Efficient designs for one-sided comparisons of two or three treatments with a control in a one-way layout

BY STEVEN M. BORTNICK
Home Finance Marketing Analytics, JPMorganChase, Columbus, Ohio 43240
steve_bortnick@bankone.com
ANGELA M. DEAN and THOMAS J. SANTNER
Department of Statistics, The Ohio State University, Columbus, Ohio 43210-1247
amd@stat.ohio-state.edu tjs@stat.ohio-state.edu

SUMMARY

The problem of providing lower confidence bounds for the mean improvements of $p \geq 2$ test treatments over a control treatment is considered. The expected average and expected maximum allowances are two criteria for comparing different systems of confidence intervals or bounds. In this paper, lower bounds are derived for the expected average allowance and the expected maximum allowance of Dunnett's simultaneous lower confidence bounds for the p mean improvements. These lower bounds hold for any $p \geq 2$ and any allocation of sample sizes. For $p = 2$ test treatments, sample allocations are given for which the bounds are achievable. For $p = 3$ test treatments, a tighter set of bounds is derived which enables easy determination of the sample allocation to achieve highly efficient designs. A table of the bounds for the expected average and expected maximum allowances and the sample allocation that achieves these bounds is given for $p = 2, 3$. The theoretical results can easily be adapted to cover upper confidence bounds.

Some key words: Control treatment; Dunnett's critical values; Expected average allowance; Expected maximum allowance; Multiple comparisons; One-way layout; Optimal design

1. INTRODUCTION

Consider an experiment for the simultaneous comparison of each of $p \geq 2$ test treatments with a control treatment. As examples, in medicine, new drug formulations are usually compared with a standard formulation or a placebo and, in engineering, alternative system configurations are compared with a benchmark configuration. Typically the goal of such an experiment is to determine which test treatments, if any, are better than the control (or standard) treatment. An important component of the statistical analysis of such data is to provide lower confidence bounds for the improvement of each test treatment mean over the mean of the control treatment. In this paper we consider simultaneous confidence bounds for these mean differences, while controlling the experimentwise error rate at a given level, α.

Let n_i (≥ 1) denote the number of experimental units assigned to treatment i, $0 \leq i \leq p$, where $i = 0$ identifies the control treatment. Throughout the paper, the total sample size is fixed at N; thus, $n_0 + n_1 + \ldots + n_p = N$. Let Y_{ij} represent the response from the jth experimental unit assigned to treatment i. We assume the model $Y_{ij} = \tau_i + \epsilon_{ij}$ for the treatment response where τ_i is the ith treatment mean and where the measurement errors $\{\epsilon_{ij}\}$ are independent and identically distributed normal random variables with zero mean and unknown variance σ^2. Let S^2 denote the unbiased pooled sample estimator of σ^2 and let $\overline{Y}_{i.}$ denote the sample mean for treatment i, $0 \leq i \leq p$. Our objective is to derive simultaneous lower confidence bounds for the p differences $\tau_i - \tau_0$, $1 \leq i \leq p$, having a given confidence level $100(1-\alpha)\%$. Although not given in this paper, the theoretical results can easily be adapted to cover upper confidence bounds. Extension to two-sided bounds appears to be difficult (see Section 4).

Following Spurrier and Nizam (1990) and Bortnick, Dean and Hsu (2001), we use the expected average allowance (EAA) and expected maximum allowance (EMA) to judge the quality of the p one-sided simultaneous confidence bounds. For (two-sided) confidence intervals, the corresponding criteria minimize the average and maximum length of the intervals, respectively, and they are defined explicitly for one-sided confidence bounds in Section 2. Spurrier and Nizam (1990) showed that for $p = 2$ test treatments and a given n_0, the optimal designs under the EAA criterion are those that have an equal or almost equal number of observations on each of the test treatments. Bortnick et al. (2001, 2003) found similar results in the block design setting.

In Section 3, we derive a bound for the one-sided EAA and EMA values of Dunnett's family of simultaneous confidence bounds for comparing p (≥ 2) test treatments with a control treatment. An example is given to show that, although the bound is quite tight, it is not tight enough to pinpoint the optimal design accurately. In Section 3, we derive a tighter bound for the case of $p = 3$ which considerably narrows the optimal design search. Tables of bounds for $p = 2$ and 3 test treatments are given in Section 5. Tables of bounds for larger p can be found in Bortnick (1999).

