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Ensuring Balance with Regard to Optimality for Known Categorical Covariates and Multiple Treatment Groups

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ABSTRACT: Ensuring balanced allocation by achieving optimality for known categorical covariates into two treatment groups has been analytically established with regard to $D-$, $A-$, D_s- and A_s-optimality in Hore et al. (2020) and for $E-$ and E_s-optimality has been discussed by the authors earlier. However, the mathematical complexity of expression of the respective optimality function and mathematical computation increases with more number of treatments. In this work, the relationship between D-optimality and balancing criteria for known categorical covariates across three treatment groups is established through analytical derivation and simulation studies. It has been shown that $D-$optimality ensures a balanced allocation design, at least as a local optimal solution. Furthermore, simulation studies demonstrate that the balanced allocation design performs uniformly better than random allocation designs.

Key Words: Covariate balanced, optimal allocation design, clinical trials, local optimality, randomization.

Contents

1. Introduction

In clinical trials (Pocock and Simon, 1975; Kalish and Begg, 1985), factorial design (Branson et al., 2016), causal inference (Rubin, 2008; Morgan and Rubin, 2012), and other contexts, balanced allocation with respect to observable covariates is a desirable one. For instance, the leprosy study experiment by Snedecor and Cochran (1989, p. 377) is taken into consideration. It involves thirty patients, each of whom is assigned to one of three drug types (two antibiotics and one control), with ten patients receiving each drug. The experimenter knows each patient's initial pre-treatment score (count of bacilli) prior to the commencement of the study.

Clinical trials frequently employ adaptive designs, in which experimental units are assigned to any of the available treatment groups based on the experimental unit's covariate values after joining the experiment sequentially. This design technique induces a balance in the experimental units through their observed covariate values while allocating them to various treatment groups. Such balancing criterion entails which treatment will be assigned to the upcoming unit. To avoid the suspicion of conscious or unconscious favoritism on a particular treatment or treatment groups, a biased coin design has been suggested by Efron (1971) in which the under-represented treatment is favored through a probabilistic allocation mechanism. Initially, Efron's biased coin design (Efron, 1971) has been designed to compare two treatments. Then, Pocock and Simon (1975) and Efron (1980) introduced an overall structure that can accommodate any number of treatments and achieve balance using the observed covariates. However, Wei (1977, 1978) implemented the probabilistic allocation using the urn design. The permuted block

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design (Zelen, 1974) is a commonly used sequential allocation rule that aims for within-stratum balance. When there is equilibrium between the treatments in the stratum, the permuted block design randomly allocates a treatment to a subsequent unit.

Optimal allocation problem considering the known covariate values related to generalized linear model (GLM) is more complex in comparison to the corresponding linear model formulation (McCullagh and Nelder, 1989; MacKenzie and Peng, 2014). Because the allocation design is dependent on the parameter values of the respective model but the parameter values are unknown to the experimenter before the experiment. One popular method for getting around this issue is to develop an effective design for the best prediction of the parameter values. Chernoff (1953) first proposed the concept of "locally optimal" designs, which have been successfully applied by Yang et al. (2012) and Yang and Mandal (2015) for $D-$optimal factorial designs under the GLM frameworks and $2-$level factorial designs with binary response models, respectively. The initial estimate approach, sequential approach, constant information approach, and fiducial approach are some of the non-Bayesian methods for effectively estimating the model parameters in quantal assays (Morgan, 1992) with binary responses (Finney, 1978; Abdelbasit and Plackett, 1983). Meanwhile, the Bayesian technique for such a model is explored in a number of sources, including Freeman (1970), Tsutakawa (1972, 1980), Owen (1975), Wu (1985), Chaloner and Larntz (1989) and Chaloner and Verdinelli (1995). Yang et al. (2016) have proposed an innovative approach for obtaining a $D-$optimal allocation design as an alternative to such local optimality, in which the corresponding information matrix is substituted with its anticipation with regard to the prior distribution of parameters. Hore et al. (2025) have suggested the concept of EW $D-$optimality to achieve a $D-$optimal allocation design by taking expectation over the weights (function of the parameters) of the covariance matrix. Considering the LM setup, recently Nag et al. (2025) proposed an efficient neighborhood search method to attain balanced as well as optimal allocation design for known categorical covariates with different levels.

