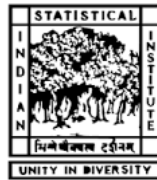


Ensuring Balance through Optimal Allocation of Experimental Units with Known Categorical Covariates into Two Treatments

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Samrat Hore, Department of Statistics, Tripura University
Anup Dewanji, Applied Statistics Unit, Indian Statistical Institute,
Kolkata
Aditya Chatterjee, Department of Statistics, University of Calcutta



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Abstract

The balanced allocation of experimental units with regard to various known covariates among several treatment groups, before the physical experiment takes place, is often considered to be the most reasonable allocation scheme in all intervention studies and clinical trials. Such allocation problems have been modeled in an ANCOVA set up by several authors. It is well-known that, for models with covariates, balancing defined through equality of covariate means corresponding to various treatment groups ensures widely used D - and A -optimality. However, it is not well-understood if the reverse (that is, ensuring balance, through an allocation of a fixed set of experimental units with known covariates to several treatments, with the objective of efficient estimation of treatment effect or covariate effect or both through commonly used D - or A -optimality) holds or not. For continuous covariates, it has been observed previously by the same authors, through a computationally intensive method, that balanced allocation (with respect to either covariate mean or number of replicates) may not always be achieved for an optimal design. In the present paper, an analytic confirmation of this reverse result with categorical covariates has been obtained with regard to D - and A -optimality.

Keywords: Balanced Allocation, ANCOVA, D -optimality, A -optimality.

1. Introduction

Balancing treatment allocation over various covariates in terms of a summarizing measure, *viz.*, covariate mean, corresponding to each treatment group, plays a vital role in intervention studies and clinical trials, as that has a direct implication towards valid comparison of various treatments (Efron, 1971; Pocock and Simon, 1975; Wu, 1981; Atkinson, 1982; Kalish and Begg, 1985; Rubin, 2008; Hu and Hu, 2012; Morgan and Rubin, 2012). Efficient estimation of treatment effect, or covariate effect, or both, with regard to several optimality criteria such as D - and A -optimality (Kiefer, 1959), may be achieved through balancing. In Shah and Sinha (1989), it had been established that a balanced design with regard to equality of covariate means over different treatments ensures D -optimality and, if additionally the

design is equi-replicate as well, it also ensures A -optimality. Our objective of this paper is to study whether these optimality criteria ensure balanced allocation design for the known categorical covariates. Note that, while allocating units with known categorical covariates, balancing with respect to covariate mean is equivalent to equi-proportional allocation. In presence of covariates, a balanced design ensuring similar group sizes is also expected to possess similar distribution for covariate values across several treatment groups (Kundt, 2009; Su, 2011).

Balancing over categorical covariates for various treatment groups, obtained as a consequence of allocation design satisfying various optimality criteria, has not been exhaustively studied. We have considered an one-way ANCOVA model, where the problem is to allocate the fixed set of experimental units with known categorical covariates into various treatment groups by satisfying the well-known optimality criteria. If the categorical covariate data are available before units are exposed to treatments, it has been shown that the optimal allocation design ensures balance not only for the overall experiment, but also for each level of the corresponding category, before the physical experiment takes place, as required in Rubin (2008) for the intervention studies. Besides the well-known D - and A -optimality, this is true for D_s - and A_s -optimality also, where the optimality is required with respect to a subset of the parameters and is based on the respective submatrix of the dispersion matrix.

In Section 2, the problem has been formulated in an *ANCOVA* framework. The properties of the allocation design with regard to D - and A -optimality by considering estimation of both treatment effects and categorical covariate effects have been studied in Section 3. In Section 4, the case of only treatment effects in terms of D_s - and A_s -optimality has been formulated and the preservation of balanced allocation through such optimalities has been discussed. The paper concludes in Section 5 with some relevant observations and scopes for further research.

2. Problem Formulation

Consider the one-way ANCOVA model with r treatments and S covariates whose values are assumed to be known for the fixed set of n experimental units. The linear model for the analysis is given by

$$y_{li} = \mu_l + \sum_{s=1}^S \beta_s x_{lis} + \epsilon_{li}, \text{ for } i = 1(1)n_l, \quad l = 1, \dots, r \quad (2.1)$$

where n_l (≥ 1) denotes the number of experimental units receiving the l^{th} treatment and $\sum_{l=1}^r n_l = n$. Here, y_{li} , μ_l , β_s , x_{lis} and ϵ_{li} denote the response from i^{th} experimental unit receiving the l^{th} treatment, the l^{th} treatment effect, the regression coefficient for the s^{th}

covariate, the value of the s^{th} covariate corresponding to i^{th} experimental unit receiving the l^{th} treatment, and the observational error, assumed to follow *iid* $N(0, \sigma^2)$ distribution, respectively.