2. Optimality Criteria

Throughout the remainder of the paper, we let n denote $(n_0, n_1, \ldots, n_p)$. We compare the p test treatments with the control treatment by means of Dunnett's (1955) simultaneous lower confidence bounds

$$\tau_i - \tau_0 \geq \overline{Y}_{i.} - \overline{Y}_{0.} - d_{p,\alpha,n}\, S\,(n_0^{-1} + n_i^{-1})^{1/2}, \quad 1 \leq i \leq p\,. \tag{1}$$

The critical value $d_{p,\alpha,n} = d(p, \alpha, n_0, n_1, \ldots, n_p)$ in (1) is defined to be the solution of

$$pr\{T_i \leq d_{p,\alpha,n};\ 1 \leq i \leq p\} = 1 - \alpha \tag{2}$$

where $(T_1, \ldots, T_p)^\top$ has the multivariate Student t-distribution with mean vector zero, unit variances, correlation matrix $R = (\rho_{ij})$ having elements

$$\rho_{ij} \equiv cor(T_i, T_j) = (\lambda_i \, \lambda_j)^{1/2}, \quad 1 \leq i \neq j \leq p \,, \tag{3}$$

where $\lambda_i = n_i/(n_i + n_0)$, and $N - p - 1$ degrees of freedom (Dunnett and Sobel, 1954). The quantity λ_i can be interpreted as a correlation ratio because it can be easily computed that $\lambda_i = \rho_{ij}\rho_{ik}/\rho_{jk}$ for any j and k. In the application to (1), the ρ_{ij} are the correlations among the contrasts $\overline{Y}_{i.} - \overline{Y}_{0.}$, $1 \leq i \leq p$. Distributional results and related computational algorithms for obtaining $d_{p,\alpha,n}$ can be found in Dunnett and Sobel (1955), Spurrier and Nizam (1990) and Hsu (1996, Chapter 3). The SAS® procedure *PROBMC* can be used to calculate $d_{p,\alpha,n}$.

We judge the quality of the p one-sided simultaneous confidence bounds in (1) by their expected average allowance and by their expected maximum allowance, where the one-sided allowance of the treatment i comparison is the distance *below* the point estimator $\overline{Y}_{i.} - \overline{Y}_{0.}$ of the lower bound in (1). The one-sided expected average allowance of the bounds (1) is defined to be

$$\text{EAA}(\alpha, n_0) = d_{p,\alpha,n} \; E(S) \; h_1(n), \;\; \text{where} \;\; h_1(n) = \frac{1}{p} \sum_{i=1}^{p} \left(n_0^{-1} + n_i^{-1} \right)^{1/2} , \tag{4}$$

and the *expected maximum allowance* is defined to be

$$\text{EMA}(\alpha, n_0) = d_{p,\alpha,n} \; E(S) \; h_2(n), \;\; \text{where} \;\; h_2(n) = \max_{1 \leq i \leq p} \left(n_0^{-1} + n_i^{-1} \right)^{1/2} . \tag{5}$$

The notation EAA(α, n_0) and EMA(α, n_0) emphasizes the dependence on the control sample size but suppresses the dependence of these quantities on the test treatment sample sizes. For a given α (and possibly n_0), the EAA-optimal and EMA-optimal sample allocations are those choices of n that minimize EAA(α, n_0) and EMA(α, n_0), respectively, for fixed total sample size N. Observe that $E(S)$ in (4) and (5) can be ignored when comparing the EAA- and EMA-efficiency of competing treatment allocations for fixed N and p because $E(S)$ depends only on N, p and the unknown σ^2. Thus, EAA(α, n_0) and EMA(α, n_0) depend only on n through the product of $d_{p,\alpha,n}$ and $h_1(n)$ or $h_2(n)$, respectively.

3. Bounding the EAA and EMA values

Spurrier and Nizam (1990) derived the global minimum of $h_1(n)$ in (4), as follows.

Lemma 1 (Spurrier and Nizam, 1990) For any $p \geq 2$ and any fixed (N, n_0) satisfying $N > n_0 + p$, the function $h_1(n)$ is minimized for any configuration $(n_1, n_2, \ldots, n_p)$ in which $n_1, \ldots, n_p$ differ by at most 1.

In words, $h_1(n)$ is minimized when $n_1, \ldots, n_p$ are chosen to be as equal as possible, subject to the constraint $N - n_0 = n_1 + \cdots + n_p$. The following lemma gives an analagous result for $h_2(n)$ in expression (5) of the EMA.

Lemma 2 For any $p \geq 2$ and any fixed (N, n_0) satisfying $N > n_0 + p$, the function $h_2(n)$ is minimized for any configuration n having $\min_{1 \leq i \leq p} n_i = \lfloor (N - n_0)/p \rfloor$ where $\lfloor \cdot \rfloor$ denotes the greatest integer function.