Such importance of balanced allocation and optimality for known covariate values under the LM and GLM frameworks motivate us to establish the relationship between optimal allocation and its balanced counter part for categorical covariates. Ensuring balanced allocation by achieving optimality for known categorical covariates into two treatment groups has been analytically established with regard to $D-$, $A-$, D_s- and A_s-optimality in Hore et al. (2020) and for $E-$ and E_s-optimality in Nag and Hore (2024). But, the mathematical complexity of expression of the respective optimality function and mathematical computation increases with more number of treatments. In this study, we have carried out to establish the relationship between $D-$optimality and balancing criteria for categorical covariates under three treatment groups. Simulation study has been also carried out to check the efficacy of the balanced allocation design compare to randomized allocation design with regard to $D-$optimality criterion.

The study has been classified into four different sections, starting with Introduction in Section 1. Structural format of the respective linear model has been derived in Section 2. Analytical establishment of $D-$optimality for three treatment groups and simulation study have been carried out in Section 3 and 4, respectively. The study ends with limitation of the work and some concluding remarks with Section 5.

2. Problem Formulation

Let us consider the linear model, as reported in the previous study

$$Y \quad = \quad \mathcal{U}\theta + \epsilon = Z\mu + X\beta + \epsilon, \tag{2.1}$$

where $\mathcal{U} = (Z : X)$, $\theta = (\mu : \beta)$. Here Y is the $n-$dimensional response vector, Z is the $(n \times r)$ matrix of unit row vectors corresponding to the indicator variables for the treatments with one entry to be *unity* for each row, μ is the vector of r treatment effects, X is the matrix of covariates of order $(n \times s)$ associated with the $s-$dimensional vector of regression coefficients β and the error vector ϵ is assumed to follow $N_n(0, \sigma^2 I)$ distribution, where $\sigma^2 (> 0)$ is the unknown constant variance. The optimality criteria depend on the information matrix $(\mathcal{U}^T\mathcal{U})$ of order $(r+s) \times (r+s)$. For efficient estimation of both treatment and covariate effects with regard to $D-$optimality, we need to maximize the determinant of the information matrix $(\mathcal{U}^T\mathcal{U})$ or minimizing the determinant of the dispersion matrix $(\mathcal{U}^T\mathcal{U})^{-1}$. Generally, maximization of the information matrix is preferable compare to the minimization of the dispersion matrix, because the inverse notations of matrix becomes more computational complex. For this reason, we have limited our discussion to $D-$optimality only and $A-$optimality has been left as future research interest.

Borrowing the notations and concepts from the previous study, we have extended for $r = 3$ and $s = K$ in the present set-up by considering a single categorical covariate involving $(K + 1)$ levels $A_1, \cdots, A_{K+1}$ (*i.e.* $s = K$, owing to the presence of K independent dummy variables to indicate the $K + 1$ levels). Hence, the non-singular information matrix $\mathcal{U}^T\mathcal{U}$ of order $(3+K)\times(3+K)$, excepting the constant σ^{-2}, may be written as

$$\mathcal{U}^T\mathcal{U} \quad = \quad \begin{pmatrix} \Lambda_n & M \\ M^T & \Lambda_m \end{pmatrix}, \tag{2.2}$$

where $\Lambda_n = diag\ (n_1, n_2, n_3)$ is a 3×3 diagonal matrix, $\Lambda_m = diag\ (m_1, m_2, \cdots, m_K)$ is a $K \times K$ diagonal matrix and $M = ((m_{lj}))$ is a $3 \times K$ dimensional matrix with elements m_{lj}, for $l = 1, 2, 3$, and $j = 1, \cdots, K$. The above matrix is independent of the term $m_{l\ \overline{K+1}}$, as $m_{l\ \overline{K+1}} = n_l - \sum_{j=1}^{K} m_{lj}$, $l = 1, 2, 3$. For s categorical covariates with $k_1, \cdots, k_s$ levels respectively, the total number of level combinations is $k_1 \times ... \times k_s = K + 1$, say. If balanced allocation, in terms of number of replicates, is achieved within each cell of such s-way classification, then corresponding marginal balance of any order is a natural consequence by summing over the required cells. Therefore, any order's marginal balance can be guaranteed by cell level balance. Hence, for s categorical covariates with $k_1, \cdots, k_s$ levels, individual and marginal balance of any order can be guaranteed by attaining balance at each level of a single hypothetical covariate with $k_1 \times ... \times k_s = K + 1$ levels. Let us demonstrate a hypothetical educational intervention study as an illustration in Table 1, in which 180 students are to be assigned to three different teaching methods (A, B and C). For each student, two different categorical covariates are observed: school type (3 levels, e.g., Public, Private, and Charter) and grade level (2 levels, e.g., Grade 9 and Grade 10). Here, $K + 1 = 3 \times 2 = 6$. Suppose the number of students from each school type is 90, 45, and 45 respectively; 120 students are in Grade 9, and 60 are in Grade 10. Thus, students can be categorized into 6 distinct groups based on the combination of these covariates. Balancing across covariates would involve allocating equi-proportionals of the students within each of the 6 categories to Teaching Method A, Teaching Method B and the remaining to Teaching Method C are shown in Table 1. This ensures that the assignment is balanced not only across the combined covariate structure but also individually across School Type and Grade Level.