The linear *ANCOVA* model, as stated in (2.1), may be reframed in matrix format as follows:

$$Y = W\theta + \epsilon = Z\mu + X\beta + \epsilon \quad (2.2)$$

where $W = (Z : X)$, $\theta = (\mu : \beta)$. 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 depends on the information matrix $(W^T W)$ of order $(r + S) \times (r + S)$. For efficient estimation of both treatment and covariate effects, we need to minimize the determinant and trace of the dispersion matrix $(W^T W)^{-1}$ for D - and A -optimality, respectively. Similarly, D_s - and A_s -optimality correspond to minimization of the determinant and trace, respectively, of the dispersion matrix of the selected subset of parameters, for example, corresponding to the r treatment effects when efficient estimation of only the treatment effects is of interest.

In practice, the covariates may be binary or categorical (nominal or ordinal) and, for the sake of mathematical convenience, we consider the allocation of experimental units into two (*i.e.* $r = 2$) treatments, while extension to general r treatments requires routine but involved mathematics. Also, for simplicity, let us consider a single categorical covariate (*i.e.* $S = 1$) involving $(K + 1)$ levels A_1, \dots, A_{K+1} . Note that, when there is only one categorical covariate, the model is same as that of a two-way ANOVA, one for the treatment and the other for the covariate. Here also, the extension to general S may be achieved by considering all possible level combinations of the S categorical covariates as the different levels of a new single categorical covariate. For the sake of exposition, we confine ourselves to a single covariate. The specific problem is then to allocate the n experimental units with known levels of the categorical covariate to either of the two treatments in an optimal way. We consider the *ANCOVA* model given in (2.1) with x_{lis} denoting the value of the *dummy variable* for the single (since $S = 1$, here s takes only one value) categorical covariate for the i^{th} experimental unit in the l^{th} treatment group. To avoid the dummy variable trap or perfect multi-collinearity (Chatterjee et al., 2000), x_{lis} is taken as a K dimensional column vector with all *zero*'s and at most one *unity*, as there are $(K + 1)$ levels for a single covariate. Let n_l be the number of experimental units in the l^{th} treatment group and m_{lj} be the number of experimental units in the l^{th} treatment group belonging to the category

A_j , $l = 1, 2$ and $j = 1, \dots, K + 1$, with $m_l \overline{K+1} = n_l - \sum_{j=1}^K m_{lj}$, and $n_1 + n_2 = n$. Note that $m_j = \sum_{l=1}^2 m_{lj}$ is the fixed number of experimental units corresponding to the covariate level A_j , for $j = 1, \dots, K + 1$. The non-singular information matrix $W^T W$, excepting the constant σ^{-2} , may be written as

$$W^T W = \begin{pmatrix} n_1 & 0 & m_{11} & m_{12} & \dots & m_{1K} \\ 0 & n_2 & m_{21} & m_{22} & \dots & m_{2K} \\ m_{11} & m_{21} & m_1 & 0 & \dots & 0 \\ m_{12} & m_{22} & 0 & m_2 & \dots & 0 \\ \vdots & \vdots & \dots & \dots & \dots & \vdots \\ m_{1K} & m_{2K} & 0 & 0 & \dots & m_K \end{pmatrix}. \quad (2.3)$$

The above matrix is independent of the term $m_l \overline{K+1}$, as $m_l \overline{K+1} = n_l - \sum_{j=1}^K m_{lj}$, $l = 1, 2$. For S categorical covariates with k_1, k_2, \dots, k_S levels respectively, the total number of level combinations is $k_1 \times k_2 \times \dots \times k_S = K + 1$, say. If balanced allocation, in terms of number of replicates, is achieved for every treatment 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. Thus, cell level balance is adequate to ensure marginal balance of any order. As such, by taking a single covariate with $(K + 1)$ levels is sufficient to ensure individual and marginal balance of any order for S categorical covariates with k_1, k_2, \dots, k_S levels, respectively, for the fixed set of experimental units.

3. Optimality with respect to both treatment and covariate effects

Here, we consider the optimum allocation of n experimental units with known values of a single categorical covariate with $K + 1$ levels with regard to D - and A -optimality based on the information matrix $W^T W$ (without the constant σ^{-2}) as given in (2.3).

3.1 D -optimality :

For D -optimality, we have to maximize $\det(W^T W)$ with respect to (n_1, n_2) and (m_{1j}, m_{2j}) , for $j = 1, \dots, K$, subject to the conditions $n = n_1 + n_2$ and $m_j = \sum_{l=1}^2 m_{lj}$, $j = 1, \dots, K$, where

$$\det(W^T W) = \left(\prod_{j=1}^K m_j \right) \left[n_1 n_2 - n_1 \sum_{j=1}^K \frac{m_{2j}^2}{m_j} - n_2 \sum_{j=1}^K \frac{m_{1j}^2}{m_j} + \left(\sum_{j=1}^K \frac{m_{2j}^2}{m_j} \right) \left(\sum_{j=1}^K \frac{m_{1j}^2}{m_j} \right) - \left(\sum_{j=1}^K \frac{m_{1j} m_{2j}}{m_j} \right)^2 \right].$$