Proof: Let $r = \lfloor (N - n_0)/p \rfloor$ and t be the remainder of this division so that $0 \leq t < p$. Suppose $n_{[1]} \leq \cdots \leq n_{[p]}$ are the ordered values corresponding to a given configuration of sample sizes $n_1, \ldots, n_p$ satisfying $N - n_0 = n_1 + \cdots + n_p$, then

$$h_2(n) = \max_{1 \leq i \leq p} \left(n_0^{-1} + n_i^{-1} \right)^{1/2} = \left(n_0^{-1} + n_{[1]}^{-1} \right)^{1/2} .$$

Then, $h_2(n)$ is minimized by selecting n to have the maximum possible value of $n_{[1]}$. For every configuration n, it must be that $n_{[1]} \leq r$ otherwise $\sum_{i=1}^{p} n_i > N - n_0$. Hence $h_2(n)$ is minimized for any configuration n, satisfying $n_{[1]} = r$. □

Let $h_1^{\min}$ and $h_2^{\min}$ denote the minimum values of $h_1(n)$ and $h_2(n)$ identified by Lemmas 1 and 2 corresponding to a given (N, n_0) satisfying $N > n_0 + p$. Then the critical value $d_{p,\alpha,n}$ is the remaining factor which must be considered in deriving bounds for EAA and EMA. From Theorems 2.1.1 and 3.1.1 of Tong (1980) concerning Slepian's inequality, $d_{p,\alpha,n}$ is strictly decreasing in each correlation given by (3) when all other correlations are held fixed (see also Slepian, 1962). It follows that a lower bound for $d_{p,\alpha,n}$ is obtained by setting each ρ_{ij} to the maximum possible value (for fixed N and n_0). This maximum correlation is identified next.

Lemma 3 For any $p \geq 2$, and any fixed (N, n_0) satisfying $N > n_0 + p$, the correlation ρ_{ij} $(1 \leq i \neq j \leq p)$ is bounded above by

$$\rho^{\dagger} = \frac{N - n_0 - (p - 2)}{N + n_0 - (p - 2)} . \tag{6}$$

Proof: Without loss of generality, consider ρ_{12}. From (3), it is straightforward to show that ρ_{12} is increasing in each of n_1 and n_2. Treating n_1 and n_2 as continuous and fixing $n_1 + n_2 = c$, ρ_{12} is maximized when $n_1 = n_2 = c/2$. By assumption, each test treatment is allocated to at least one experimental unit. It then follows that ρ_{12} is maximized when $n_3 = \ldots = n_p = 1$ and $n_1 = n_2 = [N - n_0 - (p - 2)]/2$. Replacing n_1 and n_2 in (3) by $[N - n_0 - (p - 2)]/2$, and simplifying, completes the proof. □

The upper bound (6) can be sharpened when $[N - n_0 - (p - 2)]$ is odd by observing that only the two integral choices for n_1 and n_2 with $|n_1 - n_2| = 1$ need be considered. Lemma 3 uses a componentwise argument and, when all ρ_{ij} are set to $\rho^{\dagger}$, a conservative lower bound for $d_{p,\alpha,n}$ results. Let $d_{p,\alpha}^{\dagger}$ denote the critical value that is obtained by setting each ρ_{ij} equal to its maximum, $\rho^{\dagger}$. Then, for fixed n_0,

$$\begin{aligned} \text{EAA}^{\dagger}(\alpha, n_0) \;&\equiv\; h_1^{\min} d_{p,\alpha}^{\dagger}\, E(S) \leq \text{EAA}(\alpha, n_0) \\ \text{and} \qquad & \\ \text{EMA}^{\dagger}(\alpha, n_0) \;&\equiv\; h_2^{\min} d_{p,\alpha}^{\dagger}\, E(S) \leq \text{EMA}(\alpha, n_0) \end{aligned} \tag{7}$$

are lower bounds for the average and maximum allowances. When $p = 2$, these lower bounds are achievable, as shown below.

Lemma 4 (Spurrier and Nizam, 1990) For fixed (N, n_0) with $N > n_0 + 2$, and $p = 2$, Dunnett's critical value $d_{2,\alpha,n}$ is minimized when n_1 and n_2 differ by at most 1.

Lemma 4 shows that, when $p = 2$, the allocation of $n_1 = n_2$ for $(N - n_0)$ even, or allocation of $|n_1 - n_2| = 1$ for $(N - n_0)$ odd, minimizes $d_{p,\alpha,n}$ for fixed α, N and n_0. Lemmas 1 and 2 show that the *same* allocation minimizes both $h_1(\cdot)$ and $h_2(\cdot)$ and, thus, the lower bounds for EAA(α, n_0) and EMA(α, n_0) are achievable. For example, if $(N, n_0) = (25, 13)$, then $n_1 = n_2 = 6$ is the EAA- and EMA-optimal test treatment allocation for any α. Similarly, both $n_1 = 6$ and $n_1 = 7$ (with $n_2 = N - n_0 - n_1$) are EAA- and EMA-optimal test treatment allocations when $(N, n_0) = (25, 12)$.

