat{R}_{k,j+1}$ for all $j = kn_0,\ kn_0+1,\ .....,\ n-1$ for all k=1(1)K.

An illustration of a function generating the $\hat{R}_{k,j+1}$ values using R can be as follows :

```
#---R_k_hat for proposed tule---

R <- function(theta_a_hat, theta_b_hat, theta_c_hat){
  del_a = 0
  del_b = 0
  del_c = 0

  A = rexp(500, theta_a_hat)
  B = rexp(500, theta_b_hat)
  C = rexp(500, theta_c_hat)

  for(i in 1:500){
    if(A[i] > max(B[i], C[i])){
      del_a = del_a + 1
    }
    else if(B[i] > max(A[i], C[i])){
      del_b = del_b + 1
    }
    else{
      del_c = del_c + 1
    }
  }
  R_a_hat = del_a/500
  R_b_hat = del_b/500
  R_c_hat = del_c/500
  return(c(R_a_hat, R_b_hat, R_c_hat))
}
```

Response adaptive allocation probability for competitor-1 ($\hat{R}_{k,j+1}$) as defined in ( ) for all $j = kn_0,\ kn_0 + 1,\ .....,\ n - 1$ and for all k=1(1)K is computed as follows :

- After initially allocating the treatments to a small number of patients, we cumulatively check the sums of the observations (denoted by X_i) and the number of allocations to each treatment arm.
- Next, we generate $\hat{R}_k,\ k = A, B, C$ by taking the proportion of the mean observation corresponding to the k^{th} treatment to the sum of the same for all the treatments k=A,B,C, as suggested by the allocation rule.
- Thus, updation is done after every allocation till the end.

An illustration from an R code can be as follows :

```
#Estimating Parameters
theta_a = 1/mean(X[1:5])
theta_b = 1/mean(X[6:10])
theta_c = 1/mean(X[11:15]) #---15 patients allocated

delta_a[1:5] <- c(rep(1,5)) #---Initializing the indicators
delta_b[6:10] <- c(rep(1,5))
delta_c[11:15] <- c(rep(1,5))

sum_a = sum(X[1:5]) #---Initiliazing sum variables
sum_b = sum(X[6:10])
sum_c = sum(X[11:15])

R_a = (sum_a/sum(delta_a))/(sum_a/sum(delta_a) + sum_b/sum(delta_b) + sum_c/sum(delta_c))
R_b = (sum_b/sum(delta_b))/(sum_a/sum(delta_a) + sum_b/sum(delta_b) + sum_c/sum(delta_c))
R_c = (sum_c/sum(delta_c))/(sum_a/sum(delta_a) + sum_b/sum(delta_b) + sum_c/sum(delta_c))
```

Response adaptive allocation probability for competitor-2 ($\hat{R}_{k,j+1}$) as defined in ( ) for all $j = kn_0,\ kn_0 + 1,\ .....,\ n - 1$ and for all k=1(1)K is computed by simply assigning value equal to $\frac{1}{K},\ K = no.\ of\ treatments = 3$ to each treatment arm i.e. $\frac{1}{3} = 0.3333$ to each treatment arm.

Updation of parameter(s) :

Here, we have worked with the assumption of exponential distribution, $exp(\theta),\ \theta = Rate\ parameter$(say). So, taking the reciprocal of the mean might give us an estimate of θ. Now, whenever a new allocation takes place, that value is updated to the mean corresponding to it's treatment arm and hence, the parameter estimate is updated.

An R code suggesting the above can be as follows :

```
theta_a = 1/(((1/theta_a)*(sum(delta_a)-1) + X[i])/sum(delta_a))
```

Allocating an individual :

With the values of allocation probabilities for each treatment, which sum up to 1, to allocate $(j+1)^{th}$patient, for all $j = kn_0,\ kn_0+1,\ .....,\ n-1$.

- We shall partition the interval [0,1] in a way like, $[0, \hat{R}_{A,j})$, $[\hat{R}_{A,j},\ \hat{R}_{A,j} + \hat{R}_{B,j})$, $[\hat{R}_{A,j} + \hat{R}_{B,j}, 1]$.
- Generate a $Unif(0,1)$ sample.
- Check in which partition does the uniform sample belong.
- Allocate that treatment.

An R code suggesting the above can be as follows :

```
for(i in 16:800){
    r = runif(1)
    if(r <= R_a_hat){
      X[i] = rexp(1, theta_a)
      delta_a[i] = 1
      theta_a = 1/(((1/theta_a)*(sum(delta_a)-1) + X[i])/sum(delta_a))
      R_estim = R(theta_a_hat = theta_a, theta_b_hat = theta_b, theta_c_hat = theta_c)
      R_a_hat = R_estim[1]
      R_b_hat = R_estim[2]
      R_c_hat = R_estim[3]
    }
    else if((r > R_a_hat )&&(r <= (R_a_hat + R_b_hat))){
      X[i] = rexp(1, theta_b)
      delta_b[i] = 1
      theta_b = 1/(((1/theta_b)*(sum(delta_b)-1) + X[i])/sum(delta_b))
      R_estim = R(theta_a_hat = theta_a, theta_b_hat = theta_b, theta_c_hat = theta_c)
      R_a_hat = R_estim[1]
      R_b_hat = R_estim[2]
      R_c_hat = R_estim[3]
    }
    else{
      X[i] = rexp(1, theta_c)
      delta_c[i] = 1
      theta_c = 1/(((1/theta_c)*(sum(delta_c)-1) + X[i])/sum(delta_c))
      R_estim = R(theta_a_hat = theta_a, theta_b_hat = theta_b, theta_c_hat = theta_c)
      R_a_hat = R_estim[1]
      R_b_hat = R_estim[2]
      R_c_hat = R_estim[3]
```

```
    }
  }
```