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 $p = \frac{n_1}{n}$, $1 - p = \frac{n_2}{n}$ and $q_j = \frac{m_{1j}}{m_j}$, $1 - q_j = \frac{m_{2j}}{m_j}$, for $j = 1, \dots, K$, which are fractions and hence may be treated as continuous. Let us write $q_{K+1} = \frac{m_{1, K+1}}{m_{K+1}}$, $1 - q_{K+1} = \frac{m_{2, K+1}}{m_{K+1}}$ and denote $\prod_{j=1}^K m_j = m$. Now, denoting $\det(W^T W)$ as ϕ_D , a function of p, q_1, \dots, q_K , we have

$$\begin{aligned} \phi_D(p, q_1, \dots, q_K) &= m \left[n^2 p(1-p) - np \sum_{j=1}^K m_j (1-q_j)^2 - n(1-p) \sum_{j=1}^K m_j q_j^2 \right] \\ &\quad + m \left[\left(\sum_{j=1}^K m_j q_j^2 \right) \left(\sum_{j=1}^K m_j (1-q_j)^2 \right) - \left(\sum_{j=1}^K m_j q_j (1-q_j) \right)^2 \right]. \end{aligned}$$

Equating the partial derivative of $\phi_D(p, q_1, \dots, q_K)$ with respect to p to zero and after some routine algebra, we get

$$\left[n(1-2p) - \sum_{j=1}^K m_j + 2 \sum_{j=1}^K m_j q_j \right] = 0. \quad (3.1)$$

Similar operation over $\phi_D(p, q_1, \dots, q_K)$ with respect to q_j yields

$$np - q_j m_{K+1} - \sum_{j'=1}^K m_{j'} q_{j'} = 0, \quad (3.2)$$

for $j = 1, \dots, K$. Multiplying (3.2) by m_j and summing over $j = 1, \dots, K$, we have

$$p = \frac{\sum_{j=1}^K m_j q_j}{\sum_{j=1}^K m_j}. \quad (3.3)$$

Using the expression of p in (3.2) and after some simplification, we have

$$q_j = \frac{\sum_{j'=1}^K m_{j'} q_{j'}}{\sum_{j'=1}^K m_{j'}}, \quad j = 1, \dots, K. \quad (3.4)$$

Comparing (3.3) and (3.4), we see that, p and q_j , $j = 1, \dots, K$, have the same solution. Therefor replacing, q_j by p in (3.1), we get the solution as $p = \frac{1}{2}$, which implies $q_j = \frac{1}{2}$, $j = 1, \dots, K$, and also $q_{K+1} = \frac{1}{2}$.

To check the optimality, i.e to check that $\det(W^T W)$ attains maximum at the fixed points obtained from the first order conditions, we have to show that the corresponding Hessian matrix is negative definite at that fixed point. It can be easily seen that, while evaluated at $p = q_1 = \dots = q_K = \frac{1}{2}$; $\frac{\partial^2 \phi_D}{\partial p^2} = -2mn^2 < 0$, $\frac{\partial^2 \phi_D}{\partial q_j^2} = -2mm_j(m_j + m_{K+1}) < 0$, $\frac{\partial^2 \phi_D}{\partial p \partial q_j} = 2mnm_j$, $\frac{\partial^2 \phi_D}{\partial q_j \partial q_{j'}} = -2mm_j m_{j'}$, for $j \neq j' = 1, \dots, K$. Thus, the Hessian matrix, evaluated

at the fixed point $p = q_1 = \dots = q_K = \frac{1}{2}$, is

$$H_D = 2m \begin{pmatrix} -n^2 & nm_1 & nm_2 & \dots & nm_K \\ nm_1 & -m_1(m_1 + m_{K+1}) & -m_1m_2 & \dots & -m_1m_K \\ nm_2 & -m_1m_2 & -m_2(m_2 + m_{K+1}) & \dots & -m_2m_K \\ \vdots & \vdots & \dots & \dots & \vdots \\ nm_K & -m_1m_K & -m_2m_K & \dots & -m_K(m_K + m_{K+1}) \end{pmatrix}.$$

The above matrix can be written as sum of the two matrices $H_D^{(1)}$ and $H_D^{(2)}$ as

$$H_D = 2m [H_D^{(1)} - H_D^{(2)}], \quad (3.5)$$

where $H_D^{(1)} = \text{diag}(0, -m_1m_{K+1}, -m_2m_{K+1}, \dots, -m_Km_{K+1})$, a $(K+1) \times (K+1)$ diagonal negative definite matrix and $H_D^{(2)} = (-n, m_1, \dots, m_K)^T (-n, m_1, \dots, m_K)$, a positive definite matrix. Thus, H_D is negative definite and hence D -optimality ensures a balanced design with regard to a single categorical covariate with multiple levels for allocation of n experimental units to two treatment groups and the maximum value of $\det(W^T W)$ for attaining this D -optimality is $(\prod_{j=1}^K m_j) \frac{nm_{K+1}}{4}$.

