AUSTRIAN JOURNAL OF STATISTICS
Volume 36 (2007), Number 3, 189–205

Fixed Width Confidence Interval of $\mathrm{P}(\mathrm{X} < \mathrm{Y})$ under a Data Dependent Adaptive Allocation Design

Uttam Bandyopadhyay[1] and Radhakanta Das[2]

[1] Department of Statistics, University of Calcutta, India
[2] Department of Statistics, Bankura Sammilani College, India

Abstract: The present article is related to a nonparametric fixed-width confidence interval estimation of the parameter $\theta = P(X < Y) = \int F(y)dG(y)$, where F and G are two unknown continuous distribution functions. The estimation procedure is based on a sample obtained under some non-iid adaptive situation. We provide various asymptotic results related to the proposed procedure and compare it with a non-adaptive procedure.

Zusammenfassung: Dieser Artikel bezieht sich auf eine nicht-parametrische fixed-width Konfidenzintervall Schätzung des Parameters $\theta = P(X < Y) = \int F(y)dG(y)$, wobei F und G zwei unbekannte stetige Verteilungsfunktionen sind. Die Schätzprozedur basiert auf eine Stichprobe, welche unter einer non-iid adaptiven Situation erhalten wurde. Wir liefern verschiedene asymptotische Resultate bezüglich der vorgeschlagenen Prozedur und vergleichen diese mit einer nicht-adaptiven Prozedur.

Keywords: Standard Brownian Motion Process, Martingale Difference Array, Asymptotic Power.

1 Introduction

Suppose a clinical trial is conducted for comparing two competing treatments, say A and B. Here each entering patient (subject) is to receive one of the treatments once by using a data-dependent adaptive allocation design. Such an allocation is sequential in nature. It can be seen that the design is balanced when the two treatment effects are identical, and it becomes skewed if there is a treatment difference and a larger number of patients is expected to be treated by the better treatment in course of this allocation. Let Z_i be the response of the i-th entering patient. We assume that $Z_i \sim F$ or G according as the i-th patient receives treatment A or B using the adaptive design, where F and G are two unknown continuous distribution functions (d.f.'s). Obviously, the Z_i's are neither independently nor identically distributed. Here, using a data dependent adaptive allocation design, we consider a fixed-width confidence interval estimation of $\theta = P(X < Y) = \int F(y)dG(y)$. Here, this type of inference would be worthwhile to compare the remission times by the two drugs A and B. Specifically, it is intended to make an inference about the probability of requiring lower remission time by one drug than the other. This type of inference is, however, very common in clinical trial setting.

With increasing popularity of adaptive designs in phase III clinical trials, the real life applications of such designs are gradually increasing (see e.g. Bartlett et al., 1985, Tamura et al., 1994, Ware, 1989, Rout et al., 1993, Muller and Schafer, 2001, and Biswas and Dewanji, 2004). In order to have a better understanding, different theoretical properties of such designs were studied and examined by a number of research workers. These are mostly on binary responses. But our present work is related to continuous response adaptive design. In an adaptive design, we have a sequence of indicator variables $\delta_1, \delta_2, \ldots,$ such that $\delta_i = 0$ or 1 according as A or B is used to treat the i-th entering patient, and δ_{n+1} is allowed to depend on $\{(\delta_i, Z_i), i = 1, 2, \ldots, n\}$ or $\{\delta_i, i = 1, 2, \ldots, n\}$. The present framework is related to the first case only. We write

$$Z_i = (1 - \delta_i)X_i + \delta_i Y_i$$

so that

$$\delta_i = \begin{cases} 0 \Rightarrow Z_i = X_i \sim F\,, \\ 1 \Rightarrow\ Z_i = Y_i \sim G\,. \end{cases}$$

We set $\delta_1 = 1, \delta_2 = 0$ and, for each $n \geq 2$, we find, respectively, the numbers of patients treated by A and B up to the n-th stage as

$$N_{An} = \sum_{i=1}^{n} (1 - \delta_i) \qquad \text{and} \qquad N_{Bn} = \sum_{i=1}^{n} \delta_i\,,$$

and

$$T_n = \sum_{i=1}^{n} \sum_{j=1}^{n} u(Z_i, Z_j)$$

counting the number of times an X-observation is smaller than a Y-observation up to the n-th stage, where

$$u(Z_i, Z_j) = \begin{cases} 1 \text{ if } Z_i < Z_j \text{ and } \delta_i < \delta_j\,, \\ 0 \text{ otherwise.} \end{cases}$$

We note that for any n

$$N_{An} + N_{Bn} = n\,.$$

Then an appropriate estimator of θ is given by

$$\hat{\theta}_n = \frac{T_n}{N_{An} N_{Bn}}\,. \tag{1}$$

Suppose $\hat{\theta}_n$ is strongly consistent for θ. Then, for given $d > 0$ there exists a stopping variable (finite with probability one) defined by

$$N_a(d) = \sup\{n \geq 1 : |\hat{\theta}_n - \theta| \geq d\} \tag{2}$$

which can easily be related to a sequential fixed-width confidence interval of θ based on $\hat{\theta}_n$.

Many researchers worked on the variables of the type (2) under various non-adaptive situations. These are e.g. Hjort and Fenstad (1992) and Ghosh et al. (1997). In the present situation, assuming continuous responses, our work is also related to (2) by considering an adaptive design which allows δ_n to depend on all the previous allocations and observations in order to achieve some ethical gain in terms of a larger proportion of allocation to the better treatment. In this connection, one can also go through the work by Rosenberger and

Sriram (1997) for an application of adaptive design to the variable of the type (2) using binary responses.

The rest of the paper is organized as follows. In Section 2, we describe our adaptive allocation rule along with some results. Some asymptotics related to the random variable $N_a(d)$ are studied in Section 3. In Section 4, we briefly discuss some asymptotics related to the variable of the type (2) under non-adaptive equal allocation scheme. Two natural sequential fixed-width confidence intervals are constructed in Section 5. Section 6 contains some numerical computations for comparing the two schemes. Finally some concluding remarks are given in Section 7.