When $p \geq 3$, the bounds (7) may not be (very) sharp due to the conflicting nature of the optimizing n for $h_i(n)$ and $d_{p,\alpha,n}$. Furthermore, in this case of multiple ρ_{ij}, each ρ_{ij} will usually be maximized by a different allocation, n. Therefore, the correlation bound (6) can never be attained simultaneously by every ρ_{ij} associated with any specific test treatment allocation.

Example 1 Consider an experiment to compare $p = 3$ test treatments with a control treatment. Suppose that $N = 30$ observations can be taken and that 95% simultaneous confidence bounds are desired for $\tau_i - \tau_0$, $i = 1, 2, 3$. Suppose that the optimal allocation n_0, n_1, n_2, n_3 for the control and test treatments is required that minimizes EAA$(.05, n_0)$ defined by (4). From Lemma 1, $h_1(n)$ is minimized by setting n_1, n_2 and n_3 as equal as possible for each n_0. Designs with this test treatment allocation are likely to be extremely efficient even if they do not use the optimal n_0 (c.f. Bortnick et al. 2001). For example, if $n_0 = 11$, we set $n_1 = n_2 = 6$ and $n_3 = 7$ to obtain a *most balanced* (MB) design. Then, from (4) and (6), $h_1(6, 6, 7) = 0.4995$, $\rho_{12} = .3529$, $\rho_{13} = \rho_{23} = 0.3705$, and $d_{3,.05,n} = 2.1913$. This design has EAA$(.05, 11)/E(S) = 1.0946$. If $n_0 = 10$, then the most balanced design has $n_1 = 6$ and $n_2 = n_3 = 7$ and similar calculations give EAA$(.05, 10)/E(S) = 1.0937$. Values of EAA$(.05, n_0)/E(S)$ for other n_0 are shown by the symbol ■ in Figure 1. It can be verified that $n_0 = 10$ gives the minimum EAA$(.05, n_0)$ value amongst all most balanced designs.

The bound $EAA^{\dagger}(.05, n_0)$ in (7) is calculated using the same value of $h_1^{\min}$ as for the exact EAA$(\alpha, n_0)/E(S)$ value, but with $d_{p,\alpha,n}$ determined by $\rho_{12} = \rho_{13} = \rho_{23} = \rho^{\dagger}$ where $\rho^{\dagger}$ is the maximum correlation given by (6). For $n_0 = 11$, $\rho^{\dagger} = .45$, $d_{3,.05,n} = 2.1735$, we obtain EAA$^{\dagger}(.05, 11)/E(S) = 1.0857$ which is shown on Figure 1 using the ♦ symbol. Since the bound 1.0857 is lower than $EAA(.05, 10)/E(S)$ for the most balanced (MB) design with $n_0 = 10$, it is possible that a better design exists with $n_0 = 11$. In fact, Figure 1 shows that the optimal design could have $n_0 = 9, 10, 11, 12$. So, although the MB design with $n_0 = 10$ has efficiency 1.0836/1.0937 = 0.9908 with respect to the bound EAA$^{\dagger}(.05, 10)/E(S) = 1.0836$, a fairly extensive search within these classes is still needed in order to find *the* EAA-optimal design for $\alpha = 0.05$.

In Section 4, we provide a sharper bound for the case of $p = 3$ test treatments versus a control which helps to narrow the search for optimal designs.

4. A Sharper Bound for EAA and EMA when $p = 3$

The lower bound $d^{\dagger}_{p,\alpha}$ for $d_{p,\alpha,n}$ derived in Section 3 relies on Slepian's inequality which requires the marginal bounding of every element of the correlation matrix R (for fixed N and n_0). In this section, we obtain a sharper bound for $d_{p,\alpha,n}$ when $p = 3$. Lemma 5 and Theorem 1 give restrictions on the optimal values of the correlations. All proofs are given in the Appendix of Bortnick et al (2004).

Lemma 5 For fixed (N, n_0), $p = 3$, *and any allocation* n,
(i)

$$\rho_{ij} \le \frac{N - n_0 - 1}{N + n_0 - 1} \quad \textit{for} \quad 1 \le i \ne j \le 3\,; \tag{8}$$

(ii) Each correlation ratio satisfies

$$\frac{\rho_{ij}\ \rho_{ik}}{\rho_{jk}} \le (N - n_0 - 2)/(N - 2), \tag{9}$$

$(1 \le i \ne j \ne k \le 3)$.
(iii) The correlation sum $(\rho_{12} + \rho_{13} + \rho_{23})$ *satisfies*

$$\rho_{12} + \rho_{13} + \rho_{23} \le 3(N - n_0)/(N + 2n_0). \tag{10}$$

To state Theorem 1, we require the notion of majorization of vectors.