Table 1. 60 patients in a 3×2 Design.

School	Grade Level		Marginal
	Grade 9	Grade 10	Total
Public	60 (A:B:C=20:20:20)	30 (A:B:C=10:10:10)	90
Private	30 (A:B:C=10:10:10)	15 (A:B:C=5:5:5)	45
Charter	30 (A:B:C=10:10:10)	15 (A:B:C=5:5:5)	45
Marginal Total	120	60	180

3. Optimality with respect to both treatment and covariate effects

The optimum allocation of n experimental units with a known single categorical covariate values with $K+1$ levels regarding $D-$optimality has been formulated on the information matrix $(\mathcal{U}^T\mathcal{U})$ (without the constant σ^{-2}) as given in (3.2.2) can be written as

$$\mathcal{U}^T\mathcal{U} = \begin{pmatrix} n_1 & 0 & 0 & m_{11} & m_{12} & \cdots & m_{1K} \\ 0 & n_2 & 0 & m_{21} & m_{22} & \cdots & m_{2K} \\ 0 & 0 & n_3 & m_{31} & m_{32} & \cdots & m_{3K} \\ m_{11} & m_{21} & m_{31} & m_1 & 0 & \cdots & 0 \\ m_{12} & m_{22} & m_{32} & 0 & m_2 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ m_{1K} & m_{2K} & m_{3K} & 0 & 0 & \cdots & m_K \end{pmatrix}, \quad (3.1)$$

3.1. $D-$optimality

For $D-$optimality, we have to maximize the information matrix $det(\mathcal{U}^T\mathcal{U})$ with respect to (n_1, n_2, n_3) and (m_{1j}, m_{2j}, m_{3j}), for $j = 1, \cdots, K$, subject to the conditions $n = n_1 + n_2 + n_3$ and $m_j = \sum_{l=1}^{3} m_{lj}$, $j = 1, \cdots, K$. By applying the formula of partitioned matrix (Rao, 1973, p 32; Rao and Bhimasankaran, 2000, p 246), the determinant of the information matrix $(\mathcal{U}^T\mathcal{U})$ can be written as follows

$$det(\mathcal{U}^T\mathcal{U}) = (\prod_{j=1}^{K} m_j)\ det\left[\begin{pmatrix} n_1 & 0 & 0 \\ 0 & n_2 & 0 \\ 0 & 0 & n_3 \end{pmatrix} - \begin{pmatrix} \sum_{j=1}^{K} \frac{m_{1j}^2}{m_j} & \sum_{j=1}^{K} \frac{m_{1j}m_{2j}}{m_j} & \sum_{j=1}^{K} \frac{m_{1j}m_{3j}}{m_j} \\ \sum_{j=1}^{K} \frac{m_{2j}m_{1j}}{m_j} & \sum_{j=1}^{K} \frac{m_{2j}^2}{m_j} & \sum_{j=1}^{K} \frac{m_{2j}m_{3j}}{m_j} \\ \sum_{j=1}^{K} \frac{m_{3j}m_{1j}}{m_j} & \sum_{j=1}^{K} \frac{m_{3j}m_{2j}}{m_j} & \sum_{j=1}^{K} \frac{m_{3j}^2}{m_j} \end{pmatrix}\right],$$

