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PLAY THE WINNER BINOMIAL SELECTION

by

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A THESIS

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled .....

PLAY THE WINNER BINOMIAL SELECTION

.....

.....

submitted by RAMAKRISHNAN SUGAVANAM

in partial fulfilment of the requirements for the degree of

Master of .....

Carl Nordbrock

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Supervisor

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Date May 9, 1973.

ABSTRACT

A truncated procedure for selecting the better of two binomial populations is formulated. The procedure uses play the winner rule and the selection is based on the difference in the proportion of successes at termination. The trials are terminated whenever either population is sampled completely or when the difference in the proportion of successes exceeds a critical value, based on the failures on both populations. It is shown that, when the average of the two population probabilities of success is less than 0.5, the expected number of observations on the poorer treatment is smaller for this procedure than for any procedure currently known.

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TABLE OF CONTENTS

LIST OF TABLES

CHAPTER I

INTRODUCTION

The theory of clinical trials is of considerable interest to theoretical and applied statisticians. The idea behind most of the newer techniques is the ethical one of not prolonging a trial longer than necessary, for a trial which is unduly prolonged may result in an excessive number of patients being given the less beneficial treatment. The doctor treating a patient in a clinical trial is not only obliged to derive information about the best treatment, but is also obliged to treat each patient in the best way possible. This ethical consideration has motivated the development of several statistical techniques for selecting the best treatment, or equivalently the selection of the best of several binomials.

The past work in selecting the better of two binomial populations falls into three categories: (a) aspects of the allocation problem, (b) two-armed-bandit problem and (c) alternate ways of conducting clinical trials by adopting the sampling technique.

In the two-armed-bandit problem, we deal with a slot machine. When the left arm is pulled, the machine

pays one unit with probability p, while a pull on the right arm pays one unit with probability p'. The problem with a two-armed bandit is which arm to pull. Assuming the probabilities of pay-off of the two arms are constant, a strategy which will maximize the expected winnings for a sequence of pulls is desired.

In the allocation problem, the total number of patients waiting for the treatment is known. Each patient is to be treated with one of the two treatments. The first n patients are used to select the better drug and the remaining patients are treated with the one selected as being better.

In practice, no knowledge about the number of patients is available. Zelen[11] modified the allocation model by assuming that (a) two (or more) similar groups are to be observed where the groups differ only in the treatments received; (b) the construction of the groups is by random allocation; (c) the response is dichotomous and the results are observed without delay. He suggested the use of sampling techniques to reduce the number of patients put on the poorer treatment. Zelen applied Play-the-Winner(PW) rule to the clinical trials; it prescribes that a success with a given treatment generates a further trial on the same treatment while a failure generates a trial on the alternative treatment.This is

a very simple rule to use that introduces bias in favor of testing the better treatment.

Sobel and Weiss[9] compared different procedures for selecting the better treatment. A procedure is specified by the sampling and termination rule. A comparison of PW rule was made with Vector-at-a-time(VT) rule; VT consists of taking two observations at each stage, one from each population and one does not consider stopping between these two trials. The situation where a physician wishes to compare two or more treatments using the patients he ordinarily encounters, and the problem of selecting the most effective dose of a particular drug are two among the several practical situations where these simple methods can be applied. Most of the investigations are done by formulating the selection of the better of two binomial populations (i.e. the one with the highest probability of success p on a single trial) as follows: for preassigned constants p^* and Δ^* with $0.5 \leq p^* < 1$ and $0 < \Delta^* < 1$, it is required that the probability of correct selection(CS) be at least P*when the true difference in p-values (denoted by Δ) is at least Δ^* . i.e. we want a procedure R such that

$$P(CS/R) \geq P^* \quad \text{whenever} \quad \Delta \geq \Delta^* .$$

Among the procedures satisfying this requirement, the one with the smallest expected number of patients on the less

beneficial treatment is declared to be the better treatment.

In chapter II, a review of the recent work done on the binomial selection problem is made. In chapter III, we discuss a procedure R(DPPW) using PW sampling where the rule is based on the difference in the proportion of successes. The performance of this procedure is evaluated in chapter IV.

CHAPTER II

A REVIEW OF THE RECENT RESULTS ON BINOMIAL SELECTION PROBLEM

In this chapter, we will briefly review the recent work on selecting the better of two binomial populations. The results mentioned in this chapter will be used for comparison with the results of the next chapter. Let us denote by

$S(i)$, $F(i)$, and $N(i)$ the number of successes, failures and trials respectively on the i^{th} population for $i = A,B$.