Definition (Marshall and Olkin 1979) Let x and y be vectors in $\mathbb{R}^m$, with ordered elements $x_{[1]} \le \cdots \le x_{[m]}$ and $y_{[1]} \le \cdots \le y_{[m]}$, respectively. Then x *is majorized by* y, denoted by $x \prec y$, if and only if

$$\sum_{i=j}^{m} x_{[i]} \le \sum_{i=j}^{m} y_{[i]} \ \text{ for } j = 2, \ldots, m\,, \ \text{ and } \ \sum_{i=1}^{m} x_{[i]} = \sum_{i=1}^{m} y_{[i]}\,. \tag{11}$$

Theorem 1 For fixed α, N, *and* $p = 3$, *the critical value* $d_{p,\alpha,n}$ *defined by (2) is monotonically decreasing in the majorization ordering "*$\prec$*" of the vector of correlations* $(\rho_{12}, \rho_{13}, \rho_{23})$ *obtained from* R.

Lemma 5 will now be used in conjunction with Theorem 1 to obtain a set of correlations that sharpen the lower bound $d^{\dagger}_{p,\alpha}$ for $d_{p,\alpha,n}$ when $p = 3$. To simplify the discussion that follows assume, without loss of generality, that $\rho_{12} \ge \rho_{13} \ge \rho_{23}$; also let

$$a = \left(\frac{N - n_0 - 2}{N - 2}\right)\left(\frac{N + n_0 - 1}{N - n_0 - 1}\right) \ \text{ and } \ b = 3\left(\frac{N - n_0}{N + 2n_0}\right) - \left(\frac{N - n_0 - 1}{N + n_0 - 1}\right)\,.$$

First, we find a set of correlations that simultaneously attain equality in (8)–(10) of Lemma 5. These correlations will be denoted by ρ^*_{12}, ρ^*_{13} and ρ^*_{23}. To attain the bound (8) of Lemma 5, we require

$$\rho^*_{12} = \frac{N - n_0 - 1}{N + n_0 - 1}\ . \tag{12}$$

Next, after substituting (12) for ρ_{12} in the lefthand side of (9), we require

$$\rho^*_{13} = a \times \rho^*_{23} \tag{13}$$

to attain the bound (9) of Lemma 5. Finally, after again substituting (12) for ρ_{12}, the bound (10) of Lemma 5 is achieved when

$$\rho^*_{13} + \rho^*_{23} = b. \tag{14}$$

Solving (13) and (14) simultaneously gives

$$\rho^*_{23} = b/(a+1) \tag{15}$$

and

$$\rho^*_{13} = ab/(a+1) \tag{16}$$

For given (N, n_0) and (p, α), let $d^*_{p,\alpha}$ denote the $d_{p,\alpha,n}$ value in (2) that results from using the correlations ρ^*_{12}, ρ^*_{13} and ρ^*_{23}. The following theorem now establishes the fact that $d^*_{p,\alpha}$ is a lower bound for $d_{p,\alpha,n}$. The proof is given in the Appendix of Bortnick et al. (2004).

Theorem 2 Suppose $p = 3$ *and* α *are specified, then*

$$d_{p,\alpha,n} \geq d^*_{p,\alpha}$$

for any sample size allocation n *corresponding to a given* N *and* n_0.

Extension of Theorem 1 to the two-sided case appears to be difficult. The end-points of the intervals as well as the correlations are to be optimized as functions of n. However, two-sided results in the literature, such as those of Sidak (1968, Theorem 1) state how the multivariate normal probability content of a hyper-rectangle with *fixed* end-points varies as a function of the correlations.

4.1. *Bounding EAA and EMA When* $p = 3$

When $p = 3$ and (N, n_0, α) is fixed, we obtain

$$\mathrm{EAA}(\alpha, n_0) \geq h_1^{\min} d^*_{p,\alpha}\, E(S) \equiv \mathrm{EAA}^*(\alpha, n_0) \ \text{ and }$$
$$\mathrm{EMA}(\alpha, n_0) \geq h_2^{\min} d^*_{p,\alpha}\, E(S) \equiv \mathrm{EMA}^*(\alpha, n_0) \tag{17}$$

by applying the appropriate $h_i(n)$ bound, $h_i^{\min}$, and Theorem 2. Example 2 demonstrates the sharpness of the bound.