Tests corresponding to the allocation rules :

Here, we conduct test as mentioned in **Part-C** to check for the superior treatment.

Now, we compute the statistics $D_{1,n}$ & $D_{2,n}$ as defined in (ii) from the simulated values as follows :

- During the simulation, we run all the allocations for a significantly large number of iterations say 1000.
- At the end of each of the iterations, we calculate estimated values of $\hat{\theta}_k$ for k=A,B,C.
- Using the estimated values, calculate $\hat{\theta}_n$ & hence $D_{1,n},\ D_{2,n}$ accordingly as defined in **Part-C**.
- Thus, using all $D_{1,n},\ D_{2,n}$ values and corresponding $D_n = max\{D_{1,n},\ D_{2,n}\}$ values, we perform our test.

Now, since this is a simulation study here, we assume equal values of parameters corresponding to treatments to find *critical value* empirically and then with suitable alternative choices of parameters we can conduct the test by calculating power, p-value etc. Thus, from the obtained D_n values, we formulate the mentioned test.

An R code to illustrate the above can be as follows :

```
    .
    .
    .
  d1[b] =  sqrt(800)*((1/theta_a - 1/theta_b)/(sqrt(6)*theta_hat))  #---D_1,n
  d2[b] =  sqrt(800)*((1/theta_a - 1/theta_c)/(sqrt(6)*theta_hat))  #---D_2,n
  d[b] = max(d1[b], d2[b])   #---D_n
}

C=quantile(d, p = 0.95)
#---0.95th quantile(C) = Critical value, with assumption of parameters under null hypothesis
```

Computation of mean proportions of allocation of the treatments and powers :

- As mentioned in the previous sections, in this simulation study, we repeat the allocations for a significantly large number of iterations. In each of the iterations, we calculate the respective proportions of allocations of treatments A,B and C. Hence, the means of proportions of all the iterations will give a representative idea corresponding to an allocation rule's efficiency in tracing out the superior treatment. So, we shall compute the **mean proportion of allocations** corresponding to treatments for all the allocation rules.
- Previously we discussed about computing critical values with assumption of parameters under null hypothesis. Now, we repeat the iterations with assumption of parameters under alternative hypothesis. We look for the proportion of values of D_n exceeding the critical value to calculate the **power of the test** under the assumptions.

An R code to illustrate the above can be as below :

```
sum(as.numeric(d>=C))/1000
#---With assumption of parameters under alternative
```

Comparison amongst the allocation rules using Tables and Visualizations :

It is explained above how we shall perform the whole computation algorithmically supplied with some suggestions using R. Now, we shall compare the allocation rules.

Our objectives are to compare (i) **Mean proportion of allocations for the superior treatment** (treatment A here) and (ii) **Powers of the corresponding tests** for variate choices of parameters.

Choice-1 : *Under* H_0*:* $\theta_A = \theta_B = \theta_C = 40$*,* θ_k*'s denoting means corresponding to treatment* k*,* $k = A, B, C$*.*

Table 1.

Choice of Parameters (θ_k = the mean for the k^{th} treatment, k = A, B, C)	Proposed Allocation Rule			Competitor 1			Competitor 2		
	Mean Proportion A (Standard Error)	Power	Crit. Val.	Mean Proportion A (Standard Error)	Power	Crit. Val	Mean Proportion A (Standard Error)	Power	Crit. Val.
θ_A = 200 θ_B = 120 θ_C = 40	0.54273(0.16233)	0.421	(for $H_0: \theta_A=\theta_B=\theta_C=40$) 5.911111	0.51465(0.155546)	0.396	(for $H_0: \theta_A=\theta_B=\theta_C=40$) 6.190233	0.33392(0.0321964)	0.451	(for $H_0: \theta_A=\theta_B=\theta_C=40$) 8.158355
θ_A = 400 θ_B = 120 θ_C = 40	0.67967(0.14358)	0.435		0.65402(0.1322911)	0.724		0.33209(0.0316446)	0.767	
θ_A = 600 θ_B = 120 θ_C = 40	0.74521(0.12305)	0.874		0.724505(0.1187099)	0.861		0.33488(0.032963)	0.891	
θ_A = 800 θ_B = 120 θ_C = 40	0.78517(0.10555)	0.93		0.764635(0.10669)	0.91		0.3334(0.03248)	0.95	
θ_A = 1000 θ_B = 120 θ_C = 40	0.810775(0.09336)	0.959		0.796255(0.09282295)	0.925		0.3345(0.031408)	0.976	
θ_A = 1200 θ_B = 120 θ_C = 40	0.83141(0.08303)	0.98		0.812305(0.085563)	0.906		0.332105(0.032169)	0.986	

The above table shows the variate values of mean proportion of allocation for treatment-A (shown in red), standard error in the suffix (shown in black), critical values (shown in green) under null obtained for tests upon the three allocation rules and powers (shown in blue) corresponding to the alternative choices as shown in the first column. For the other choices of parameters considered, the tables are formed in this manner only.