$N = N(A) + N(B)$, the total number of observations on both populations.

$\Delta = p - p'$ where p and p' are the probabilities of success on a single trial on population A and B respectively; let $p \geq p'$.

$q = 1 - p$; $q' = 1 - p'$.

CS - correct selection, namely identifying population A as the better one.

(2.1)

(P^*, Δ^*) - preassigned constants such that

$0.5 < P^* < 1$ and $0 < \Delta^* < 1$.

We need a procedure R for selecting the population with the larger probability of success on a single trial such that

(2.2) $P[\ CS/R\ ] \geq P^*$ whenever $\Delta \geq \Delta^*$.

Sobel and Weiss [9] considered procedures R[DPW] and R[DVT] with the termination rule based on the difference in successes at each stage. The procedure R[DPW] uses play-the-winner (PW) sampling and declares treatment i as the better one when S(i) - S(j) = r, where j is the other treatment, while R[DVT] uses vector-at-a-time (VT) sampling and makes the same decision when S(i) - S(j) = s. The integers r and s are chosen to be the smallest such that (2.2) is satisfied for preassigned constants (P^*, Δ^*) satisfying (2.1).

The probability of correct selection under R[DPW] is calculated by defining

(2.3) $P(n) = P[\ CS/\ S(A) - S(B) = n,\ NT = A\ ]$

$Q(n) = P[CS/\ S(A) - S(B) = n,\ NT = B\ ]$

where NT = A (NT = B) denotes the next treatment is on A(B). Since the first treatment is chosen at random, the P(CS) at termination is given by

(2.4) $P(CS/R[DPW]) = \frac{1}{2}\ [\ P(0) + Q(0)\ ]$

Under R[DPW], letting q = 1 - p, and q' = 1 - p', we obtain

$$P(n) = p\,P(n+1) + q\,Q(n)$$

(2.5)

$$Q(n) = p'Q(n-1) + q'P(n)$$

with the boundary conditions $P(r) = 1$, $Q(-r) = 0$.

The solution to (2.5) satisfying the boundary conditions is given by

$$(2.6)\quad Q(n) = \frac{q'(1-\lambda^{r+n})}{q'-q\lambda^{2r}}\quad,\quad P(n) = \frac{q'-q\lambda^{r+n}}{q'-q\lambda^{2r}}$$

where $\lambda = (p'/p) < 1$. Setting $P(CS)=P^*$, we obtain from (2.6) and (2.4)

$$(2.7)\qquad q' - \frac{1}{2}(q+q')\lambda^{r} = P^*(q'-q\lambda^{2r})$$

as the equation determining r. Thus given any p and p', (2.7) determines r such that $P(CS)=P^*$. Since it is desired that (2.2) be satisfied when p and p' are unknown, it is necessary to find the Least Favourable (LF) configuration of p and p' which satisfies (2.2). By LF we mean p and p' which minimizes P(CS) subject to the restriction $p-p' \geq \Delta^*$. It is shown in [9] that, when $P^* \to 1$, the value of r under LF can be approximated by

$$r_m = \left[\frac{\log\{2(1-P^*)\}}{\log(1-\Delta^*)}\right] + 1$$

where [.] denotes 'the largest integer contained in'.

Under the procedure R[DVT], using VT sampling, we stop when $S(i)-S(j)=s$ and choose the treatment i as the better. We let $P(n) = P(CS/S(A)-S(B)=n)$; thus

$P(CS/R[DVT]) = P(0)$; and it is obtained by solving the difference equation

$$(2.8) \qquad P(n) = pq'P(n+1)+qp'P(n-1)+(pp'+qq')P(n)$$

with the boundary conditions $P(s)= 1$ and $P(-s)=0$.