2 The Design and The Related Results

There are several adaptive designs primarily for phase III clinical trials. These are, e.g., play-the-winner rule (Zelen, 1969), biased coin design (Efron, 1971), randomized play-the-winner rule (Wei and Durham, 1978), generalized Polya's urn design (Wei, 1979), and the success driven design (Durham et al., 1998). Also Hu and Zhang (2004) worked with the doubly adaptive biased coin design. These designs are for binary responses of the study variables. The binary response trials are also used by Rosenberger et al. (2001) in connection with an adaptive design. The designs by Rosenberger (1993, 2002) and Bandyopadhyay and Biswas (2004) are for continuous responses of the study variables. In the present study, we work with the allocation rule described by Bandyopadhyay and Biswas (2004). The rule is a generalization of randomized play-the-winner (RPW) rule for continuous responses. We describe the rule in the following.

The Rule: Suppose we have a sequential chain of study subjects and we are to allocate them to either of the treatments A and B. We start with allocating the treatment B to the first incoming subject and the treatment A to the second incoming subject such that $\delta_1 = 1$ and $\delta_2 = 0$. At the n-th ($n > 2$) allocation we make use of an urn which has generated $\alpha + \beta T_n$ and $\alpha + \beta(N_{An}N_{Bn} - T_n)$ balls of kinds B and A, respectively, yielding a total of $2\alpha + \beta N_{An}N_{Bn}$ balls in the urn, where α and β are some positive integers. We draw a ball from the urn and allocate the entering subject by the treatment identified by the drawn ball. Then we add $\beta(T_{n+1} - T_n)$ and $\beta(N_{An+1}N_{Bn+1} - N_{An}N_{Bn} - T_{n+1} + T_n)$ balls of kinds B and A to the urn. This process is continued, and hence, the conditional probability of $\{\delta_{n+1} = 1\}$ given the earlier data is

$$\hat{\pi}_{n+1} = P\left(\delta_{n+1} = 1 | Z_{(n)}, \delta_{(n)}\right) = \frac{\alpha + \beta T_n}{2\alpha + \beta N_{An}N_{Bn}}, \qquad n > 2, \tag{3}$$

where $Z_{(n)} = (Z_1, \ldots, Z_n)'$ and $\delta_{(n)} = (\delta_1, \ldots, \delta_n)'$. More formally, denoting $I\{.\}$ as an indicator function, we have

$$\delta_{n+1} = I\{U_{n+1} < \hat{\pi}_{n+1}\},$$

where U_n, $n \geq 1$, are independently and identically distributed according to the uniform(0, 1) distribution and are independent of (X_n, Y_n), $n \geq 1$. Now we prove some propositions related to the above adaptive allocation design.

Proposition 2.1: *As $n \to \infty$, almost surely,*

$$N_{kn} \to \infty\,, \qquad k = A, B\,.$$

Proof: We establish the result for $k = B$ only and the other follows in a similar way. For this we note that, for any $n > 2$, $T_n \geq 0$, $N_{An} + N_{Bn} = n$, $N_{An}N_{Bn} \leq n^2/2$,

$$\begin{aligned} \{N_{Bn}\text{does not tend to } \infty\} &= \bigcup_{m=1}^{\infty} \{N_{Bn} = N_{Bm} \text{ for all } n > m\} \\ P\{N_{Bn} = N_{Bm} \text{ for all } n > m\} &= P\{U_{n+1} \geq \hat{\pi}_{n+1} \text{ for all } n \geq m\}\,. \end{aligned}$$

Also, for every m, we find under the event $\{N_{Bn} = N_{Bm} \text{ for all } n > m\}$

$$\begin{aligned} \hat{\pi}_{n+1} &= \frac{\alpha + \beta T_n}{2\alpha + \beta N_{Bm}(N_{Am} + n - m)} \\ &\geq \alpha\{2\alpha + \beta N_{Am}N_{Bm} + \beta n N_{Bm}\}^{-1} \\ &\geq \alpha \left\{ 2\alpha + \frac{\beta m^2}{4} + \beta m n \right\}^{-1} = u_n(m)\,, \end{aligned}$$

say. Then we have

$$P\{N_{Bn} \text{ does not tend to } \infty\} \leq \sum_{m=1}^{\infty} P\{U_{n+1} \geq u_n(m) \text{ for all } n \geq m\}\,.$$

It is easy to see that, for every m, $\sum_{n=1}^{\infty} u_n(m)$ is divergent. Hence, using the same technique as in the proof of the Borel-Cantelli lemma (see Laha and Rohatgi, 1979, p.72), we get the required result. □

Proposition 2.2: *Let, for each $n > 2$ and under the proposed adaptive set-up, $F_{N_{An}}(x)$ be the sample d.f. based on X-observations. Then, writing*

$$D(N_{An}) = \sup_x |F_{N_{An}}(x) - F(x)|\,, \tag{4}$$

we have, for any $\epsilon > 0$,

$$\lim_{\nu \to \infty} P\{\sup_{n \geq \nu} D(N_{An}) > \epsilon\} = 0\,.$$

Proof: Suppose, for each n, there are fixed positive integers $n_k(n) = n_k$, $k = A, B$ with the properties

(i) $n_A + n_B = n$,

(ii) n_k $(k = A, B)$ is non-decreasing, and

(iii) $n_k \to \infty$ as $n \to \infty$, $k = A, B$.

Then, by Glivenko-Cantelli's lemma, we can find, for given $\epsilon, \delta > 0$, a positive integer M such that

$$P\left\{\sup_{n:n_A \geq M} D^*(n_A) > \epsilon\right\} < \frac{\delta}{2}\,, \tag{5}$$

where $D^*(n_A)$ is given by (4) under a non-adaptive set-up using the fixed pairs (n_A, n_B). By virtue of (ii) and (iii), we can also find, for given M, a positive integer ν_0 such that $n_A(\nu_0) = M$ and $n_A(\nu) \geq M$ for all $\nu > \nu_0$. Hence, (5) implies

$$P\left\{\sup_{n \geq \nu_0} D^*(n_A) > \epsilon\right\} < \frac{\delta}{2}\,. \tag{6}$$