Choice-2 : *Under* H_0*:* $\theta_A = \theta_B = \theta_C = 30$*,* θ_k*'s denoting means corresponding to treatment* k*,* $k = A, B, C$*.*

Table 2.

Choice of Parameters (θ_k = the mean for the kth treatment, k = A, B, C)	Proposed Allocation Rule			Competitor 1			Competitor 2		
	Mean Proportion A (Standard Error)	Power	Crit. Val.	Mean Proportion A (Standard Error)	Power	Cr. Val	Mean Proportion A (Standard Error)	Power	Crit. Value
θ_A = 90 θ_B = 30 θ_C = 30	0.680405(0.14883)	0.431	(for, H_0: θ_A=θ_B=θ_C=30) 5.91111	0.55935(0.14701)	0.449	(for, H_0: θ_A=θ_B=θ_C=40) 6.026934	0.333365(0.03267)	0.483	(for, H_0: θ_A=θ_B=θ_C=30) 7.807418
θ_A = 150 θ_B = 30 θ_C = 30	0.76378(0.1398)	0.643		0.65499(0.13089)	0.692		0.332485(0.0331452)	0.735	
θ_A = 250 θ_B = 30 θ_C = 30	0.80832(0.1111166)	0.842		0.73262(0.11654)	0.867		0.332565(0.031436)	0.915	
θ_A = 350 θ_B = 30 θ_C = 30	0.83667(0.09040216)	0.91		0.787465(0.0968)	0.943		0.33454(0.03144562)	0.955	
θ_A = 450 θ_B = 30 θ_C = 30	0.87885(0.0743696)	0.955		0.81481(0.08425)	0.967		0.33252(0.031606)	0.979	
θ_A = 750 θ_B = 30 θ_C = 30	0.58036(0.05100964)	0.984		0.85858(0.06423)	0.986		0.33095(0.030984)	0.996	

Choice-3 : *Under* H_0*:* $\theta_A = \theta_B = \theta_C = 100$*,* θ_k*'s denoting means corresponding to treatment* k*,* $k = A, B, C$*.*

Table 3.

Choice of Parameters (θ_k = the mean for the kth treatment, k = A, B, C)	Proposed Allocation Rule			Competitor 1			Competitor 2		
	Mean Proportion A (Standard Error)	Power	Cr. Val	Mean Proportion A (Standard Error)	Power	Cr. Val.	Mean Proportion A (Standard Error)	Power	Cr. Val
θ_A = 300 θ_B = 100 θ_C = 170	0.516565(0.1648546)	0.311	(for, H_0: θ_A=θ_B=θ_C= 100) 5.911111	0.489465(0.1524)	0.284	(for, H_0: θ_A=θ_B=θ_C= 100) 6.190236	0.331455(0.031308)	0.304	(for, H_0: θ_A=θ_B=θ_C= 100) 8.356584
θ_A = 600 θ_B = 100 θ_C = 170	0.66006(0.1438273)	0.612		0.63367(0.13949)	0.61		0.331655(0.03137)	0.652	
θ_A = 900 θ_B = 100 θ_C = 170	0.728325(0.125645)	0.789		0.700595(0.1203)	0.762		0.33258(0.0310146)	0.823	
θ_A = 1200 θ_B = 100 θ_C = 170	0.772035(0.108958)	0.877		0.74304(0.112885)	0.824		0.333385(0.03188)	0.902	
θ_A = 1500 θ_B = 100 θ_C = 170	0.801395(0.0951758)	0.908		0.774765(0.1035)	0.855		0.333575(0.03185)	0.938	

So, we can see patterns in the observed values in the table. To make some conclusive idea about the comparison amongst the three allocation rules, we take help of the following visualizations.