3.2 A -optimality :

For A -optimality, we require to minimize $\text{trace}(W^T W)^{-1}$ subject to the conditions $n_1 + n_2 = n$ and $\sum_{l=1}^2 m_{lj} = m_j, j = 1, \dots, K$. From (2.3) and using the result of matrix inverse through partitioned matrix (Rao, 1973, pp 33) and, as before, instead of the discrete design variables n_l and m_{lj} , considering the corresponding proportions p and $q_j, j = 1, \dots, K$, as defined in Section 3.1, we have $\text{trace}(W^T W)^{-1}$, denoted by $\phi_A(p, q_1, \dots, q_K)$, as

$$\phi_A(p, q_1, \dots, q_K) = \sum_{j=1}^K \frac{1}{m_j} + \frac{\phi_{A,1}(p, q_1, \dots, q_K)}{\phi_{A,2}(p, q_1, \dots, q_K)}, \quad (3.6)$$

where

$$\phi_{A,1}(p, q_1, \dots, q_K) = m_{K+1} \left(\sum_{j=1}^K q_j^2 + 1 \right) - 2(np - \sum_{j=1}^K m_j q_j) \left(\sum_{j=1}^K q_j + 1 \right) + (K+2) \left(np - \sum_{j=1}^K m_j q_j \right)^2$$

and

$$\phi_{A,2}(p, q_1, \dots, q_K) = m_{K+1} \left(np - \sum_{j=1}^K m_j q_j \right)^2 - \left(np - \sum_{j=1}^K m_j q_j \right)^2.$$

The minimization of $\text{trace}(W^T W)^{-1}$ requires finding the fixed point solutions, by setting the partial derivatives of the expression given in (3.6) with respect to p, q_1, q_2, \dots, q_K to zero.

Now, equating the first order partial derivative of $\phi_A(p, q_1, \dots, q_K)$ with respect to p , denoted by $\phi_{A,p}(p, q_1, \dots, q_K)$, to zero gives

$$\phi_{A,2}(p, q_1, \dots, q_K)\phi_{A,1p}(p, q_1, \dots, q_K) = \phi_{A,1}(p, q_1, \dots, q_K)\phi_{A,2p}(p, q_1, \dots, q_K), \quad (3.7)$$

where

$$\begin{aligned} \phi_{A,1p}(p, q_1, \dots, q_K) &= n \sum_{j=1}^K (1 - 2q_j) \text{ and} \\ \phi_{A,2p}(p, q_1, \dots, q_K) &= n[m_{K+1} - 2(np - \sum_{j=1}^K m_j q_j)] \end{aligned}$$

are the first order partial derivatives of $\phi_{A,1}(p, q_1, \dots, q_K)$ and $\phi_{A,2}(p, q_1, \dots, q_K)$, respectively, with respect to p . Similarly, equating the first order partial derivative of $\phi_A(p, q_1, \dots, q_K)$ with respect to q_j to zero, for $j = 1, \dots, K$, we have

$$\phi_{A,2}(p, q_1, \dots, q_K)\phi_{A,1q_j}(p, q_1, \dots, q_K) = \phi_{A,1}(p, q_1, \dots, q_K)\phi_{A,2q_j}(p, q_1, \dots, q_K), \quad (3.8)$$

where

$$\begin{aligned} \phi_{A,1q_j}(p, q_1, \dots, q_K) &= 2[m_{K+1}q_j - (np - \sum_{j'=1}^K m_{j'}q_{j'}) + m_j(\sum_{j'=1}^K q_{j'} + 1) - (K+2)m_jq_j] \text{ and} \\ \phi_{A,2q_j}(p, q_1, \dots, q_K) &= 2m_j[(np - \sum_{j'=1}^K m_{j'}q_{j'}) - m_{K+1}q_j]. \end{aligned}$$