$$\text{or, } det(\mathcal{U}^T\mathcal{U}) = (\prod_{j=1}^{K} m_j)\ det\left[\begin{pmatrix} n_1 - \sum_{j=1}^{K} \frac{m_{1j}^2}{m_j} & -\sum_{j=1}^{K} \frac{m_{1j}m_{2j}}{m_j} & -\sum_{j=1}^{K} \frac{m_{1j}m_{3j}}{m_j} \\ -\sum_{j=1}^{K} \frac{m_{2j}m_{1j}}{m_j} & n_2 - \sum_{j=1}^{K} \frac{m_{2j}^2}{m_j} & -\sum_{j=1}^{K} \frac{m_{2j}m_{3j}}{m_j} \\ -\sum_{j=1}^{K} \frac{m_{3j}m_{1j}}{m_j} & -\sum_{j=1}^{K} \frac{m_{3j}m_{2j}}{m_j} & n_3 - \sum_{j=1}^{K} \frac{m_{3j}^2}{m_j} \end{pmatrix}\right].$$

For the sake of mathematical convenience, instead of considering the discrete design variables n_l and m_{lj} as integers, we consider the corresponding proportions given by $p_1 = \frac{n_1}{n}$, $p_2 = \frac{n_2}{n}$, $1 - p_1 - p_2 = \frac{n_3}{n}$ and $q_{1j} = \frac{m_{1j}}{m_j}$, $q_{2j} = \frac{m_{2j}}{m_j}$, $1 - q_{1j} - q_{2j} = \frac{m_{3j}}{m_j}$, for $j = 1, \cdots, K$, which are fractions and hence may be treated as continuous. Let us write $q_{1\overline{K+1}} = \frac{m_{1\overline{K+1}}}{m_{K+1}}$, $q_{2\overline{K+1}} = \frac{m_{2\overline{K+1}}}{m_{K+1}}$, $1 - q_{1\overline{K+1}} - q_{2\overline{K+1}} = \frac{m_{3\overline{K+1}}}{m_{K+1}}$ and denote $\prod_{j=1}^{K} m_j = m$. A brief summary table of the relation between key symbols (p_i, q_{ij}), and (n_i, m_{ij}), for $i = 1, 2, 3$ and $j = 1, 2, \cdots, K + 1$ is performed in Table 2 to understand the relation between the transformation from discrete variables to continuous variables for quick readability.

Table 2. Transformation of discrete variables to continuous variables.

Discrete	Continuous
n_1	$n \times p_1$
n_2	$n \times p_2$
n_3	$n \times (1 - p_1 - p_2)$
m_{1j}	$m_j \times q_{1j}$
m_{2j}	$m_j \times q_{2j}$
m_{3j}	$m_j \times (1 - q_{1j} - q_{2j})$

.

Now, by writing $det(\mathcal{U}^T\mathcal{U})$ as ϕ_D, a function of $\mathbf{p} = (p_1, p_2)$, $\mathbf{q_{1j}} = (q_{11}, \cdots, q_{1K})$ and $\mathbf{q_{2j}} = (q_{21}, \cdots, q_{2K})$, we have

$$\begin{aligned}\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) \quad = \quad & m\left[(np_1 - \sum_{j=1}^{K} m_j q_{1j}^2)(np_2 - \sum_{j=1}^{K} m_j q_{2j}^2)\{n(1-p_1-p_2) - \sum_{j=1}^{K} m_j(1-q_{1j}-q_{2j})^2\}\right] \\ & -m\{n(1-p_1-p_2) - \sum_{j=1}^{K} m_j(1-q_{1j}-q_{2j})^2\}(\sum_{j=1}^{K} m_j q_{1j} q_{2j})^2 \\ & -m\left[(np_1 - \sum_{j=1}^{K} m_j q_{1j}^2)\{\sum_{j=1}^{K} m_j q_{2j}(1-q_{1j}-q_{2j})\}^2\right] \\ & -m\left[(np_2 - \sum_{j=1}^{K} m_j q_{2j}^2)\{\sum_{j=1}^{K} m_j q_{1j}(1-q_{1j}-q_{2j})\}^2\right] \\ & -2m\left[\{\sum_{j=1}^{K} m_j q_{1j} q_{2j}\}\{\sum_{j=1}^{K} m_j q_{1j}(1-q_{1j}-q_{2j})\}\{\sum_{j=1}^{K} m_j q_{2j}(1-q_{1j}-q_{2j})\}\right]. \quad (3.1)\end{aligned}$$