By Proposition 2.1 we can find, for given M and δ, a positive integer $\nu_1 = \nu_1(M, \delta)$ such that

$$P\{N_{A\nu_1} < M\} < \frac{\delta}{2}\,. \tag{7}$$

Now

$$\begin{aligned} P\left\{\sup_{n\geq\nu} D(N_{An}) > \epsilon\right\} &\leq P\left\{\sup_{n\geq\nu} D(N_{An}) > \epsilon,\ N_{A\nu} \geq M\right\} + P(N_{A\nu} < M) \\ &\leq P\left\{\sup_{n\geq\nu_0} D^*(n_A) > \epsilon\right\} + P(N_{An} < M) \end{aligned}$$

which by (5) and (6) is less than or equal to δ for all ν exceeding $\nu^* = \max\{\nu_0, \nu_1\}$ and hence the required result follows. □

Theorem 2.1: *For every* $\epsilon > 0$,

$$\lim_{\nu\to\infty} P\left\{\sup_{n\geq\nu} |\hat{\theta}_n - \theta| > \epsilon\right\} = 0\,.$$

Proof: Let $1 \leq \alpha_1 < \alpha_2 < \cdots < \alpha_{N_{An}} \leq n$ and $1 \leq \beta_1 < \beta_2 < \cdots < \beta_{N_{Bn}} \leq n$ be two sets of positive, increasing, integer valued, almost surely finite random variables with $P(\alpha_i = \beta_j) = 0$ for all i, j. Then, we have $\{(\delta_i, Z_i), i = 1, \ldots, n\} = \{X_{\alpha_i}, i = 1, \ldots, N_{An}\} \bigcup \{Y_{\beta_j}, j = 1, \ldots, N_{Bn}\}$. Hence, using Theorem 2.1 of Melfi and Page (2000), X_{α_i}'s are iid with d.f. F and are independent of Y_{β_j}'s, which are iid with d.f. G. Thus, we can re-write $\hat{\theta}_n$ as

$$\hat{\theta}_n = \frac{1}{N_{An}N_{Bn}} \sum_{i=1}^{N_{An}} \sum_{j=1}^{N_{Bn}} u(X_{\alpha_i}, Y_{\beta_j}) = \frac{1}{N_{Bn}} \sum_{j=1}^{N_{Bn}} F_{N_{An}}(Y_{\beta_j})\,.$$

Now, defining $V_j = F(Y_{\beta_j}) - \theta$, for $j \geq 1$, we have

$$\begin{aligned} |\hat{\theta}_n - \theta| &\leq \frac{1}{N_{Bn}} \sum_{j=1}^{N_{Bn}} |F_{N_{An}}(Y_{\beta_j}) - F(Y_{\beta_j})| + \left|\frac{1}{N_{Bn}} \sum_{j=1}^{N_{Bn}} V_j\right| \\ &\leq D(N_{An}) + \left|\frac{1}{N_{Bn}} \sum_{j=1}^{N_{Bn}} V_j\right|\,. \end{aligned}$$

So, for every positive ϵ,

$$P\left\{\sup_{n\geq\nu}|\hat{\theta}_n-\theta|\right\}\leq P\left\{\sup_{n\geq\nu}D(N_{An})>\frac{\epsilon}{2}\right\}+P\left\{\sup_{n\geq\nu}|\frac{1}{N_{Bn}}\sum_{j=1}^{N_{Bn}}V_j|>\frac{\epsilon}{2}\right\}. \quad (8)$$

The random variables $V_1, V_2, \ldots$ are iid with mean 0 and finite variance. Hence, using Theorem 3.1 of Melfi and Page (2000), the second term of the right hand member of (8) converges to zero as $n \to \infty$. Then, by applying Proposition 2.2, the required result follows. □

Note: From (3) we write

$$\begin{aligned}\hat{\pi}_n &= \frac{\alpha+\beta T_n}{2\alpha+\beta N_{An}N_{Bn}}\\ &= \left(\frac{2\alpha}{N_{An}N_{Bn}}+\beta\right)^{-1}\left(\frac{\alpha}{N_{An}N_{Bn}}+\beta\hat{\theta}_n\right),\end{aligned}$$

which by Proposition 2.1 and Theorem 2.1 tends to θ almost surely as $n \to \infty$.
Theorem 2.2: *As $n \to \infty$, almost surely,*

$$\frac{N_{Bn}}{n} \to \theta\,.$$

The proof, using the above note, directly follows from Theorem 1 of Melfi, Page, and Geraldes (2001).

3 Asymptotic Results Related To $N_a(d)$

In this section we study asymptotic behaviors of $N_a(d)$. For this we have for every $\upsilon > 0$

$$\begin{aligned}P\{d^2N_a(d)\geq\upsilon\} &= P\{N_a(d)\geq r\}\\ &= P\{\sqrt{r}\sup_{n\geq r}|\hat{\theta}_n-\theta|\geq\sqrt{\upsilon_0}\}\,,\end{aligned} \quad (9)$$

where r is the smallest integer larger or equal υ/d^2, and $\upsilon_0 = rd^2$ satisfies $\upsilon_0 - d^2 < \upsilon \leq \upsilon_0$. Thus, we have to study the limiting distribution of $\sqrt{r}\sup_{n\geq r}|\hat{\theta}_n-\theta|$. Let $\widetilde{\theta}_n$ be given by (1) under a non-adaptive set-up using the fixed pairs (n_A, n_B) as defined in the proof of Proposition 2.2. Then, as in Sen (1981), we have

$$\sqrt{n}[(\widetilde{\theta}_n-\theta)-\frac{1}{n_A}\sum_{i=1}^{n_A}(\bar{G}(X_{\alpha_i})-\theta)-\frac{1}{n_B}\sum_{j=1}^{n_B}(F(Y_{\beta_j})-\theta)]\to 0 \quad (10)$$

almost surely as $n \to \infty$, where $(\alpha_1, \alpha_2, \ldots, \alpha_{n_A})$ and $(\beta_1, \beta_2, \ldots, \beta_{n_B})$ are defined in Section 2, and $\bar{G}(x) = 1 - G(x)$. Hence, by the same technique as in the proof of Proposition 2.2, it follows that

$$D_n=\sqrt{n}[(\hat{\theta}_n-\theta)-\frac{1}{N_{An}}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)-\frac{1}{N_{Bn}}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)]\to 0 \quad (11)$$

almost surely. But

$$\sqrt{r}\left|\sup_{n\geq r}|\hat{\theta}_n-\theta|-\sup_{n\geq r}\left\{\left|\frac{1}{N_{An}}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)+\frac{1}{N_{Bn}}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)\right|\right\}\right|$$
$$\leq \sup_{n\geq r}|D_n| \tag{12}$$

and

$$\begin{aligned}
&\sqrt{r}\sup_{n\geq r}\left|\frac{1}{N_{An}}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)+\frac{1}{N_{Bn}}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)\right.\\
&\left.-\frac{1}{n(1-\theta)}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)-\frac{1}{n\theta}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)\right|\\
&\leq \sup_{n\geq r}\left|\frac{n}{N_{An}}-\frac{1}{1-\theta}\right|\cdot\sup_{n\geq r}\frac{\sqrt{r}}{N_{An}}\left|\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)\right|\\
&+\sup_{n\geq r}\left|\frac{n}{N_{Bn}}-\frac{1}{\theta}\right|\cdot\sup_{n\geq r}\frac{\sqrt{r}}{N_{Bn}}\left|\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)\right|.
\end{aligned}\tag{13}$$