Visualizing Mean Proportions of all allocations of Treatment-A :

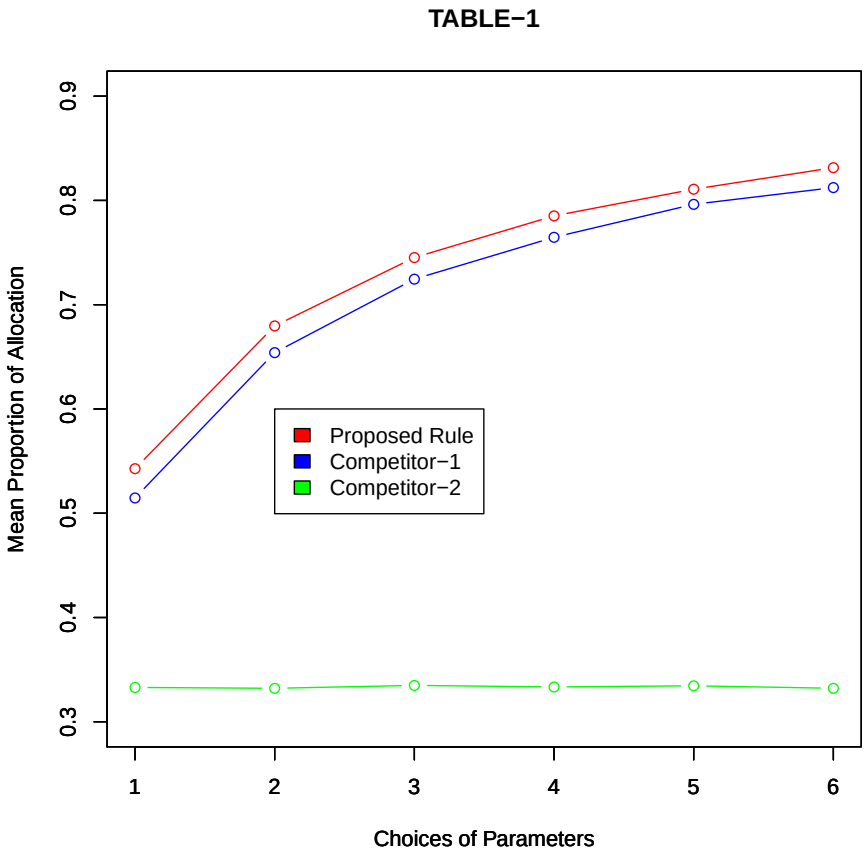

Figure-1 : Plot showing mean proportions of allocation of treatment-A for alternative choices of parameters in Table-1.

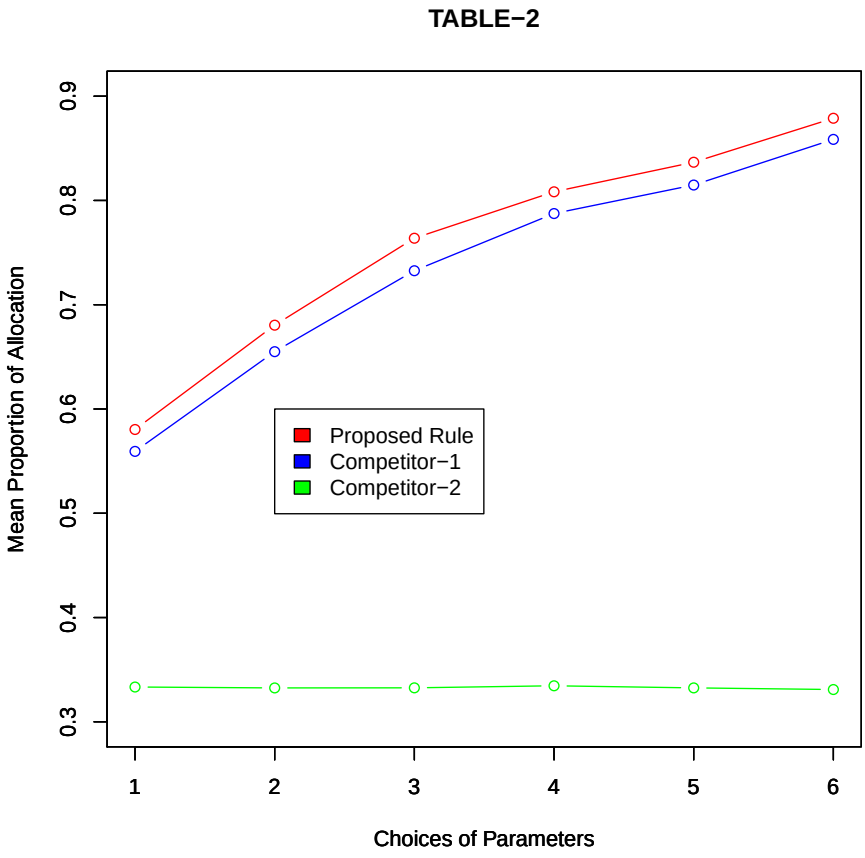

Figure-2 : Plot showing mean proportions of allocation of treatment-A for alternative choices of parameters in Table-2.