The above equation can be written as

$$\begin{aligned}\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) \quad = \quad & m\left[(\phi_{D_1}\phi_{D_2} - \phi_{D_{12}}^2)(\phi_{D_3} - \phi_{D_4}) - \phi_{D_1}(\phi_{D_{23}})^2 - \phi_{D_2}(\phi_{D_{13}})^2\right] \\ & -2m\left[\phi_{D_1}\phi_{D_2}\phi_{D_3}\right], \quad (3.2)\end{aligned}$$

where,

$$\phi_{D_1} = (np_1 - \sum_{j=1}^{K} m_j q_{1j}^2), \quad (3.3)$$

$$\phi_{D_2} = (np_2 - \sum_{j=1}^{K} m_j q_{2j}^2), \quad (3.4)$$

$$\phi_{D_3} = n(1-p_1-p_2), \quad (3.5)$$

$$\phi_{D_4} = \sum_{j=1}^{K} m_j(1-q_{1j}-q_{2j})^2, \quad (3.6)$$

$$\phi_{D_{12}} = \sum_{j=1}^{K} m_j q_{1j} q_{2j}, \quad (3.7)$$

$$\phi_{D_{13}} = \sum_{j=1}^{K} m_j q_{1j}(1-q_{1j}-q_{2j}), \quad (3.8)$$

$$\phi_{D_{23}} = \sum_{j=1}^{K} m_j q_{2j}(1-q_{1j}-q_{2j}). \quad (3.9)$$

For the sake of mathematical convenience, partial derivative of above small terms with respect to p_1, p_2, q_{1j}, q_{2j}, for $j = 1, 2, \cdots, K$, we get
$\phi'_{D_1|p_1} = n$, $\phi'_{D_2|p_1} = 0$, $\phi'_{D_3|p_1} = -n$ and $\phi'_{D_4|p_1} = \phi'_{D_{12}|p_1} = \phi'_{D_{13}|p_1} = \phi'_{D_{23}|p_1} = 0$.
$\phi'_{D_1|p_2} = 0$, $\phi'_{D_2|p_2} = n$, $\phi'_{D_3|p_2} = -n$ and $\phi'_{D_4|p_2} = \phi'_{D_{12}|p_2} = \phi'_{D_{13}|p_2} = \phi'_{D_{23}|p_2} = 0$.
$\phi'_{D_1|q_{1j}} = -2m_j q_{1j}$, $\phi'_{D_2|q_{1j}} = 0$, $\phi'_{D_3|q_{1j}} = 0$, $\phi'_{D_4|q_{1j}} = -2m_j(1-q_{1j}-q_{2j})$, $\phi'_{D_{12}|q_{1j}} = m_j q_{2j}$, $\phi'_{D_{13}|q_{1j}} = m_j(1-2q_{1j}-q_{2j})$, $\phi'_{D_{23}|q_{1j}} = -m_j q_{2j}$.

$\phi^{'}_{D_1|q_{2j}} = 0$, $\phi^{'}_{D_2|q_{2j}} = -2m_jq_{2j}$, $\phi^{'}_{D_3|q_{2j}} = 0$ and $\phi^{'}_{D_4|q_{2j}} = -2m_j(1-q_{1j}-q_{2j})$, $\phi^{'}_{D_{12}|q_{2j}} = m_jq_{1j}$, $\phi^{'}_{D_{13}|q_{2j}} = -m_jq_{1j}$, $\phi^{'}_{D_{23}|q_{2j}} = m_j(1-q_{1j}-2q_{2j})$.
Now equating the partial derivative of $\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}})$ with respect to p_1 to zero and after some routine algebra, we get

$$\begin{aligned}\phi^{'}_{D|p_1}(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) &= 0,\\ \Rightarrow mn\left[\phi_{D_2}(\phi_{D_3}-\phi_{D_4}) - (\phi_{D_1}\phi_{D_2}-\phi^2_{D_{12}}) - \phi^2_{D_{23}}\right] &= 0. \qquad (3.10)\end{aligned}$$

Considering balanced allocation in each level of covariate, i.e., for $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, the values of the equations (3.3.3) to (3.3.9) are