However, the solutions of the equations given in (3.7) and (3.8) subject to the stated conditions are mathematically intractable and devoid of any closed form. We start by trying to identify a fixed point of the above equations. Note that, when we have $p = q_1 = \dots = q_K = 1/2$, we have balance with respect to the number of replicates at each level of the covariate and the two treatment groups in the corresponding allocation design. It is to be observed that the solution $(p, q_1, \dots, q_K) = \frac{1}{2}J_{K+1}$ is also a fixed point solution of the equations (3.7) and (3.8). Here J_{K+1} is the $(K+1)$ -dimensional unit vector. In order to obtain optimality, we have to establish positive definiteness of the corresponding Hessian matrix at this fixed point solution. Now, at this observed fixed point, the elements of the corresponding Hessian matrix H_A are $\frac{\partial^2 \phi_A}{\partial p^2} = \frac{2n^2 \psi_1}{\psi_2^2} > 0$, $\frac{\partial^2 \phi_A}{\partial q_j^2} = \frac{2(m_j(m_j + m_{K+1})\psi_1 + (m_{K+1} - Km_j)\psi_2)}{\psi_2^2} > 0$, $\frac{\partial^2 \phi_A}{\partial p \partial q_j} = \frac{-2n(m_j \psi_1 + \psi_2)}{\psi_2^2}$ and $\frac{\partial^2 \phi_A}{\partial q_j \partial q_{j'}} = \frac{2(m_j m_{j'} \psi_1 + (m_j + m_{j'}) \psi_2)}{\psi_2^2}$, for $j \neq j' = 1, \dots, K$, where $\psi_1 = \frac{n(K+2) + 2m_{K+1}}{4}$ and $\psi_2 = \frac{nm_{K+1}}{4}$. Note that H_A is a symmetric matrix and it can be easily proved that the determinants of all the principal order minors are greater than zero, which establishes positive definiteness of the Hessian matrix H_A (Rao, 1973, pp 52). Hence, this fixed point $(p, q_1, \dots, q_K) = \frac{1}{2}J_{K+1}$ is at least a local minima of (3.6). In order to establish that A -optimality ensures unique balanced allocation design, we have to show that

there is no other optimal solution except the fixed point solution given by $\frac{1}{2}J_{K+1}$. Let us assume that, $p^* = \{p, q_1, \dots, q_K\} \in (0, 1)^{K+1}$ be a set of any arbitrary allocation ratio other than $\frac{1}{2}J_{K+1}$. The difference between the functional values at these two points is

$$\begin{aligned}
\phi_A(p^*) - \phi_A(\frac{1}{2}J_{K+1}) &= \sum_{j=1}^K \frac{1}{m_j} + \frac{\phi_{A,1}(p, q_1, \dots, q_K)}{\phi_{A,2}(p, q_1, \dots, q_K)} - \sum_{j=1}^K \frac{1}{m_j} - \frac{n(K+2)+2m_{K+1}}{n m_{K+1}}, \\
&= \frac{m_{K+1}(\sum_{j=1}^K q_j^2 + 1) - 2(np - \sum_{j=1}^K m_j q_j)(\sum_{j=1}^K q_j + 1) + (K+2)(np - \sum_{j=1}^K m_j q_j^2)}{m_{K+1}(np - \sum_{j=1}^K m_j q_j^2) - (np - \sum_{j=1}^K m_j q_j)^2} - \frac{n(K+2)+2m_{K+1}}{n m_{K+1}} \\
&= \frac{m_{K+1}(\sum_{j=1}^K q_j^2 + 1) - 2(m_{K+1}q_{K+1})(\sum_{j=1}^K q_j + 1) + (K+2)(np - \sum_{j=1}^K m_j q_j^2)}{m_{K+1}(np - \sum_{j=1}^K m_j q_j^2) - (m_{K+1}q_{K+1})^2} - \frac{n(K+2)+2m_{K+1}}{n m_{K+1}} \\
&= \frac{m_{K+1}^2 [n(\sum_{j=1}^K q_j^2 + 1) - 2nq_{K+1}(\sum_{j=1}^K q_j + 1) + \{n(K+2)+2m_{K+1}\}q_{K+1}^2 - 2(m_{K+1}q_{K+1} + \sum_{j=1}^K m_j(q_j - q_j^2))] }{\{m_{K+1}(np - \sum_{j=1}^K m_j q_j^2) - (np - \sum_{j=1}^K m_j q_j)^2\}nm_{K+1}} \\
&= \frac{n \sum_{j=1}^K (q_j - q_{K+1})^2 + 2(n+m_{K+1})(q_{K+1} - \frac{1}{2})^2 + 2 \sum_{j=1}^K m_j (q_j - \frac{1}{2})^2}{\{m_{K+1}(np - \sum_{j=1}^K m_j q_j^2) - (np - \sum_{j=1}^K m_j q_j)^2\}nm_{K+1}} > 0. \tag{3.9}
\end{aligned}$$

Observe that the numerator of the equation (3.9) is greater than zero, while its denominator is same as $nm_{K+1}^2 \{m_{K+1}q_{K+1}(1 - q_{K+1}) + \sum_{j=1}^K m_j q_j(1 - q_j)\}$, a positive quantity. Hence, the right hand side of (3.9) is greater than zero. This ensures that $\phi_A(p, q_1, q_2, \dots, q_K)$ attains minimum at $\frac{1}{2}J_{K+1}$ which establishes that A -optimality achieves the unique balanced allocation for the experimental units into the two treatment groups and at each level of the categorical covariates, with respect to number of replicates. The corresponding A -optimal value of the objective function at that optimal point is $\sum_{j=1}^K \frac{1}{m_j} + \frac{n(K+2)+2m_{K+1}}{n m_{K+1}}$.