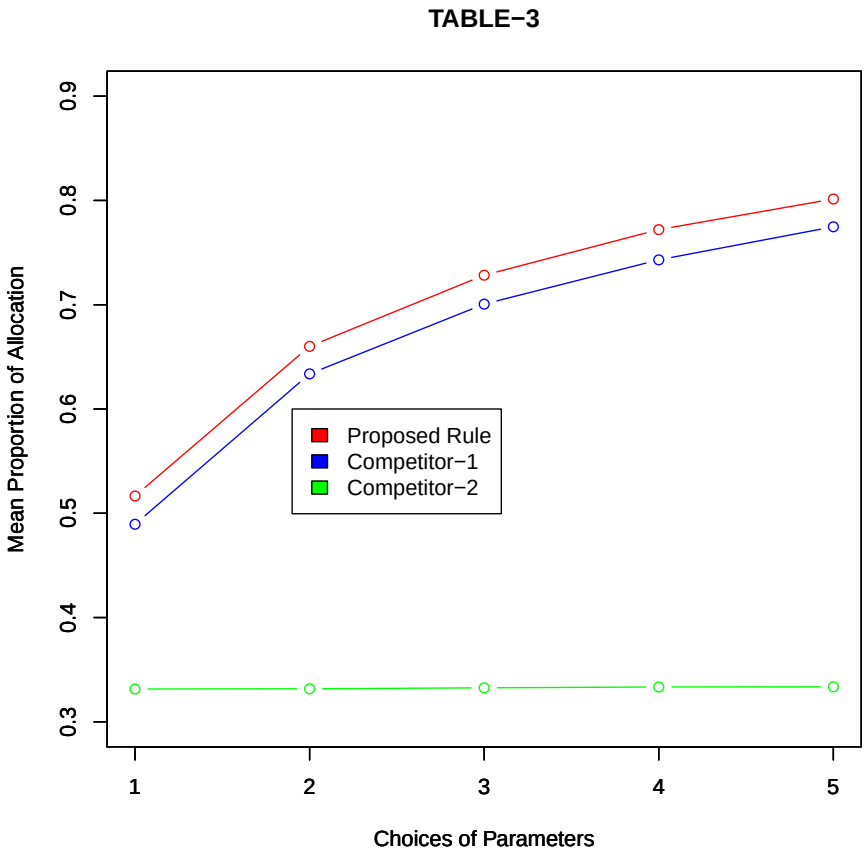

Figure-3 : Plot showing mean proportions of allocation of treatment-A for alternative choices of parameters in Table-3.

Remarks :

In all of the cases considered above, we have observed ***very similar patterns*** and hence leads to similar conclusions as follows :

1. ***Our proposed rule of allocation has allocated the maximum number of individuals to the superior treatment, A*** for every choice of alternative hypothesis, followed by competitor-1 and competitor-2 respectively.

2. Both ***Proposed allocation rule*** and ***Competitor-1*** have allocated treatment-A with superiority followed by Treatment-B and Treatment-C respectively resulting in ***Ethical Allocation***. Hence, combining with the previous point, ***the Proposed allocation rule is the most Ethically Efficient one.***

3. For competitor-2 i.e. equal probability allocation rule, there is no question of ethical allocation and ***hence not preferable according to our interest***.

4. In the ethical allocation rules, the increasing nature of mean proportion of allocations justifies the fact that more the difference between the parameters corresponding to each treatment arm i.e. more the mean for treatment-A, more is the allocation for treatment-A. So in simple words, ***the better Treatment-A works for the disease than Treatment-B and C, more will be the allocation for treatment-A if the Proposed rule or the Competitor-1 rule is implemented***.

5. Simply, just by comprehending these plots, ***our proposed allocation rule stands out to be preferable***.

Visualizing Powers corresponding to the Tests constructed :

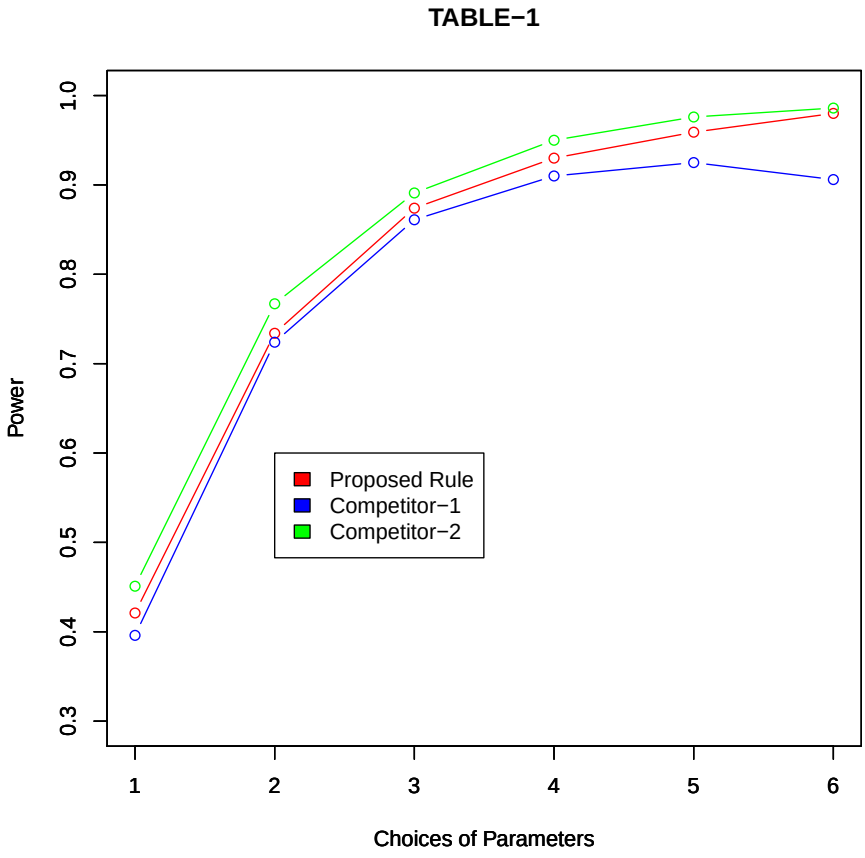

Figure-4 : Plot showing power of tests corresponding to alternative choices of parameters in Table-1.