Thus, the right hand member of (13) converges to zero in probability, provided the random variables

$$\sup_{n\geq r}\left\{\frac{\sqrt{r}}{N_{An}}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta)\right\}\qquad\text{and}\qquad\sup_{n\geq r}\left\{\frac{\sqrt{r}}{N_{Bn}}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)\right\}$$

are bounded with probability 1. Hence, writing

$$\theta_n^*=\frac{1}{n(1-\theta)}\sum_{i=1}^{n}(1-\delta_i)(\bar{G}(Z_i)-\theta)+\frac{1}{n\theta}\sum_{i=1}^{n}\delta_i(F(Z_i)-\theta),$$

and using (10), (11), and (12), we get that $\sup_{n\geq r}\{\sqrt{r}|\hat{\theta}_n-\theta|\}$ and $\sup_{n\geq r}\{\sqrt{r}|\theta_n^*-\theta|\}$ asymptotically behave the same.

To study the asymptotic distribution of $\sup_{n\geq r}\{\sqrt{r}|\theta_n^*-\theta|\}$, we follow Hjort and Fenstad (1990) under martingale set-up. For this, we set for each real (c_1,c_2),

$$Z_k^a=c_1(1-\delta_k)(\bar{G}(Z_k)-\theta)+c_2\delta_k(F(Z_k)-\theta)$$

and

$$S_k^a=\sum_{i=1}^{k}Z_k^a,\qquad k\geq 1.$$

Also for each $c>1$ we define the stochastic process $W_{rc}^a=\{W_{rc}^a(t),\ 1\leq t\leq c\}$ as

$$W_{rc}^a(t)=\frac{1}{\sqrt{r}}S_{[rt]}^a,\quad 1\leq t\leq c$$

which belongs to $D[1,c]$ equipped with the Skorokhod topology.

Theorem 3.1: *Let* $W = \{W(t),\ t \geq 0\}$ *be a standard Brownian motion process. Then*

$$\sup_{n \geq r}\{\sqrt{r}|\theta_n^* - \theta|\} \to \left(\frac{\sigma_1^2}{1-\theta} + \frac{\sigma_2^2}{\theta}\right)^{1/2} \sup_{0 \leq t \leq 1} |W(t)|$$

in distribution as $r \to \infty$*, where*

$$\sigma_1^2 = \int_{-\infty}^{\infty} \bar{G}^2(x) dF(x) - \theta^2 \qquad \textit{and} \qquad \sigma_2^2 = \int_{-\infty}^{\infty} F^2(y) dG(y) - \theta^2 \, .$$

The proof of Theorem 3.1 depends on the following propositions.
Proposition 3.1: *For any* $1 \leq t_1 \leq t_2 \leq \cdots \leq t_d \leq c$*, as* $r \to \infty$*,*

$$(W_{rc}^a(t_1), \ldots, W_{rc}^a(t_d))' \to \gamma_\theta (W(t_1), \ldots, W(t_d))'$$

in distribution, where

$$\gamma_\theta^2 = c_1^2 \sigma_1^2 (1-\theta) + c_2^2 \sigma_2^2 \theta \, .$$

Proof: For any real vector $\mathbf{l} = (l_1, l_2, \ldots, l_d)'$, we consider

$$T_r^a = \sum_{k=1}^{d} l_k W_{rc}^a(t_k) = \frac{1}{\sqrt{r}} \sum_{k=1}^{d} l_k \sum_{i=1}^{[rt_k]} Z_i^a = \sum_{i=1}^{[rt_d]} \bar{Z}_i^a \, ,$$

say, where

$$\bar{Z}_i^a = \left(\frac{1}{\sqrt{r}} \sum_{k=j}^{d} l_k\right) Z_i^a \, , \qquad [rt_{j-1}] + 1 \leq i \leq [rt_j] \, , \quad j = 1, \ldots, d$$

with $t_0 = 0$. Then it can be easily shown that $\{\bar{Z}_i^a,\ 1 \leq i \leq [rt_d],\ r \geq 1\}$ form a martingale difference array from a zero-mean-square-integrable martingale. Hence, as in Wei et al. (1990) (see also Theorems 3.13 and 2.13 of Hall and Heyde (1980), we have after some routine calculations

$$T_r^a \to \mathcal{N}(0, \eta^2)$$

in distribution, where $(T_r^a)^2$ converges in probability to

$$\begin{aligned}
\eta^2 &= \left[\left(\sum_{k=1}^{d} l_k\right)^2 t_1 + \left(\sum_{k=2}^{d} l_k\right)^2 (t_2 - t_1) + \cdots + l_d^2 (t_d - t_{d-1})\right] \gamma_\theta^2 \\
&= \left[\sum_{k=1}^{d} l_k^2 t_k + 2 \sum_{1 \leq k < k' \leq d} l_k l_{k'} t_k\right] \gamma_\theta^2 \, ,
\end{aligned}$$

as $r \to \infty$. Here $\mathcal{N}(\mu, \sigma^2)$ represents a random variable having normal distribution with mean μ and variance σ^2. Hence, by Cramer-Wold device the required result follows. □