Example 2 Consider the setting of Example 1 where $p = 3$, $\alpha = 0.05$ and $N = 30$. For $n_0 \in \{8, 9, 10, 11, 12, 13\}$, Figure 1 compares $\text{EAA}(.05, n_0)/E(S)$ for the design having most balanced test treatment allocation to the bound $\text{EAA}^{\dagger}(.05, n_0)/E(S)$ in (7) and the sharper bound $\text{EAA}^{*}(.05, n_0)/E(S)$ of (17). For example, when $n_0 = 11$, $\rho^*_{12} = 0.45$, $\rho^*_{13} = 0.3711$, $\rho^*_{23} = 0.2751$ and $d^*_{p,\alpha} = 2.1898$ So the bound $\text{EAA}^{*}(.05, 11)$ is $1.0938\, E(S)$, as compared with the Section 3 bound $\text{EAA}^{\dagger}(.05, 11) = 1.0857\, E(S)$. Because this sharper lower bound is greater than the EAA value of the MB treatment design with $n_0 = 10$ (whose exact EAA(.05,10)/E(S) value is 1.0937) we may conclude that the optimal design does not have $n_0 = 11$ observations on the control treatment. Similarly, we may rule out $n_0 = 9$ and $n_0 = 12$ (see Figure 1). The optimal design must have $n_0 = 10$ observations on the control treatment. Furthermore, without any additional searching, it is evident that using the most balanced test treatment allocation with $n_0 = 10$ control treatments will produce a design that, at a minimum, is extremely efficient. The bound EAA*(.05,10) is $1.0928\, E(S)$. So the efficiency of the MB design is at least (1.0928)/(1.0937) = 0.9992.

5. Tables of Lower Bounds

To obtain lower bounds for $\text{EAA}(\alpha, n_0)$ for general N, $p \in \{2, 3\}$ and α, we calculated $\text{EAA}^{\dagger}(\alpha, n_0)/E(S)$ for $p = 2$ and $\text{EAA}^{*}(\alpha, n_0)/E(S)$ for $p = 3$, for each $1 \leq n_0 \leq N - p$. We then selected the minimum among this set of bounds. A similar procedure was used to find a lower bound for $\text{EMA}(\alpha, n_0)$. Table 1 lists these bounds for $\alpha \in \{0.05, 0.1\}$, for $10 \leq N \leq 50$, and for $p = 2, 3$. The value of n_0 achieving the corresponding minimum bound is also listed. For $p = 2$ test treatments, the Section 3 bounds are achieved by the EAA- or EMA-optimal design which always has the most balanced test treatment allocation. In particular, the optimal solutions when $\alpha = 0.05$ correspond to those in Table 1 of Spurrier and Nizam (1990). For $p = 3$, although the designs most balanced in the test treatments for the listed values of n_0 may not be the optimal designs, they are extremely efficient. Additional optimal bounds for $p = 2, 3$ can be found in Bortnick et al. (2004) while tables of bounds based on the lower bound (7) of Section 3, are available in Bortnick (1999) for $4 \leq p \leq 10$.

EAA- or EMA-optimal or efficient designs can be constructed from the information given in Table 1 as follows. For $p = 2$ and $\alpha = 0.05$ or 0.10, if the listed values of N and n_0 result in $N - n_0$ even, then the optimal design may be obtained by taking n_0 observations on the control and $n_1 = n_2 = (N - n_0)/2$ observations on each of the test treatments. If $(N - n_0)$ is odd, then an optimal design has $n_1 = (N - n_0 - 1)/2$ and $n_2 = (N - n_0 + 1)/2$ observations, respectively, on the two test treatments. For example, from Table 1, an EAA(.05)-optimal design with $N = 25$ observations has $n_0 = 10, n_1 = 7, n_2 = 8$, while the EMA(.05)-optimal design has $n_0 = 9, n_1 = n_2 = 8$

Similarly, for $p = 3$, to obtain a highly efficient design, $N - n_0$ is divided as evenly as possible between n_1, n_2, n_3. Thus, from Table 1, an EAA(.05)-efficient design with $N = 25$ observations has $n_0 = 9$ observations on the control, $n_1 = n_2 = 5$ and $n_3 = 6$ observations, respectively, on the three test treatments, whereas an EAA(.10)-efficient design has $n_0 = 8, n_1 = 5, n_2 = n_3 = 6$ and an EMA(.05)-efficient design has $n_0 = 10, n_1 = n_2 = n_3 = 5$.