The solution to (2.8) is given by

$$P(n) = \frac{1 - \delta^{s+n}}{1 - \delta^{2s}} \qquad \text{where } \delta = \frac{p'q}{pq'} < 1.$$

It is shown that $\min P(CS/R[DVT])$ for $\Delta \geq \Delta^*$ is attained by setting $\Delta = \Delta^*$ and $p = (1+\Delta^*)/2$. The required s is the solution of

$$(2.9) \qquad \left(\frac{(1-\Delta^*)}{(1+\Delta^*)}\right)^{2s} = \left\{\frac{1-P^*}{P^*}\right\}$$

It is shown in [9] that, when $P^* \to 1$, the value of s under LF can be approximated by

$$(2.10) \qquad s_m = \left[\frac{\log(1-P^*)}{2\log\left(\frac{(1-\Delta^*)}{(1+\Delta^*)}\right)}\right] + 1$$

The procedures R[DPW] and R[DVT] are compared by the expected number of trials on the poorer treatment. Defining

$$(2.11) \qquad \begin{aligned} R(n) &= E(\, N(B)/\, S(A)-S(B)=n,\ NT=A) \\ S(n) &= E(\, N(B)/\, S(A)-S(B)=n,\ NT=B) \end{aligned}$$

then $E(N(B)/R[DPW]) = \frac{1}{2}\{\, R(0)+S(0)\}$.

Under R[DPW] we obtain

$$R(n) = pR(n+1) + qS(n)$$
$$S(n) = p'S(n-1) + q'R(n) + 1 \qquad (2.12)$$

with the boundary conditions $R(r) = S(-r) = 0$.

Solving (2. 12) we obtain

$$E(N(B)/\ DPW) \quad = \quad \frac{1}{\Delta} \left\{ \frac{(p+2qr)(1-\lambda^r)\ (q'-q\lambda^r)}{2\ (q'-q\lambda^{2r})} \right\}$$

where $\lambda = p'/p$. Under R[DVT], we define

$$G(n) = E(N(B)/\ S(A)-S(B) = n \ ) \qquad (2.13)$$

we obtain therefore

$$G(n) = pq'G(n+1) + qp'G(n-1) + (pp'+qq')G(n)+1 \qquad (2.14)$$

with the boundary conditions $G(s) = G(-s) = 0$. Solving (2.14) we obtain

$$E(N(B)/R[DVT]) \quad = \quad \frac{1}{\Delta} \left\{ \frac{s(1-\delta^s)}{1+\delta^s} \right\}$$

where $\delta = p'q/\ pq'$. Further it was shown in [9] that for P^* close to 1 and Δ^* small, R[DPW] is preferable to R[DVT] when $p > \{ \frac{3}{4} - \frac{\Delta^*}{8} \}$; otherwise R[DVT] is preferred. Numerical results of E(N(B)) for different (P^*, Δ^*) combinations are given in Tables 6, 7, 8 and 9.

Sobel and Weiss [8] considered an inverse stopping rule which terminates the trials when any one population has r successes. The procedure R[ISPW] uses

PW sampling with inverse sampling as the termination rule. It was shown in [8] that

$$P(CS/R[ISPW]) = \frac{1}{2} E_r \{I_{q'}(X,r)+I_{q'}(X+1,r)\}$$

where

$$I_q(j,r) = \frac{\Gamma(j+r)}{\Gamma(j)\Gamma(r)} \int_0^q t^{j-1} (1-t)^{r-1} dt$$

and $E[f(X)]$ is the expectation of $f(X)$ where X is a (negative binomial) random variable denoting the number of failures before the r^{th} success. A normal approximation to minimum of $P(CS/R[ISPW])$ when $r \to \infty$ is given by

$$\text{Min } P(CS/R[ISPW]) \simeq \Phi\{\Delta\sqrt{\frac{27r}{8}}\} \text{ for } \Delta \geq \Delta^* \tag{2.15}$$

where $\Phi(x)$ is the standard normal c.d.f. We solve for r by putting $\Delta=\Delta^*$ in (2.15) and setting the result equal to P^*. If $\lambda = \lambda(P^*)$ denotes the solution of $\Phi(\lambda) = P^*$, then we obtain

$$r = \frac{8}{27}\{\frac{\lambda}{\Delta^*}\}^2 \tag{2.16}$$

An asymptotic ($r \to \infty$) normal approximation to $E[N(B)]$ under $R[ISPW]$ is given by

$$E(N(B)/R[ISPW]) \simeq \frac{r}{q'}\{\frac{q}{p}\Phi(y) + \frac{q'}{p'}(1-\Phi(y))\} + \frac{1}{2q'}\Phi(y) \tag{2.17}$$

where $y = \Delta\sqrt{\frac{r}{D}}$, $D = q(p')^2 + q'(p)^2$. As seen in tables 6,7,8 and 9, the inverse sampling rule requires a large number of observations on the poorer treatment when the success probabilities are small. Another procedure R[IFPW] resulting in smaller E(N(B)) when the success probabilities are small, is obtained by changing the termination rule so that the experimenter will wait for a fixed number of failures instead of successes. Under R[IFPW], one waits for r failures from each population and selects the one with most successes as being best, using randomization when there is a tie. It was shown that P(CS/R[IFPW) = P(CS/R[ISPW]) and the critical values r are given by (2.16). It was further shown, when $r \to \infty$, $E(N(B)/R[IFPW]) \simeq r/q'$. Tables 6, 7, 8 and 9 give E(N(B)) for different (P^*, Δ^*) combinations.