4. Optimality with regard to only treatment effects

Such optimality criteria consider the dispersion matrix of the least square estimates of the selected subset of the parameters corresponding to ‘only treatment effects’. There are D_s - and A_s -optimality, corresponding to D - and A -optimality, respectively, but based on the corresponding dispersion matrix, which is the corresponding submatrix of $(W^T W)^{-1}$, with the covariate effect parameter β playing the role of nuisance parameter. Let us partition the matrix $(W^T W)^{-1}$ as

$$(W^T W)^{-1} = \begin{pmatrix} W^{11} & W^{12} \\ W^{21} & W^{22} \end{pmatrix}, \tag{4.1}$$

where $W^{11}\sigma^2$ is the (2×2) dispersion matrix of the least squares estimate of μ , and the matrix $W^{11} = (Z^T P Z)^{-1}$ is derived through the projection operator $P = I - X(X^T X)^{-1}X^T$, the

ortho-complement of the column space of X (Cook and Nachtsheim, 1989). To achieve the D_s - and A_s -optimality, we have to minimize the determinant and the trace of W^{11} , respectively. From (2.3)

$$Z^T P Z = \begin{pmatrix} n_1 - \sum_{j=1}^K \frac{m_{1j}^2}{m_j} & - \sum_{j=1}^K \frac{m_{1j} m_{2j}}{m_j} \\ - \sum_{j=1}^K \frac{m_{1j} m_{2j}}{m_j} & n_2 - \sum_{j=1}^K \frac{m_{2j}^2}{m_j} \end{pmatrix}. \quad (4.2)$$

4.1 D_s -Optimality :

For D_s -optimality, the minimization of $\det(Z^T P Z)^{-1}$ is equivalent to maximization of $\det(Z^T P Z)$, with respect to (n_1, n_2) and (m_{1j}, m_{2j}) subject to the constraints as given in Subsection 3.1. As before, instead of considering the discrete design variables n_l and m_{lj} , for $l = 1, 2$, let us consider the corresponding proportions given by $p = \frac{n_1}{n}$, $q_j = \frac{m_{1j}}{m_j}$, for $j = 1, \dots, K$, and $q_{K+1} = \frac{m_{1, \overline{K+1}}}{m_{K+1}}$. Expressing the determinant of $(Z^T P Z)$ in terms of p and q_1, \dots, q_K , we have the objective function to be maximized as

$$\begin{aligned} \phi_{D_s}(p, q_1, \dots, q_K) &= \left[n^2 p(1-p) - np \sum_{j=1}^K m_j (1-q_j)^2 - n(1-p) \sum_{j=1}^K m_j q_j^2 \right] \\ &+ \left[\left(\sum_{j=1}^K m_j q_j^2 \right) \left(\sum_{j=1}^K m_j (1-q_j)^2 \right) - \left(\sum_{j=1}^K m_j q_j (1-q_j)^2 \right) \right]. \end{aligned}$$

From Subsection 3.1, we have $\phi_D(p, q_1, \dots, q_K) = m \phi_{D_s}(p, q_1, \dots, q_K)$, where $m = \prod_{j=1}^k m_j$ is a constant, independent of the decision variables. Hence, by following the same argument, we have the result and the optimum value of the objective function in this case is $\frac{nm_{K+1}}{4}$.

4.2 A_s -Optimality :

For A_s -optimality, we have to minimize $\text{trace}(Z^T P Z)^{-1}$, with respect to (n_1, n_2) and (m_{1j}, m_{2j}) subject to the constraints as mentioned in Subsection 3.1, where

$$\text{trace}(Z^T P Z)^{-1} = \frac{(n_1 + n_2) - \left(\sum_{j=1}^K \frac{m_{1j}^2}{m_j} + \sum_{j=1}^K \frac{m_{2j}^2}{m_j} \right)}{\left[n_1 n_2 - n_1 \sum_{j=1}^K \frac{m_{2j}^2}{m_j} - n_2 \sum_{j=1}^K \frac{m_{1j}^2}{m_j} + \left(\sum_{j=1}^K \frac{m_{2j}^2}{m_j} \right) \left(\sum_{j=1}^K \frac{m_{1j}^2}{m_j} \right) - \left(\sum_{j=1}^K \frac{m_{1j} m_{2j}}{m_j} \right)^2 \right]}.$$

As before, the continuous version of the discrete optimization problem through the transformations $p = \frac{n_1}{n}$, $q_j = \frac{m_{1j}}{m_j}$, $j = 1, \dots, K$ and $q_{K+1} = \frac{m_{1, \overline{K+1}}}{m_{K+1}}$, gives the equivalent problem of minimizing

$$\phi_{A_s}(p, q_1, \dots, q_K) = \frac{\phi_{A_s,1}(p, q_1, \dots, q_K)}{\phi_{A_s,2}(p, q_1, \dots, q_K)},$$

where $\phi_{A_s,1}(p, q_1, \dots, q_K) = n - \left(\sum_{j=1}^K m_j(1 - q_j)^2 + \sum_{j=1}^K m_j q_j^2\right)$, and

$$\begin{aligned} \phi_{A_s,2}(p, q_1, \dots, q_K) &= [n^2 p(1 - p) - np \sum_{j=1}^K m_j(1 - q_j)^2 - n(1 - p) \left(\sum_{j=1}^K m_j q_j^2\right) \\ &\quad + \left(\sum_{j=1}^K m_j q_j^2\right) \left(\sum_{j=1}^K m_j(1 - q_j)^2\right) - \left(\sum_{j=1}^K m_j q_j(1 - q_j)\right)^2]. \end{aligned}$$