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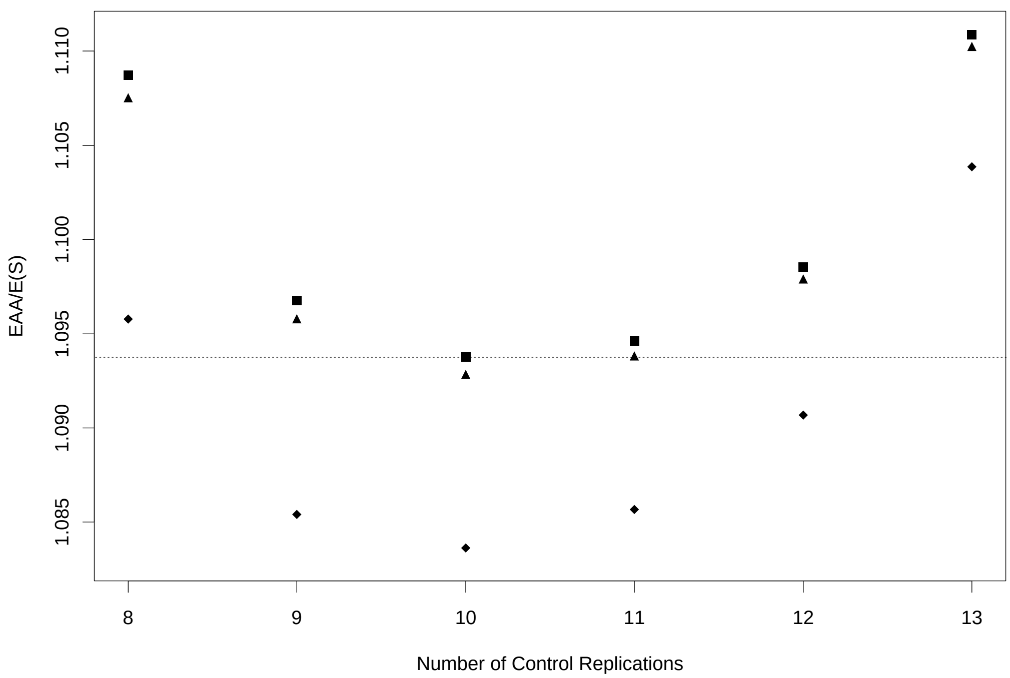

Figure 1: For $(p, \alpha, N) = (3, 0.05, 30)$ and $n_0 \in \{8, 9, 10, 11, 12, 13\}$, comparison of the exact value of $\text{EAA}(\alpha, n_0)/E(S)$ for the most balanced treatment design (■), the bound (7) of Section 3 (♦), and the bound (17) of Section 4 (▲).

Table 1: *For* $N \in \{10, \ldots, 50\}$ *and* $p \in \{2, 3\}$*, the minimum of EAA*$^{\dagger}(\alpha, n_0)/E(S)$ *and EMA*$^{\dagger}(\alpha, n_0)/E(S)$ *over* $1 \leq n_0 \leq N - p$ *and the* n_0 *that achieves these minima.*