Hoel [3] modified R[ISPW] to obtain a truncated test, R[H], that uses PW sampling. Defining

$$R(i) = S(i)+F(j) \qquad (2.18)$$
$$R(j) = S(j)+F(i)$$

R[H] terminates the trials as soon as R(i) or R(j) is equal to r, where r is chosen such that (2.2) is satisfied. If R(i) equals r, then population i is declared to be the better one. The LF configuration was found to be

$$p = \frac{1}{2} + \frac{\Delta^*}{2} \quad , \qquad p' = \frac{1}{2} - \frac{\Delta^*}{2} .$$

Under LF, the P(CS) is given by

$$P(CS/R[H]) = E_{r-1}[\, I_{q'}(X+1,\ r-X)\ ]$$

where $E_r(X)$ denotes the expectation of the binomial random variable X with parameters r and q and $I_a(b,c)$ is the incomplete beta function. We find E(N(B)/R[H]) by defining

$$T = (r-R(A),\ r-R(B)),$$

$R(A)$, $R(B)$ as in (2.18)

$$R(m,n) = E[N(B)/\ T=(m,n),\ NT=A]$$

$$S(m,n) = E[N(B)/\ T=(m,n),\ NT=B]$$

Under R[H] we obtain

$$R(m,n) = p\ R(m-1,n) + q\ S(m,n-1)$$

(2.19)

$$S(m,n) = p'S(m,n-1) + q'R(m-1,n) + 1$$

with boundary conditions $R(0,n) = S(n,0) = 0$ for $n > 0$.

Then $E[N(B)/R[H]\ ] = [\ R(r,r) + S(r,r)\ ] / 2.$

An explicit solution to (2.19) is found in [3]. Tables 6, 7, 8 and 9 show that R[H] has a larger expected sample size on population B than R[ISPW] whenever $\frac{(p+p')}{2} > \frac{1}{2}$, while when $\frac{(p+p')}{2} \leq 0.5$, R[H] is preferable to R[ISPW].

Another truncated procedure in which the maximum number of tests was specified was discussed by Kiefer and Weiss [6]. This procedure uses VT sampling. After each pair of populations is sampled, one calculates $\Delta S = S(i)-S(j)$. If at any test $t < N$ (the maximum number of tests) we have $\Delta S = s$, then we terminate, calling the population with the greater number of successes the better population. If no decision is made within the N test pairs, the populations are held to be essentially of equal value. In this truncated version the experimenter can use the parameter N as follows:

(a) Fix N and determine s so that P(CS) is maximum.

(b) Choose the smallest N consistent with (2.2).

(c) Require, in addition to (2.2), that the probability of a decision of equality be $\geq P_1^*$ when $p = p'$.

The authors were not successful in deriving an exact expression for the expected number of trials to reach a decision. Values of s that maximize P(CS) for fixed Δ^* and N are given in [6].

Hoel, Sobel and Weiss [4] discussed a two-stage sampling procedure. In the first stage N tests are conducted on each population. The type of sampling to be used in the second stage was based on a critical parameter k ; PW sampling was used in the second stage if the maximum of the number of successes in the first stage was $\geq k$; otherwise vector-at-a-time sampling (VT)

was used. The terminal decision rule was based on the difference in the successes on both populations. Expected sample sizes on the poorer population for different (P^*, Δ^*) combinations are given in chapter IV. It was shown that the two-stage procedure resulted in substantial savings on the expected samples on the poorer population compared to R[DVT] whenever $p > 0.6$. We denote this procedure by R[DTS].

Nebenzahl and Sobel [7] investigated the selection problem for fixed sample size case. The procedure R[FSPW] uses PW sampling while R[FSVT] uses VT sampling. R[FSVT] forces the sample size to be an even number. The same

Table 1.