Differentiating $\phi_{A_s}(p, q_1, \dots, q_K)$ partially with respect to p and equating with zero, we get

$$\phi_{A_s,2}(p, q_1, \dots, q_K) \phi_{A_s,1p}(p, q_1, \dots, q_K) = \phi_{A_s,1}(p, q_1, \dots, q_K) \phi_{A_s,2p}(p, q_1, \dots, q_K), \quad (4.3)$$

where the first order partial derivatives of $\phi_{A_s,1}(p, q_1, \dots, q_K)$ and $\phi_{A_s,2}(p, q_1, \dots, q_K)$ with respect to p are

$$\phi_{A_s,1p}(p, q_1, \dots, q_K) = 0, \quad \text{and} \quad (4.4)$$

$$\phi_{A_s,2p}(p, q_1, \dots, q_K) = n \left[n(1 - 2p) - \sum_{j=1}^K m_j(1 - q_j)^2 + \sum_{j=1}^K m_j q_j^2 \right], \quad (4.5)$$

respectively. Hence, using (4.4) and (4.5), and after some routine algebra, (4.3) gives

$$\left[2np - 2 \sum_{j=1}^K m_j q_j - m_{K+1} \right] = 0. \quad (4.6)$$

Similarly, taking partial derivative of $\phi_{A_s}(p, q_1, \dots, q_K)$ with respect to q_j yields

$$m_j(1 - 2q_j) \left[2m_{K+1}(np - \sum_{j'=1}^K m_{j'} q_{j'}) - 2(np - \sum_{j'=1}^K m_{j'} q_{j'})^2 - m_{K+1}^2 \right] = 0, \quad (4.7)$$

for $j = 1, \dots, K$. Substituting the value of m_{K+1} obtained from (4.6) in (4.7), we have $q_j = \frac{1}{2}$, for $j = 1, \dots, K$. Then, from equation (4.6), we have $p = \frac{1}{2}$, which results in $q_{K+1} = \frac{1}{2}$. The elements of the Hessian matrix H_{A_s} , evaluated at the fixed points $(p, q_1, \dots, q_K) = \frac{1}{2} J_{K+1}$, are $\frac{\partial^2 \phi_{A_s}}{\partial p^2} = \frac{2n^2 \xi_1}{\xi_2^2} > 0$, $\frac{\partial^2 \phi_{A_s}}{\partial q_j^2} = \frac{2m_j(m_j + m_{K+1})\xi_1 - 4m_j \xi_2}{\xi_2^2} = \frac{m_j(nm_j + m_j m_{K+1} + m_{K+1}^2)}{\xi_2^2} > 0$, $\frac{\partial^2 \phi_{A_s}}{\partial p \partial q_j} = \frac{-2nm_j \xi_1}{\xi_2^2}$, $\frac{\partial^2 \phi_{A_s}}{\partial q_j \partial q_{j'}} = \frac{2m_j m_{j'} \xi_1}{\xi_2^2}$, for $j \neq j' = 1, 2, \dots, K$, with $\xi_1 = \frac{(n+m_{K+1})}{2}$ and $\xi_2 = \frac{nm_{K+1}}{4}$. Thus the Hessian matrix H_{A_s} , evaluated at this fixed point, can be written as

$$H_{A_s} = \frac{n + m_{K+1}}{\xi_2^2} \begin{pmatrix} n^2 & -nm_1 & \dots & -nm_K \\ -nm_1 & \left(m_1^2 + \frac{m_1 m_{K+1}^2}{(n+m_{K+1})}\right) & \dots & m_1 m_K \\ -nm_2 & m_1 m_2 & \dots & m_2 m_K \\ \vdots & \vdots & \dots & \vdots \\ -nm_K & m_1 m_K & \dots & \left(m_K^2 + \frac{m_K m_{K+1}^2}{(n+m_{K+1})}\right) \end{pmatrix}.$$

Therefore, apart from a constant, H_{A_s} may be written as the sum of two matrices $H_{A_s}^{(1)}$ and $H_{A_s}^{(2)}$ as

$$H_{A_s} = \frac{n + m_{K+1}}{\xi_2^2} [H_{A_s}^{(1)} + H_{A_s}^{(2)}], \quad (4.8)$$

where $H_{A_s}^{(1)} = (n, -m_1, \dots, -m_K)^T(n, -m_1, \dots, -m_K)$ is a positive definite matrix and $H_{A_s}^{(2)} = \text{diag} \left(0, \frac{m_1 m_{K+1}^2}{(n+m_{K+1})}, \dots, \frac{m_K m_{K+1}^2}{(n+m_{K+1})} \right)$ is a diagonal and non-negative definite matrix. Therefore, H_{A_s} is a positive definite matrix. Hence, for a single covariate at $K + 1$ levels, A_s -optimal design achieves balanced allocation of experimental units in the two treatment groups at each level of the covariate, with the optimal value of the objective function being $\frac{2(n+m_{K+1})}{n m_{K+1}}$.