$\phi_{D_1} = \phi_{D_2} = \frac{(2n+m_{K+1})}{9}$, $\phi_{D_3} = \frac{n}{3}$ and $\phi_{D_4} = \phi_{D_{12}} = \phi_{D_{13}} = \phi_{D_{23}} = \frac{\sum_{j=1}^{K} m_j}{9}$.
Interestingly, $(\phi_{D_3} - \phi_{D_4}) = \frac{n}{3} - \frac{\sum_{j=1}^{K} m_j}{9} = \frac{(2n+m_{K+1})}{9}$.
By incorporating the above values at the left hand side of the equation (3.3.10) leads

$$mn\left[\left(\frac{2n+m_{K+1}}{9}\right)^2 - \left(\frac{2n+m_{K+1}}{9}\right)^2 + \left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2 - \left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2\right] = 0.$$

Similar operation over $\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}})$ with respect to p_2 yields

$$\begin{aligned}\phi^{'}_{D|p_2}(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) &= 0,\\ \Rightarrow mn\left[\phi_{D_1}(\phi_{D_3}-\phi_{D_4}) - (\phi_{D_1}\phi_{D_2}-\phi^2_{D_{12}}) - \phi^2_{D_{13}}\right] &= 0. \qquad (3.11)\end{aligned}$$

Like previous, the above equation (3.3.11) satisfies when $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, for $j = 1, 2, \cdots, K$.
Now, doing the partial derivative of $\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}})$ with respect to q_{1j} and equating to zero, gives

$$\begin{aligned}\phi^{'}_{D|q_{1j}}(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) &= 0,\\ \Rightarrow -2m_j(q_{1j}\phi_{D_2}+q_{2j}\phi_{D_{12}})(\phi_{D_3}-\phi_{D_4}) + 2m_j(1-q_{1j}-q_{2j})(\phi_{D_1}\phi_{D_2}-\phi^2_{D_{12}}) + 2m_jq_{1j}\phi^2_{23}&\\ +2m_jq_{2j}(\phi_{D_1}\phi_{D_{23}}+\phi_{D_{12}}\phi_{D_{13}}-\phi_{D_{13}}\phi_{D_{23}}) - 2m_j(1-2q_{1j}-q_{2j})\left[\phi_{D_2}\phi_{D_{13}}+\phi_{D_{12}}\phi_{D_{23}}\right] &= 0. \qquad (3.12)\end{aligned}$$

The left hand side of above equation (3.3.12) equals with 0, when $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, for $j = 1, 2, \cdots, K$. Because, if we explicit the left hand side of the equation (3.3.12), it gives at $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, for $j = 1, 2, \cdots, K$, as

$$\begin{aligned}&\left(\frac{-2m_j}{3}\right)\left[\frac{(2n+m_{K+1})}{9} - \frac{\sum_{j=1}^{K} m_j}{9}\right]\frac{(2n+m_{K+1})}{9} + \left(\frac{2m_j}{3}\right)\left[\left(\frac{2n+m_{K+1}}{9}\right)^2 - \left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2\right]\\ &+\left(\frac{2m_j}{3}\right)\left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2 + \left(\frac{2m_j}{3}\right)\left[\left(\frac{2n+m_{K+1}}{9}\right)\left(\frac{\sum_{j=1}^{K} m_j}{9}\right) + \left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2 - \left(\frac{\sum_{j=1}^{K} m_j}{9}\right)^2\right] = 0.\end{aligned}$$

Now, the partial derivative of $\phi_D(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}})$ with respect to q_{2j} and equating to zero, leads

$$\phi^{'}_{D|q_{2j}}(\mathbf{p}, \mathbf{q_{1j}}, \mathbf{q_{2j}}) = 0,$$

$$\begin{aligned}\Rightarrow & -2m_j(q_{2j}\phi_{D_1} + q_{1j}\phi_{D_{12}})(\phi_{D_3} - \phi_{D_4}) + 2m_j(1 - q_{1j} - q_{2j})(\phi_{D_1}\phi_{D_2} - \phi^2_{D_{12}}) + 2m_j q_{2j}\phi^2_{13} \\ & +2m_j q_{1j}(\phi_{D_2}\phi_{D_{13}} + \phi_{D_{12}}\phi_{D_{23}} - \phi_{D_{13}}\phi_{D_{23}}) - 2m_j(1 - q_{1j} - 2q_{2j})\left[\phi_{D_1}\phi_{D_{23}} + \phi_{D_{12}}\phi_{D_{13}}\right] = 0. \end{aligned} \tag{3.13}$$