	minimum EAA$^{\dagger}(\alpha, n_0)/E(S)$ (associated n_0)								minimum EMA$^{\dagger}(\alpha, n_0)/E(S)$ (associatedn_0)							
	$p = 2$				$p = 3$				$p = 2$				$p = 3$			
N	$\alpha = 0.05$		$\alpha = 0.10$		$\alpha = 0.05$		$\alpha = 0.10$		$\alpha = 0.05$		$\alpha = 0.10$		$\alpha = 0.05$		$\alpha = 0.10$	
10	1.744	(4)	1.371	(4)	2.267	(4)	1.805	(3)	1.744	(4)	1.371	(4)	2.267	(4)	1.807	(4)
11	1.637	(4)	1.294	(4)	2.096	(4)	1.685	(4)	1.637	(5)	1.298	(5)	2.128	(5)	1.716	(5)
12	1.539	(5)	1.223	(4)	1.953	(4)	1.579	(4)	1.541	(4)	1.223	(4)	1.971	(3)	1.586	(3)
13	1.450	(5)	1.157	(5)	1.828	(4)	1.484	(4)	1.450	(5)	1.157	(5)	1.828	(4)	1.484	(4)
14	1.384	(6)	1.111	(6)	1.733	(5)	1.416	(5)	1.384	(6)	1.111	(6)	1.733	(5)	1.416	(5)
15	1.327	(6)	1.066	(6)	1.661	(5)	1.360	(5)	1.333	(5)	1.068	(5)	1.664	(6)	1.367	(6)
16	1.272	(6)	1.023	(6)	1.594	(5)	1.307	(5)	1.272	(6)	1.023	(6)	1.613	(7)	1.320	(4)
17	1.225	(7)	0.989	(7)	1.531	(5)	1.258	(5)	1.225	(7)	0.989	(7)	1.531	(5)	1.258	(5)
18	1.186	(7)	0.958	(7)	1.470	(6)	1.212	(6)	1.189	(8)	0.962	(6)	1.470	(6)	1.212	(6)
19	1.148	(7)	0.928	(7)	1.424	(7)	1.178	(7)	1.148	(7)	0.928	(7)	1.424	(7)	1.178	(7)
20	1.112	(8)	0.901	(8)	1.383	(7)	1.145	(7)	1.112	(8)	0.901	(8)	1.388	(8)	1.151	(8)
21	1.084	(8)	0.878	(8)	1.343	(7)	1.112	(7)	1.084	(9)	0.880	(9)	1.349	(6)	1.114	(6)
22	1.055	(9)	0.855	(8)	1.304	(7)	1.081	(7)	1.055	(8)	0.855	(8)	1.304	(7)	1.081	(7)
23	1.027	(9)	0.834	(9)	1.269	(8)	1.054	(8)	1.027	(9)	0.834	(9)	1.269	(8)	1.054	(8)
24	1.003	(10)	0.816	(9)	1.241	(9)	1.031	(8)	1.003	(10)	0.816	(10)	1.241	(9)	1.033	(9)
25	0.981	(10)	0.798	(10)	1.212	(9)	1.008	(8)	0.982	(9)	0.798	(9)	1.217	(10)	1.012	(7)
26	0.959	(10)	0.780	(10)	1.185	(9)	0.985	(8)	0.959	(10)	0.780	(10)	1.186	(8)	0.985	(8)
27	0.939	(11)	0.765	(11)	1.158	(9)	0.964	(9)	0.939	(11)	0.765	(11)	1.158	(9)	0.964	(9)
28	0.921	(11)	0.750	(11)	1.134	(10)	0.946	(10	0.921	(12)	0.751	(10)	1.134	(10)	0.946	(10)
29	0.903	(11)	0.736	(11)	1.113	(10)	0.929	(10)	0.903	(11)	0.736	(11)	1.115	(11)	0.931	(11)
30	0.886	(12)	0.722	(12)	1.093	(10)	0.912	(10)	0.886	(12)	0.722	(12)	1.096	(9)	0.912	(9)
31	0.871	(12)	0.710	(12)	1.072	(10)	0.895	(10)	0.871	(13)	0.711	(13)	1.072	(10)	0.895	(10)
32	0.856	(13)	0.698	(12)	1.053	(11)	0.879	(11)	0.856	(12)	0.698	(12)	1.053	(11)	0.879	(11)
33	0.841	(13)	0.687	(13)	1.036	(12)	0.866	(11)	0.841	(13)	0.687	(13)	1.036	(12)	0.867	(12)
34	0.828	(14)	0.676	(13)	1.019	(12)	0.852	(11)	0.828	(14)	0.676	(14)	1.021	(13)	0.854	(10)
35	0.815	(14)	0.666	(13)	1.003	(12)	0.839	(11)	0.816	(13)	0.666	(13)	1.004	(11)	0.839	(11)
36	0.802	(14)	0.656	(14)	0.987	(12)	0.825	(12)	0.802	(14)	0.656	(14)	0.987	(12)	0.825	(12)
37	0.791	(15)	0.647	(15)	0.972	(13)	0.814	(13)	0.791	(15)	0.647	(15)	0.972	(13)	0.814	(13)
38	0.780	(15)	0.638	(15)	0.959	(13)	0.803	(13)	0.780	(16)	0.638	(14)	0.960	(14)	0.804	(14)
39	0.769	(15)	0.629	(15)	0.946	(13)	0.792	(13)	0.769	(15)	0.629	(15)	0.948	(12)	0.792	(12)
40	0.758	(16)	0.620	(16)	0.933	(13)	0.781	(13)	0.758	(16)	0.620	(16)	0.933	(13)	0.781	(13)
41	0.749	(16)	0.613	(16)	0.920	(14)	0.771	(14)	0.749	(17)	0.613	(15)	0.920	(14)	0.771	(14)
42	0.739	(17)	0.605	(16)	0.908	(15)	0.761	(14)	0.739	(16)	0.605	(16)	0.908	(15)	0.762	(15)
43	0.730	(17)	0.597	(17)	0.897	(15)	0.752	(14)	0.730	(17)	0.597	(17)	0.898	(16)	0.753	(13)
44	0.721	(18)	0.590	(17)	0.886	(15)	0.743	(14)	0.721	(18)	0.591	(18)	0.887	(14)	0.743	(14)
45	0.712	(18)	0.583	(17)	0.875	(15)	0.734	(15)	0.713	(17)	0.583	(17)	0.875	(15)	0.734	(15)
46	0.704	(18)	0.577	(18)	0.865	(16)	0.726	(16)	0.704	(18)	0.577	(18)	0.865	(16)	0.726	(16)
47	0.696	(19)	0.570	(18)	0.856	(16)	0.718	(16)	0.696	(19)	0.571	(19)	0.856	(17)	0.718	(17)
48	0.689	(19)	0.564	(18)	0.846	(17)	0.710	(16)	0.689	(20)	0.564	(18)	0.847	(18)	0.710	(15)
49	0.681	(19)	0.558	(19)	0.837	(17)	0.702	(16)	0.681	(19)	0.558	(19)	0.837	(16)	0.702	(16)
50	0.674	(20)	0.552	(20)	0.827	(17)	0.694	(17)	0.674	(20)	0.552	(20)	0.827	(17)	0.694	(17)