Comparison of R[FSPW] and R[FSVT] for the pair

$(p,p') = (0.5 + 0.5\ \Delta^* , 0.5 - 0.5\ \Delta^*)$

P^*	$\Delta^* = 0.1$			$\Delta^* = 0.2$		
	N	{E(N(B)/ R[FSVT]}	{E(N(B)/ R[FSPW]}	N	{E(N(B)/ R[FSVT]}	{E(N(B)/ R[FSPW]}
0.990	540	270	243.0	134	67	53.6
0.975	384	192	172.8	96	48	38.4
0.950	270	135	121.5	68	34	27.2

terminal decision rule is used for both procedures,namely to select the population with most successes and to randomise when we get equality in the number of successes. The fixed sample size N for both procedures is determined so that (2.2) is satisfied. Table 1 gives N needed under R[FSPW] and E[N(B)] under R[FSPW] and R[FSVT] for different (P^*, Δ^*) combinations.

Another procedure R[IT] due to Berry and Sobel [2] modifies the inverse sampling procedure R[ISPW] by terminating the trials either after c failures on each population or when there are r successes on any population, whichever occurs sooner. In either case the population with the larger number of successes is selected. The E[N(B)] when r = c is given in tables 6, 7 and 8.

CHAPTER III

A TRUNCATED PROCEDURE FOR CHOOSING THE BETTER OF TWO BINOMIAL POPULATIONS

The different procedures discussed earlier are distinguished by the sampling and termination rules. The termination rule was specified by a decision function, defined by the current number of successes and/or failures on either or both populations, and a critical value r, a preassigned constant chosen to satisfy (2.2). In this chapter we analyse a truncated procedure using PW sampling, in which a maximum number of tests on each population is specified.

Consider two bernoulli populations, one having probability of success p on a single trial and probability of failure $q = 1 - p$; denote it by A; the other is B with parameters p' $(p > p')$ and $q' = 1 - p'$ .The parameters p and p' are both unknown and our sampling and termination rule will not depend on the knowledge of which population is A. At the outset one of the two populations is chosen at random. Procedure R[DPPW] uses the PW sampling with the selection based on the difference in the proportion of successes at termination. Before the trials are started, the maximum number of tests, N, on each population

and c, the critical parameter are specified. Using the notation in chapter II, the procedure R[DPPW] has the following stopping rule: sampling is terminated whenever either population has been sampled completely or when

$$(3.1) \qquad \left| \frac{S(A)}{N(A)} - \frac{S(B)}{N(B)} \right| \geq \frac{c}{F(A)+F(B)}$$

whichever is earlier, where the constants (N,c) are chosen to be the smallest integers satisfying the condition

$$(3.2) \quad P(CS/R[DPPW]) \geq P^* \quad \text{whenever} \quad \Delta \geq \Delta^*$$

for preassigned constants (P^*, Δ^*) satisfying (2.2). The population with the larger proportion of successes at termination is declared as the better. This procedure is truncated, since at most 2N-1 trials will be required. The results of the total sample size required for the fixed sample size binomial selection procedure R[FSPW] given in Table 2 were used as follows to specify (N,c). For any specified (P^*, Δ^*) combination, N was taken to be slightly greater than half the total samnle in the fixed sample procedure with

$$(3.3) \qquad P(CS/R[DPPW]) \geq P^* \quad \text{when} \quad \Delta = \Delta^*$$

Then, for this N, the smallest integer c satisfying (3.3) was found; then,for this value of c, the smallest

N satisfying (3.3) was found. The combination (N,c) found thus was taken to be the final choice of (N,c).

Table 2

Total Samples N required under R[FSPW]

Δ^* \ P^*	.99	.975	.95	.90	.85	.80	.75
.1	540	384	270	164	108	71	46
.2	134	96	68	41	27	18	12

The expected sample sizes on the poorer population, when the population probability of successes are small, are considerably reduced by this procedure.

To calculate P(CS/R[DPPW]), let

NT=A(NT=B) denote the next trial is on population A(B).