Remarks :

1. We can see for all choices of parameters under alternative hypothesis in Table-1, ***the power corresponding to equal probability allocation rule is maximum*** followed by the proposed allocation rule and the competitor-1 respectively. Hence, ***only by comparing the powers, the equal probability allocation rule works the best***.

2. Leaving aside the equal probability allocation, ***observing the powers of the other two, the proposed allocation rule stands out to be***

acceptable given the choice of alternative hypothesis.

3. The increase in power signifies that, the more the difference between the parameters corresponding to the treatments, more is the power when tested accordingly. ***So, in simpler words, the better treatment-A works, the more the tests i.e. the proposed allocation rules traces how better treatment-A is than the rest of the two.***

TABLE−2

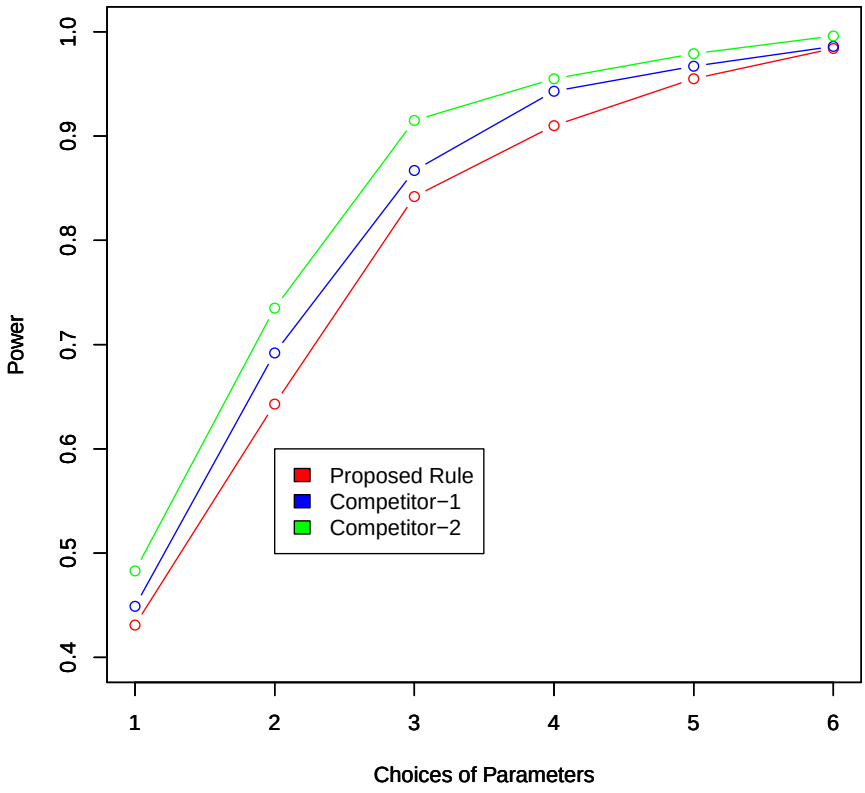

Figure-5 : Plot showing power of tests corresponding to alternative choices of parameters in Table-2.

Remarks :

1. Here , we can see that, for all choices of parameters under alternative hypothesis, ***the power corresponding to equal probability allocation rule is maximum*** here also, but ***followed by the competitor-1 and***

the proposed allocation rule respectively. Hence, only by comparing the powers, the equal probability allocation rule works the best.

2. Leaving aside the equal probability allocation, observing the powers of the other two, the ***Competitor-1 stands out to be acceptable*** given the choice of alternative hypothesis.