Proposition 3.2: *The sequence* $\{W_{rc}^a\}$ *is tight.*

Proof: Take any $1 \le s \le t \le u \le c$. Then, using the martingale theory as used in the proof of Proposition 3.1, we have

$$\begin{aligned}
& E\left[(W_{rc}^a(t) - W_{rc}^a(s))^2 (W_{rc}^a(u) - W_{rc}^a(t))^2\right] \\
&= r^{-2} E\left[\left(\sum_{i=[rs]+1}^{[rt]} Z_i^a\right)^2 \left(\sum_{i=[rt]+1}^{[ru]} Z_i^a\right)^2\right] \\
&= r^{-2}\left\{c_1^2\sigma_1^2 \sum_{i=[rs]+1}^{[rt]} P(\delta_i = 0) + c_2^2\sigma_2^2 \sum_{i=[rs]+1}^{[rt]} P(\delta_i = 1)\right\} \\
&\quad \cdot \left\{c_1^2\sigma_1^2 \sum_{i=[rt]+1}^{[ru]} P(\delta_i = 0) + c_2^2\sigma_2^2 \sum_{i=[rt]+1}^{[ru]} P(\delta_i = 1)\right\} \\
&\le r^{-2}\gamma_1^4([rt] - [rs])([ru] - [rt]) \\
&\le r^{-2}\gamma_1^4\left([ru] - [rs]\right)^2 ,
\end{aligned}$$

where $\gamma_1^2 = c_1^2\sigma_1^2 + c_2^2\sigma_2^2$. Hence, by using Theorem 15.6 of Billingsley (1968), the required result follows. □

Proposition 3.3: *For every* $\epsilon > 0$

$$\lim_{c\to\infty} \lim\sup_{r\to\infty} P\left\{\sup_{n\ge rc}\left|\frac{S_n^a}{n}\right| > \frac{\epsilon}{\sqrt{r}}\right\} = 0 .$$

Proof: Let us write

$$P_r(c) = P\left\{\sup_{n\ge rc}\left|\frac{S_n^a}{n}\right| > \frac{\epsilon}{\sqrt{r}}\right\} .$$

Then, for every fixed $c \ge 1$ there exists a non-negative integer k such that $2^k \le c \le 2^{k+1}$, and hence

$$P_r(c) \le \sum_{i=k}^{\infty} P\left\{\sup_{r2^i\le n\le r2^{i+1}} |S_n^a - S_{r2^i}^a| > \frac{\epsilon}{2}2^i\sqrt{r}\right\} + \sum_{i=k}^{\infty} P\left\{\sup_{r2^i\le n\le r2^{i+1}} |S_{r2^i}^a| > \frac{\epsilon}{2}2^i\sqrt{r}\right\} . \tag{14}$$

The second member of the right hand side (r.h.s.) of (14) equals

$$\sum_{i=k}^{\infty} P\left\{\frac{|S_{r2^i}^a|}{\sqrt{r2^i}} > \frac{\epsilon}{2}2^{i/2}\right\} ,$$

which by the same technique as in Wei et al. (1990) tends to

$$\sum_{i=k}^{\infty} P\left\{|\mathcal{N}(0,1)| > \frac{\epsilon}{2\gamma_\theta}2^{i/2}\right\} \le \sum_{i=k}^{\infty} \frac{4\gamma_1^2}{\epsilon^2}\frac{1}{2^i} = \frac{8\gamma_1^2}{2^k\epsilon^2} \le \frac{8\gamma_1^2}{c\epsilon^2} . \tag{15}$$

Using Hall and Heyde (1980, p.22) the first member on the r.h.s. of (14) is for some $K > 0$

$$\leq \sum_{i=k}^{\infty} \frac{4}{\epsilon^2} \frac{K}{r2^{2i}} \left[c_1^2 \sigma_1^2 \sum_{k=r2^i}^{r2^{i+1}} P(\delta_k = 0) + c_2^2 \sigma_2^2 \sum_{k=r2^i}^{r2^{i+1}} P(\delta_k = 1) \right]$$

$$\rightarrow \frac{4\gamma_1^2 K}{\epsilon^2} \sum_{i=k}^{\infty} \frac{1}{2^i} = \frac{8\gamma_1^2 K}{2^k \epsilon^2} \leq \frac{8\gamma_1^2 K}{c\epsilon^2} \,. \tag{16}$$

So, combining (15) and (16) we get

$$\limsup_{r\to\infty} P_r(c) \leq \frac{8\gamma_1^2}{c\epsilon^2}(K+1) \rightarrow 0 \qquad \text{as} \quad c \rightarrow \infty \,.$$

Hence we get the required result. □

Proof of Theorem 3.1: Using Propositions 3.1 and 3.2 we get on $D[1, c]$

$$W_{rc}^a \rightarrow \gamma_\theta \{W(t),\ t \in [1, c]\}$$

in distribution as $r \rightarrow \infty$, and hence

$$\left\{ \frac{\sqrt{r} S_{[rt]}^a}{[rt]},\ t \in [1, c] \right\} \rightarrow \gamma_\theta \left\{ \frac{W(t)}{t},\ t \in [1, c] \right\}$$

in distribution on $D[1, c]$. This implies

$$\sqrt{r} \sup_{r \leq n \leq rc} \frac{|S_n^a|}{n} \rightarrow \gamma_\theta \sup_{1 \leq t \leq c} \frac{|W(t)|}{t} \tag{17}$$

in distribution and since the distribution of

$$\sup_{1 \leq t \leq c} |t^{-1} W(t)| = \sup_{c^{-1} \leq s \leq 1} |s W(s^{-1})|$$

is the same as that of $\sup_{c^{-1} \leq t \leq 1} |W(t)|$, we get by using Proposition 3.3, as in Theorem 4.1 of Billingsley (1968),

$$\sqrt{r} \sup_{n \geq r} \frac{|S_n^a|}{n} \rightarrow \gamma_\theta \sup_{0 \leq t \leq 1} |W(t)|$$

in distribution. Now, taking $c_1 = 1/(1-\theta)$ and $c_2 = 1/\theta$, we get

$$\gamma_\theta^2 = \frac{\sigma_1^2}{1-\theta} + \frac{\sigma_2^2}{\theta} \,.$$