Like previous description, above equation (3.3.13) equals with 0, when $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, for $j = 1, 2, \cdots, K$. Because, by expanding the left hand side of the equation (3.3.13), at $p_1 = p_2 = q_{1j} = q_{2j} = \frac{1}{3}$, for $j = 1, 2, \cdots, K$, it yields

$$\begin{aligned}&\left(\frac{-2m_j}{3}\right)\left[\frac{(2n + m_{K+1})}{9} - \frac{\sum\limits_{j=1}^{K} m_j}{9}\right]\frac{(2n + m_{K+1})}{9} + \left(\frac{2m_j}{3}\right)\left[\left(\frac{2n + m_{K+1}}{9}\right)^2 - \left(\frac{\sum\limits_{j=1}^{K} m_j}{9}\right)^2\right] \\ &+ \left(\frac{2m_j}{3}\right)\left(\frac{\sum\limits_{j=1}^{K} m_j}{9}\right)^2 + \left(\frac{2m_j}{3}\right)\left[\left(\frac{2n + m_{K+1}}{9}\right)\left(\frac{\sum\limits_{j=1}^{K} m_j}{9}\right) + \left(\frac{\sum\limits_{j=1}^{K} m_j}{9}\right)^2 - \left(\frac{\sum\limits_{j=1}^{K} m_j}{9}\right)^2\right] = 0.\end{aligned}$$

Comparing all the equations (3.3.10) to (3.3.13), we get the solution as $p_1 = p_2 = \frac{1}{3}$ and $q_{1j} = q_{2j} = \frac{1}{3}$, $j = 1, \cdots, K$, which implies $q_{1\overline{K+1}} = q_{2\overline{K+1}} = \frac{1}{3}$. These relations leads to local optimal solution but to attain global optimality (maximum), we have to show that the corresponding Hessian matrix at this stationary or fixed point is a negative definite matrix (Apostol, 1974, p 376-379 ; Rao, 2009, p 68-73) for which we have to do second order partial derivative with respect to the decision variables p_1, p_2, q_{1j}, q_{2j}, for $j = 12, \cdots, K$. But due to mathematical complexity of the second order partial derivatives require to formulate Hessian matrix, we have left this work for future research work. Wherever, simulation study has been carried out to find out the efficiency of the balanced allocation design compare to the random allocation design.