3. Like the previous plot, here also ***the graphs are of increasing nature***. Hence, the same interpretation.

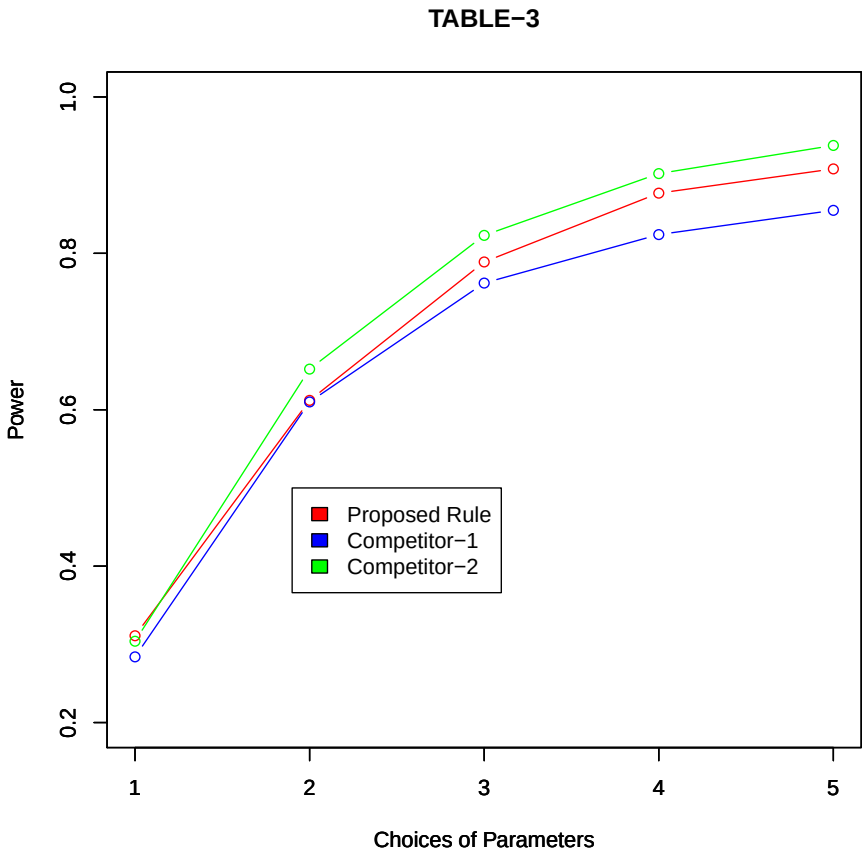

Figure-6 : Plot showing power of tests corresponding to alternative choices of parameters in Table-3.

Remarks :

Here again, ***just like the results obtained for alternative choices in Table-1***, the power corresponding to equal probability allocation rule is maxi-

mum followed by the proposed allocation rule and the competitor-1 respectively. So, the interpretations are pretty much same as obtained for Figure-4 (Table-1).

Overall remarks from Means of Proportions of Allocation and Figures-4, 5 & 6 :

1. Leaving the Equal probability allocation aside, ***we have seen more power corresponding to Proposed allocation rule in two cases (Table-1 & 3) and seen the same for Competitor-1 in the second (Table-2) case***. From here we can conclude, the majority of the three suggests, Proposed allocation rule is better than Competitor-1 w.r.t the powers calculated. ***From here, roughly we can say either the Proposed allocation rule is better between the two or the two are somewhat similar according to the powers resulting from the tests***.

2. The Equal probability allocation rule has ***the maximum power in all three cases and hence the most acceptable if our selection criterion of rules only pertains power of the test***.

3. ***Combining with the conclusions, from the plots of Mean proportion allocation, the Equal probability allocation does not end up being the best, despite having very high powers***. Our study of Adaptive allocation has the objective of tracing the superior treatment and allocating the maximum to that treatment and allocating the rest according to their superiority. The Proposed rule and the Competitor-1 rule proves to be Ethically efficient, the Proposed allocation rule being the best but ***the Equal probability allocation rule is not ethically significant at all***. Hence, ***we discard Competitor-2 as it violates the objective / motivation of this allocation study even though it works good in terms of power calculation***.

4. Combining Point-1 and results obtained w.r.t Mean proportion of allocation, ***we can conclude that the Proposed allocation rule proves itself to be efficient in both ways, i.e. "Ethical and Statistical". Comparing with the Competitor-1, we shall tend towards our Proposed allocation rule as it proves itself better ethically and as majority in our study suggests statistically. So, our Proposed allocation rule can allocate the maximum to the superior treatment and also traces how better our superior treatment is than the rest most efficiently.***

5. Hence, from all the studies conducted, we choose ***our Proposed allocation rule to be the best***.

Comparing the Consistency of the Performed Tests :

A test is considered to be **consistent** if the power of the test for a fixed alternative hypothesis increases to one(1) as the sample size increases.

Now, primarily for our problem, we shall look at the powers corresponding to the tests performed for variate values of sample size i.e. total number of individuals to whom treatments are allocated, with a fixed choice of alternative hypothesis.

So here, we fix our null hypothesis $H_0 : \ \theta_A = \theta_B = \theta_C = 30$ and our alternative hypothesis $H_1 : \ \theta_A = 250, \ \theta_B = 80, \ \theta_C = 30$.

For varying values of sample sizes, we construct the following table :

Table 4.

Sample Size *(n)*	Proposed Allocation Rule			Competitor 1			Competitor 2		
	Power	**S.D.**	**Crit. Val.**	**Power**	**S.D.**	**Cr. Val**	**Power**	**S.D.**	**Cr. Val.**
200	0.683	0.14573	5.91111	0.679	0.13422	6.219394	0.669	0.032463	8.383924
400	0.695	0.14863	8.222038	0.682	0.14934	8.611195	0.706	0.023313	11.65483
1000	0.746	0.14824	12.74309	0.69	0.15234	13.54952	0.730	0.01462	18.26168
1200	0.75	0.15215	14.05489	0.671	0.15822	14.75901	0.726	0.01358	20.06617
(for, H_0: θ_A=θ_B=θ_C=30, null choices of parameters) *(For, θ_A=250, θ_B=80, θ_C=30, alternative choices of θ_k , k = A, B and C)*									

The above table shows the variate values of Power (shown in red), Standard error (shown in blue), Critical values (shown in green) for the mentioned fixed hypothesis.