Hence the required result follows. □

4 Asymptotic Results in Non-adaptive Equal Allocation Design

In connection with the fixed-width interval estimation of θ, it would be quite natural to compare the adaptive allocation design with a non-adaptive equal allocation design, where the treatments A and B are equally randomized to the experimental units. For this, we briefly describe the non-adaptive 50:50 allocation rule along with the related asymptotic results. Suppose, the allocation indicators δ_i's are iid Bernoulli variables with success probability $1/2$. Then the resulting design becomes non-adaptive equal allocation. Hence, we have the observations $\{\delta_i,\ Z_i = (1-\delta_i)X_i + \delta_i Y_i,\ i \geq 1\}$ as before. Having n observations we set

$$\bar{\theta}_n = \left\{\sum_{i=1}^{n} \delta_i\right\}^{-1} \left\{\sum_{i=1}^{n}(1-\delta_i)\right\}^{-1} \sum_{i=1}^{n}\sum_{j=1}^{n}(1-\delta_i)\delta_j u(Z_i, Z_j)\,, \tag{18}$$

which is a strongly consistent estimator of θ. Using $\bar{\theta}_n$ we can also define a stopping variable $N_e(d)$, say, as in (2), which also admits expression (9) after replacing $\bar{\theta}_n$ in place of $\hat{\theta}_n$. Now, setting

$$Z_i^e = 2(1-\delta_i)(\bar{G}(Z_i) - \theta) + 2\delta_i(F(Z_i) - \theta) \qquad \text{and} \quad S_k^e = \sum_{i=1}^{k} Z_i^e\,, \quad k = 1, 2, \dots\,,$$

we introduce for every $c > 0$ and integer $r > 0$ a stochastic process $W_{rc}^e = \{W_{rc}^e(t),\ 1 \leq t \leq c\}$ defined by

$$W_{rc}^e(t) = \frac{1}{\sqrt{r}} S_{[rt]}^e\,.$$

Then by the same technique as used in Section 3 it is easy to show that

$$W_{rc}^e(t) \to \{2(\sigma_1^2 + \sigma_2^2)\}^{1/2} W(t)\,, \quad 1 \leq t \leq c$$

in distribution as $r \to \infty$. Hence we have

$$\sup_{n \geq r}\left\{\sqrt{r}|\bar{\theta}_n - \theta|\right\} \to \{2(\sigma_1^2 + \sigma_2^2)\}^{1/2} \sup_{0 \leq t \leq 1} |W(t)| \tag{19}$$

in distribution as $r \to \infty$.

5 Fixed-Width Confidence Intervals

Now we construct two sequences of fixed-width confidence intervals of θ based on the asymptotic results derived in Sections 3 and 4. These intervals are determined in the following way.

In an adaptive allocation design, we have

$$P\{d^2 N_a(d) \leq \upsilon\} = P\{\sqrt{r} \sup_{n \geq r} |\hat{\theta}_n - \theta| \leq \sqrt{\upsilon_0}\}\,,$$

which by (9) and Theorem 3.1 tends to

$$\psi_s(w_a) = P\left\{\sup_{0\le t\le 1}|W(t)| \le w_a\right\} \tag{20}$$

as $r \to \infty$, where

$$w_a = \sqrt{\upsilon}\left(\frac{\sigma_1^2}{1-\theta} + \frac{\sigma_2^2}{\theta}\right)^{-1/2} .$$

From Sen (1981, p.42) (see also Anderson, 1960) $\psi_s(w_a)$ can be computed as

$$\psi_s(w_a) = \sum_{k=-\infty}^{\infty}(-1)^k\left[\Phi((2k+1)w_a) - \Phi((2k-1)w_a)\right] ,$$

where $\Phi(x)$ represents the d.f. of a standard normal random variable. Similarly, in case of equal allocation design it is easy to find that

$$\lim_{r\to\infty} P(d^2N_e(d) \le \upsilon) = \psi_s(w_e) ,$$

where w_e is given by

$$w_e = \sqrt{\frac{\upsilon}{2}}\left(\sigma_1^2 + \sigma_2^2\right)^{-1/2} .$$

Let a_α be such that $\psi_s(a_\alpha) = 1-\alpha$ for given $0<\alpha<1$. Then, for given (α, d) we find the following stopping rules corresponding to the adaptive and equal allocation designs, respectively

$$\hat\nu_a = \min\left\{n:\ n \ge \frac{a_\alpha^2}{d^2}\left(\frac{\hat\sigma_{1n}^2}{1-\hat\theta_n} + \frac{\hat\sigma_{2n}^2}{\hat\theta_n}\right)\right\} \tag{21}$$

$$\hat\nu_e = \min\left\{n:\ n \ge \frac{2a_\alpha^2}{d^2}\left(\bar\sigma_{1n}^2 + \bar\sigma_{2n}^2\right)\right\} , \tag{22}$$

where $\hat\sigma_{kn}$ and $\bar\sigma_{kn}$, $k=1,2$, are the consistent estimators of σ_1 and σ_2 in adaptive and equal allocation designs, respectively. The forms of the estimators are

$$\hat\sigma_{1n}^2 = \left(\sum_{i=1}^n(1-\delta_i)\right)^{-1}\left(\frac{\sum_{i=1}^n\delta_i}{2}\right)^{-1}\sum_{i=1}^n\sum_{1\le j<j'\le n}(1-\delta_i)\delta_j\delta_{j'}u(Z_i,Z_j)u(Z_i,Z_{j'}) - \hat\theta_n^2$$

$$\hat\sigma_{2n}^2 = \left(\frac{\sum_{i=1}^n(1-\delta_i)}{2}\right)^{-1}\left(\sum_{i=1}^n\delta_i\right)^{-1}\sum_{1\le i<i'\le n}\sum_{j=1}^n(1-\delta_i)(1-\delta_{i'})\delta_j u(Z_i,Z_j)u(Z_{i'},Z_j) - \hat\theta_n^2 .$$

The estimators $\bar\sigma_{kn}^2$, $k=1,2$, have similar forms, and hence are omitted. Using martingale convergence concept it can be checked by laborious but straightforward computations that

$$\sup_{n\ge r}\left|\frac{\hat\sigma_{kn}}{\sigma_k} - 1\right| \to 0 \qquad \text{and} \qquad \sup_{n\ge r}\left|\frac{\bar\sigma_{kn}}{\sigma_k} - 1\right| \to 0 , \quad k=1,2$$

in probability as $r \to \infty$. Again, since $\psi_s(\cdot)$ is a continuous function of (σ_1, σ_2), we have as in the previous section

$$\lim_{r\to\infty} P(N_k(d) < \hat{\nu}_k) = 1 - \alpha\,, \quad k = a, e\,.$$

Hence, the sequences of fixed-width confidence intervals for θ of length $2d$ with confidence coefficient $1-\alpha$ are $(\hat{\theta}_n - d, \hat{\theta}_n + d)$, $n \geq \hat{\nu}_a$, in the adaptive design, and $(\bar{\theta}_n - d, \bar{\theta}_n + d)$, $n \geq \hat{\nu}_e$ in the equal allocation design. In the next section we carry out various numerical computations to judge the performance of the adaptive allocation relative to that of the equal allocation.