5. Concluding Remarks

The present paper is concerned with allocation of experimental units with known single categorical covariate, at multiple levels, in two treatment groups, so as to ensure various well-known optimality criteria. It has been analytically established that, under this setup, balanced allocation designs are obtained through D -, A -, D_s - and A_s -optimality criteria. Another well-known optimality criterion, namely the T -optimality (Pukelsheim, 2006) is derived by maximizing the trace of the information matrix $W^T W$. Note that $\text{trace}(W^T W) = n + \sum_{j=1}^K m_j$ is a fixed quantity, as the total number of experimental units (n) and the number of units corresponding to j^{th} covariate level (m_j), are completely known before the actual experiment commences. As a result, any allocation design is T -optimal including the balanced one. At the same time, the T_s -optimality is obtained by maximizing trace of the selected submatrix $(W^{11})^{-1}$, or trace of $(Z^T P Z)$, given by $n - \left(\sum_{j=1}^K \frac{m_{1j}^2}{m_j} + \sum_{j=1}^K \frac{m_{2j}^2}{m_j} \right)$, subject to the two constraints mentioned in Subsection 3.1. The transformed continuous version of the problem is to maximize the function $\phi_{T_s}(p, q_1, \dots, q_K) = n - \left(\sum_{j=1}^K m_j q_j^2 + \sum_{j=1}^K m_j (1 - q_j)^2 \right)$, with respect to p and q_j , for $j = 1, 2, \dots, K$. Note that the function $\phi_{T_s}(p, q_1, \dots, q_K)$ is independent of p , which means that T_s -optimality may be achieved without ensuring balance with regard to total number of experimental units allocated to the two treatments. So it remains to be seen whether balancing is achieved through T_s -optimality with regard to each level of the category. Let us first write $\phi_{T_s}(p, q_1, \dots, q_K) = \phi_{T_s^*}(q_1, \dots, q_K)$, as a function of q_1, \dots, q_K only. The first order condition by differentiating $\phi_{T_s^*}(q_1, \dots, q_K)$ partially with respect to q_j and equating to zero yields $q_j = \frac{1}{2}$, for $j = 1, \dots, K$. Thus the first order condition gives the allocation design to be balanced for the single categorical covariate for each of the K levels. To ensure T_s -optimality at the fixed point $(q_1, \dots, q_K) = \frac{1}{2} J_K$, we observe that the elements of the Hessian matrix $H_{T_s^*}$ as $\frac{\partial^2 \phi_{T_s^*}}{\partial q_j^2} = -4m_j < 0$, for $j = 1, \dots, K$, and $\frac{\partial^2 \phi_{T_s^*}}{\partial q_j \partial q_{j'}} = 0$, for $j \neq j' = 1, \dots, K$, giving $H_{T_s^*} = \text{diag}(-4m_1, \dots, -4m_K)$, a $(K \times K)$ diagonal negative definite matrix. Thus T_s -optimality ensures balance in each of the K categorical levels, but fails to provide information about allocation at the $(K + 1)^{\text{st}}$ level

(q_{K+1}) and the overall allocation (p). An allocation design consisting of any arbitrary value of the variables p and q_{K+1} , with $q_j = \frac{1}{2}$, for $j = 1, \dots, K$, and also satisfying the restriction $np - \sum_{j=1}^K m_j q_j = m_{K+1} q_{K+1}$, ensures T_s -optimality, including the balanced allocation design ($p = q_1 = \dots = q_K = \frac{1}{2}$). As an example, let us consider an allocation problem with a single binary covariate (i.e $K = 1$) for $n = 20$ experimental units, to be allocated to two treatments, where the number of experimental units corresponding to the covariate levels 0 and 1 are $m_1 = 8$ and $m_2 = n - m_1 = 12$, respectively. Here, T_s -optimality is achieved (with the same optimum value of the objective function as 16) for two different allocation designs, where the first design corresponds to an unbalanced allocation ($p = \frac{3}{10}, q_1 = \frac{1}{2}, q_2 = \frac{1}{6}$), while the second one is the balanced one with ($p = q_1 = q_2 = \frac{1}{2}$).

Analytical study of generalizations of these results to multiple treatment groups may be carried out similarly. However, the mathematical expressions and the corresponding proofs might turn out to be more involved. Efficient estimation of only covariate effects may also be of interest by considering the corresponding submatrix of $W^T W$.

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