4. Simulation Study

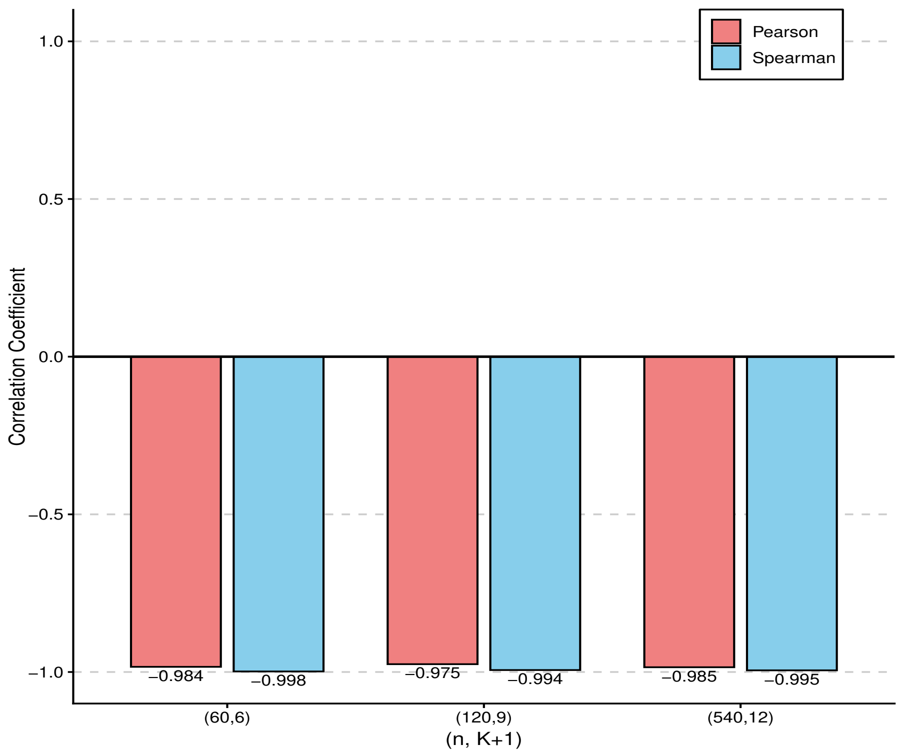
Considering the n experimental units of a categorical covariate having $(K + 1)$ levels that are to be allocated into 3 treatment groups. The efficiency of the balanced allocation design (η^B) has been compared to random allocation design (η^R) with respect to the $D-$optimality criterion is defined by $\frac{V(\eta^B)}{V(\eta^R)}$, where $V(.)$ is the respective $D-$optimality function (preferable to be maximized). Such efficiency calculation is repeated $10,000$ times and the mean efficiency is reported in the following table, along with the range of efficiency values in square bracket and variance of efficiency values in round bracket. It has been observed that the mean efficiency value is always more than unity, which means that the balanced allocation design performed uniformly better than the randomized allocation design. In addition, a measure of imbalance, named as a proportion of imbalance (PIB) measured as the 'Euclidean distance' of the random allocation design of its balanced counterpart, defined as $PIB = \sqrt{\sum\limits_{j=1}^{K+1} (\frac{1}{3} - min(m_{1j}, m_{2j}, m_{3j})/m_j)^2}$. The mean of $10,000$ such PIB values (mPIB) over the $10,000$ randomized allocation designs are also reported in the following table along with the corresponding ranges and variance. To establish the relationship between a balanced allocation design's efficiency value regarding $D-$optimality criterion and its respective imbalance measure (PIB), the Pearson and Spearman rank correlation coefficients have been calculated on $10,000$ simulations. It has been resulted as a significant negative correlation, indicating that the less imbalanced allocation design results a more efficient design.

Table 3 : Mean efficiency of balanced allocation design compared to completely randomized design (with range in square bracket and variance in round bracket) along with the corresponding mPIB value over 10,000 repetitions. (*Significant with $p-$value $< 2.2e-16$)

(n,K+1)	Efficiency	mPIB	Pearson	Spearman
(60,6)	1.562 (0.3176) [1,1.954]	0.3349 (0.1952) [0,0.672]	-0.9836*	-0.9983*
(120,9)	1.490 (0.2689) [1,1.732]	0.3288 (0.1906) [0,0.659]	-0.9752*	-0.9938*
(540,12)	1.719 (0.3414) [1,2.193]	0.3669 (0.2106) [0,0.732]	-0.9849*	-0.9947*

The correlation coefficient distributions between efficiency and PIB measures of balanced allocation design versus randomized design over Spearman and Pearson measurements are graphically represented in the Figure 1.

Fig. 1: Graphical representation of the correlation coefficients between Efficiency and PIB measures over Spearman and Pearson measurements



5. Concluding Remarks

The present study addresses about the allocation problem of experimental units with known categorical covariates are to be allocated into multiple treatment groups with regard to $D-$optimality. It has been established that, $D-$optimality ensures balanced allocation design at least as local optimal solution. Through simulation studies, it has been also shown that the balanced allocation performs uniformly better than the random allocation design. Though achieving balanced allocation in each level of different covariate combinations are prime interest in the field of clinical trials. But in real-life situation number of experimental units having different covariates along with multi-level combinations are unequal in numbers. Recently such kind of problem has been discussed in Nag et al. (2025). A real-life example has been demonstrated in that paper, where 40 units having three different covariates and multiple levels are to be allocated into 4 treatments, but number of units in each level of each covariate are lesser than the number of treatments, like $0, 1, 2, 3$. Randomization or re-randomization method may not achieve balancing in each level of covariates. An exhaustive search may be one way out but the search space becomes computationally intractable when the units in each level combinations are much smaller than the total number of treatment groups. Developing an iterative algorithm with intelligent search mechanism, like Wu (1981), Nag et al. (2025), is the best way out to overcome this situation. In the next study, we have discussed about such type of problem and proposed an efficient search algorithm for obtaining an optimal allocation design as well as balanced allocation design in each level combinations of the covariates.

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