6 Numerical Study

Here we give a numerical comparison between the adaptive allocation design and its non-adaptive counterpart in terms of the minimum sample sizes required to obtain the fixed width confidence intervals of θ. The true values of these minimum sample sizes are, respectively, given by

$$\nu_a = \frac{a_\alpha^2}{d^2}\left(\frac{\sigma_1^2}{1-\theta} + \frac{\sigma_2^2}{\theta}\right) \qquad \text{and} \qquad \nu_e = \frac{2a_\alpha^2}{d^2}\left(\sigma_1^2 + \sigma_2^2\right)\,.$$

So we compute ν_a and ν_e at different choices of (F, G, d). In case of the adaptive design we also compute the proportion of allocation of the observations to the better treatment. Here we take $F \equiv \mathcal{N}(0,1)$ and consider the following choices of G:

(i) $\mathcal{N}(\delta, \tau^2)$

(ii) $\mathcal{C}(\delta,\ \tau)$, a Cauchy distribution with location δ and scale τ

(iii) contaminated normal having d.f.

$$G(x) = p\Phi\left(\frac{x-\delta}{\tau}\right) + (1-p)\Phi\left(\frac{x-\delta}{5\tau}\right)$$

with $0 < p < 1$ as the mixing proportion.

The value of τ is varied to see the effect of different shapes in the behaviors of ν_a and ν_e. In particular, we take $\tau = 0.5, 1, 2$, $\delta = 0.25, 0.5, 1$, $d = 0.05, 0.1$, and $p = 0.8, 0.9$. Here, treatment B is better for the above choices of δ. Denoting the proportion of the observations on treatment B by $prop_B$, we see that the true value of $prop_B$ is equal to θ. So we compute $prop_B$ for the above parametric combinations. The whole computation is done by taking $\alpha = 0.05$ for which we note that $a_\alpha = 2.242$. The results are reported in Table 1. There it is observed that for given (δ, τ) the sample size ν_a for the adaptive design is larger than the sample size ν_e corresponding to a non-adaptive equal allocation design. Also the proportion of allocation $prop_B$ to the better treatment for the adaptive design always exceeds $1/2$ which is the value of the proportion corresponding to a 50:50 allocation design. In an adaptive design it is also noted that for any τ, $prop_B$ increases with δ. That means, the larger the deviation in the locations of F and G, the higher is the ethical gain measured in terms of the proportion of allocations to the better treatment. The sampling becomes skewed in the presence of ethical gain. However, the skewness is inversely proportional to the value of τ.

Table 1: Sample sizes ν_a, ν_e, and proportion of allocation to treatment B for $d = 0.05, 0.1$

	$\delta = 1/4$			$\delta = 1/2$			$\delta = 1$		
$(F,G) \equiv$ (Normal, Cauchy)									
τ	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$
1/2	678	664	0.569	671	625	0.636	614	504	0.751
	170	166		168	157		154	126	
1	659	656	0.552	624	616	0.602	544	547	0.694
	165	162		156	147		136	130	
2	726	714	0.534	686	656	0.567	649	625	0.629
	182	191		171	169		152	141	
$(F,G) \equiv$ (Normal, Normal)									
	$\delta = 1/4$			$\delta = 1/2$			$\delta = 1$		
τ	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$
1/2	700	695	0.589	715	621	0.673	729	501	0.815
	200	174		216	157		236	110	
1	667	653	0.570	656	606	0.638	614	498	0.760
	167	163		164	152		154	112	
2	679	675	0.545	636	635	0.589	546	521	0.673
	170	179		159	174		137	156	
$(F,G) \equiv$ (Normal, contaminated Normal with $p = 0.9$)									
	$\delta = 1/4$			$\delta = 1/2$			$\delta = 1$		
τ	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$
1/2	695	680	0.583	710	617	0.663	717	670	0.797
	189	170		199	154		204	106	
1	657	658	0.565	636	619	0.628	575	588	0.742
	164	165		159	157		144	122	
2	692	630	0.541	688	673	0.582	659	652	0.659
	143	148		162	158		150	143	
$(F,G) \equiv$ (Normal, contaminated Normal with $p = 0.8$)									
	$\delta = 1/4$			$\delta = 1/2$			$\delta = 1$		
τ	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$	ν_a	ν_e	$prop_B$
1/2	699	669	0.578	708	616	0.652	720	679	0.781
	180	167		184	154		180	113	
1	653	646	0.560	635	624	0.619	551	528	0.724
	163	157		156	154		138	132	
2	706	705	0.538	663	631	0.574	656	621	0.646
	177	176		166	163		144	141	

In each of the cells corresponding to ν_a and ν_e, there are two values. The upper values correspond to $d = 0.05$ and the lower ones to $d = 0.1$.

Table 1 shows that as τ becomes larger the difference $\nu_a - \nu_e$ becomes insignificant along with the gradual decrease of $prop_B$. It indicates that the adaptive design performs equivalently with the equal allocation design. But for smaller values of τ the sample size ν_a of the adaptive design is slightly larger than the sample size ν_e of 50:50 allocation design. Simultaneously, the proportion of allocations to the better treatment takes the higher values. At the cost of drawing extra $\nu_a - \nu_e$ (which is very small except very few cases) observations, a considerable amount of ethical gain can be achieved by using the proposed adaptive design in place of the non-adaptive equal allocation design while constructing the fixed width confidence intervals of θ.