Visualizing Power with Variate Values of Sample size :

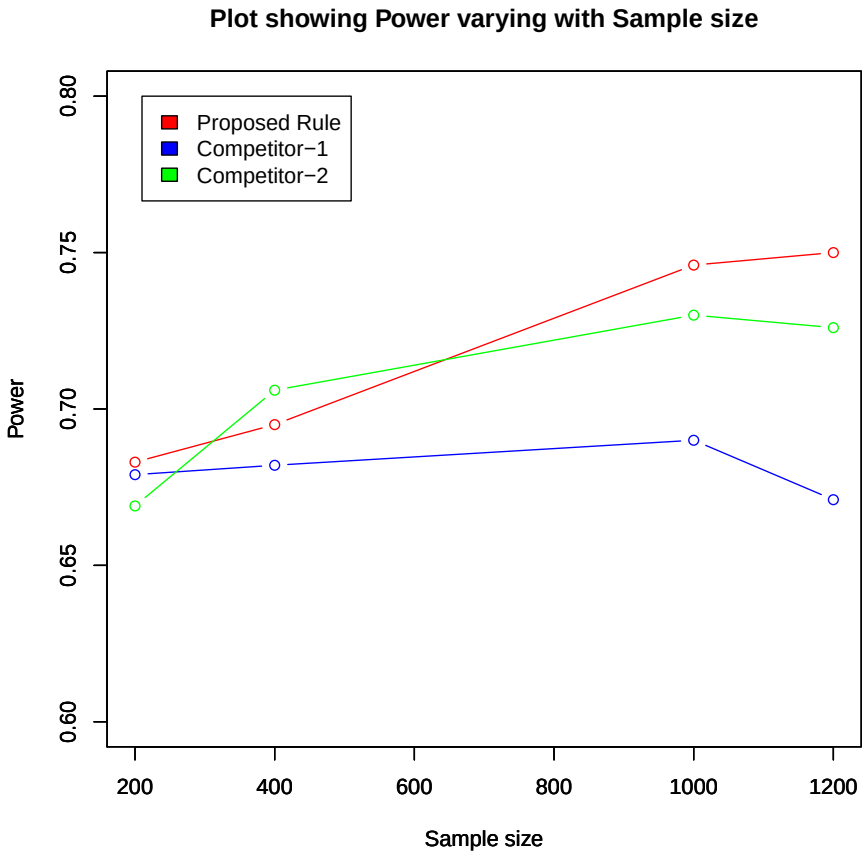

Figure-7 : Plot showing power of tests corresponding to variate values of sample size as given in Table-4.

Remark :

Theoritically as $n \to \infty$, the power increases to 1 for a **Consistent test**. Now, as we are dealing with a long tail distribution, *a monotonic increase in power with increasing sample sizes is fair enough to suggest consistency* in this practical problem of adaptive allocation.

1. We can see ***Power corresponding to our Proposed allocation rule has increased monotonically in the range in which, we have in-***

creased our sample sizes. Hence, our proposed rule can be considered Consistent.

2. If we watch the plots minutely, ***we can see both the competitors have their powers decreased at a high value of sample size (1200). Hence, it is debatable if both of them are actually consistent or not***.

3. Even though the powers corresponding to the Equal probability allocation rule, is more than the other two initially, as the sample size increases further, the Proposed allocation rule stands tall beating the other two (approximately sample size=600 onwards). So, ***the proposed allocation rule is more strongly consistent than the other two and hence, desirable over the two competitors***.

V. Conclusion:

So as our objective was to understand if our ***Proposed allocation rule*** matches it's competitors by merits of ***Ethical and Statistical efficiency*** from the results obtained.

(i) ***We have checked the means of proportions of allocations corresponding to all the allocation rules and resultantly observed that our proposed allocation rule is the most ethically efficient one***.

(ii) We have the hypothesis testing by formulating suitable statistics to test the significance of differences between the parameters corresponding to the treatments. ***Here also, the proposed allocation rule proved itself to be having strong statistical efficiency***.

(iii) As for the rest of the two competitors, ***Competitor-1 has been the tougher competitor as it was ethically and statistically significant but not quite as much as the proposed allocation rule. As said earlier, Competitor-2 i.e. Equal probability allocation design is not ethically efficient at all***.

(iv) Addition to the above, ***when we checked for the consistency of the related tests of the allocation rules, our proposed allocation rule proved itself to be consistent strongly enough***.

(v) ***In the course of the study, we formulated precised procedures of treatment allocations as per the three allocation rules, checked the above results and hence, conclusively say that our proposed allocation rule is more acceptable as per all deductions and results obtained in our study***.