7 Concluding Remarks

The efficiency of the proposed adaptive allocation design relative to the non-adaptive 50:50 allocation design can also be assessed by

$$E_r^* = \lim_{d\to 0} \frac{E(N_a(d))}{E(N_e(d))} = \frac{\lim_{d\to 0} E(d^2 N_a(d))}{\lim_{d\to 0} E(d^2 N_e(d))}$$

provided the expectations converge. Now, from the convergence of $d^2 N_a(d)$ are $d^2 N_e(d)$ in distributions discussed in Sections 3 and 4, respectively, we expect that as $d \to 0$

$$\begin{aligned} E(d^2 N_a(d)) &\to \left(\frac{\sigma_1^2}{1-\theta} + \frac{\sigma_2^2}{\theta}\right) E(W_{\max}^2) \\ E(d^2 N_e(d)) &\to 2\left(\sigma_1^2 + \sigma_2^2\right) E(W_{\max}^2)\,, \end{aligned}$$

where $W_{\max} = \sup_{0\le t\le 1} |W(t)|$. Hence, we get

$$E_r^* = \frac{\theta\sigma_1^2 + (1-\theta)\sigma_2^2}{2\theta(1-\theta)(\sigma_1^2 + \sigma_2^2)}\,.$$

Thus, one can easily determine the value of E_r^* for given F and G. But such a derivation depends on the conditions related to the uniform integrability of $d^2 N_a(d)$ and $d^2 N_e(d)$. Techniques from Hjort and Fenstad (1992) would be appropriate, but we are not going to pursue this.

Acknowledgements

The authors like to thank the editor and the referee for their valuable comments and suggestions. The second author also like to thank the authority of Bankura Sammilani College for their kind co-operation in pursuing this research work.

References

Anderson, T. W. (1960). A modification of the sequential probability ratio test to reduce the sample size. *Annals of Mathematical Statistics*, *31*, 163-197.

Bandyopadhyay, U., and Biswas, A. (2004). An adaptive allocation for continuous response using Wilcoxon-Mann-Whitney score. *Journal of Statistical Planning and Inference*, *123*, 207-224.

Bartlett, H. R., Roloff, D. W., Cornell, R. G., Andrew, A. F., Dillon, P. W., and Zwischesberger, J. B. (1985). Extracorporeal circulation in neonatal respiratory failure: A prospective randomized trial. *Pediatrics*, *76*, 479-487.

Billingsley, P. (1968). *Convergence of Probability Measures*. New York: John Wiley.

Biswas, A., and Dewanji, A. (2004). Sequential adaptive designs for clinical trials with longitudinal response. In N. Mukhopadhyay, S. Chattopadhyay, and S. Datta (Eds.), *Applied Sequential Methodologies*. New York: Marcel Dekker.

Durham, S. D., Flournoy, N., and Li, W. (1998). A sequential design for maximizing the probability of a favourable response. *Canadian Journal of Statistics*, *26*, 479-495.

Efron, B. (1971). Forcing a sequential experiment to be balanced. *Biometrika*, *58*, 403-417.

Ghosh, M., Mukhopadhyay, N., and Sen, P. K. (1997). *Sequential Estimation*. New York: John Wiely.

Hall, P., and Heyde, C. C. (1980). *Martingale Limit Theory and its Application*. New York: Academic Press.

Hjort, N. L., and Fenstad, G. (1990). *On the last n where $|\hat{\theta}_n - \theta| \geq \epsilon$* (Tech. Rep.). University of Oslo, Norway: Institute of Mathematics.

Hjort, N. L., and Fenstad, G. (1992). On the last n and the number of times an estimator is more than ϵ from its largest value. *Annals of Statistics*, *20*, 469-489.

Hu, F., and Zhang, L. X. (2004). Asymptotic properties of doubly adaptive biased coin design for multi-treatment clinical trials. *Annals of Statistics*, *32*, 268-301.

Laha, R. G., and Rohatgi, V. K. (1979). *Probability Theory*. New York: John Wiley.

Melfi, V., and Page, C. (2000). Estimation after adaptive allocation. *Journal of Statistical Planning and Inference*, *87*, 353-363.

Melfi, V., Page, C., and Geraldes, M. (2001). An adaptive randomized design with application to estimation. *Canadian Journal of Statistics*, *29*, 107-116.

Muller, H. H., and Schafer, H. (2001). Adaptive group sequential designs for clinical trials combining the advantages of adaptive and of classical group sequential approaches. *Biometrics*, *57*, 886-891.

Rosenberger, W. F. (1993). Asymptotic inference with response-adaptive treatment allocation design. *Annals of Statistics*, *21*, 2098-2107.

Rosenberger, W. F. (2002). Randomised urn models and sequential design. *Sequential Analysis*, *21*, 1-28.

Rosenberger, W. F., and Sriram, T. N. (1997). Estimation for an adaptive allocation design. *Journal of Statistical Planning and Inference*, *59*, 309-319.

Rosenberger, W. F., Stallard, N., Ivanova, A. V., Harper, C. N., and Ricks, M. L. (2001). Optimal adaptive designs for binary response trials. *Biometrics*, *57*, 909-913.

Rout, C. C., Rocke, D. A., Levin, J., Gouws, E., and Reddy, D. (1993). A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. *Anesthesiology*, *79*, 262-269.

Sen, P. K. (1981). *Sequential Nonparametrics: Invariance Principles and Statistical Inference*. New York: John Wiley.

Tamura, R. N., Faries, D. E., Andersen, J. S., and Heiligenstein, J. H. (1994). A case study of an adaptive clinical trials in the treatment of out-patients with depressive disorder. *Journal of the American Statistical Association*, *89*, 768-776.

Ware, J. H. (1989). Investigating therapies of potentially great benefit: ECMO. *Statistical Science*, *4*, 298-340.

Wei, L. J. (1979). The generalised Polya's urn for sequential medical trials. *Annals of Statistics*, *7*, 291-296.

Wei, L. J., and Durham, S. (1978). The randomized play-the-winner rule in medical trials. *Journal of the American Statistical Association*, *73*, 838-843.

Wei, L. J., Smythe, R. T., Lin, D. Y., and Park, T. S. (1990). Statistical inference with data-dependent treatment allocation rules. *Journal of the American Statistical Association*, *85*, 156-162.

Zelen, M. (1969). Play-the-winner rule and the controlled clinical trial. *Journal of the American Statistical Association*, *64*, 131-146.

Authors' addresses:

Uttam Bandyopadhyay
Department of Statistics
University of Calcutta
35, Ballygunge Circular Road, Kolkata-19
India
E-mail: ubandyopadhyay@yahoo.com

Radhakanta Das
Department of Statistics
Bankura Sammilani College
Bankura, West Bengal
India