T = (m,n,a,b) where

m = N - N(A)

n = N - N(B)

a = number of failures on A

(3.4)

b = number of failures on B

Define

$$U(m,n,a,b) = P(CS/\ T=(m,n,a,b),\ NT=A)$$

(3.5)

$$V(m,n,a,b) = P(CS/\ T=(m,n,a,b),\ NT=B)$$

Using PW sampling and using [(3.4),(3.5)] we obtain

for the procedure R[DPPW],

$$
\begin{aligned}
U(m,n,a,b) &= p\,U(m-1,n,a,b) + q\,V(m-1,n,a+1,b) \\
V(m,n,a,b) &= p'V(m,n-1,a,b) + q'U(m,n-1,a,b+1)
\end{aligned}
\tag{3.6}
$$

and the boundary conditions are

(a) $U(0,0,a,b) = 0$

$V(0,0,a,b) = 0 \qquad$ for $a,b \geq 0$

(b)
$$
U(0,n,a,b) \begin{cases} = 1 \text{ if } b = a \text{ or } a+1,\ n \neq N, b \neq 0 \\ = 1 \text{ if } b = 0,\ a = 0,\ n = N \\ = 0 \text{ if } b > N-n \end{cases}
$$

(c)
$$
V(0,n,a,b) \begin{cases} = 1 \text{ if } b = a \text{ or } a-1,\ n \neq N,\ b \neq 0 \\ = 1 \text{ if } b = 0,\ a = 1,\ n = N \\ = 0 \text{ if } b > N-n \end{cases}
$$

(d) $U(m,0,a,b) = 0$

$V(m,0,a,b) = 0 \qquad$ for $m,a,b > 0$

(e) $U(m,N,a,b) = 0 \qquad$ for $b > 0$

$V(N,n,a,b) = 0 \qquad$ for $a > 0$

(f) $U(m,n,a,b) = 1$, $V(m,n,a,b) = 1$ when $\left| \dfrac{S(A)}{N(A)} - \dfrac{S(B)}{N(B)} \right| \geq \dfrac{c}{a+b}$

for all m,n,a,b $m \neq 0$, $n \neq 0$

(3.7)

(g) $0 \le a \le N,\ 0 \le b \le N,\quad |a-b| \le 1$

The first treatment at the outset is chosen at random and hence P(CS) at termination is given by

(3.8) $P(CS/R[DPPW]) = \frac{1}{2}\left[U(N,N,0,0)+V(N,N,0,0)\right]$

An analytical solution to (3.6) with the boundary conditions(3.7) is quite complicated. We used the IBM 360 computer to numerically evaluate the P(CS/R[DPPW]) when N and c are specified. Several computations using program A (appendix) were made to find the value of c and LF configuration for preassigned (N, Δ^*, P^*) and the results are summarized below.

Table 3.

The Least Value of c for R[DPPW] satisfying (P^*, Δ^*) probability requirement for specified N

(P^*, Δ^*)	N	c	LF(p,p')
(.90,.2)	24	4	(.57,.37)
(.95,.2)	39	5	(.55,.35)
(.99,.2)	72	8	(.55,.35)
(.90,.1)	89	8	(.50,.40)

The performance of R[DPPW] was evaluated by comparing the expected number of observations on the population B

with other procedures mentioned in chapter II. For this we define

$$(3.9)\quad R(m,n,a,b) = E(N[B]/\ T=(m,n.a.b),\ NT=A)$$
$$S(m,n,a,b) = E(N[B]/\ T=(m,n,a,b).\ NT=B)$$

Using PW for R[DPPW] we obtain

$$(3.10)\quad R(m,n,a,b) = p\ R(m-1,n,a,b) + q\ S(m-1,n,a+1,b)$$
$$S(m,n,a,b) = p'S(m,n-1,a,b) + q'R(m,n-1,a,b+1) + 1$$

and the boundary conditions are

$$(a)\quad R(0,0,a,b) = 0$$
$$S(0,0,a,b) = 0 \quad \text{for } a,b \geq 0$$

$$(b)\quad R(0,n,a,b) \begin{cases} = 0 \text{ if } b=a \text{ or } a+1, n\neq N, b\neq 0 \\ = 0 \text{ if } b=0,\ a=0,\ n=N \\ = 0 \text{ if } b > N-n \end{cases}$$

$$(c)\quad S(0,n,a,b) \begin{cases} = 0 \text{ if } b=a \text{ or } a-1, n\neq N, b\neq 0 \\ = 0 \text{ if } b=0,\ a=1,\ n=N \\ = 0 \text{ if } b > N-n \end{cases}$$

$$(d)\quad R(m,o,a,b) = 0$$
$$S(m,0,a,b) = 0 \quad \text{for } m,a,b > 0$$

$$(e)\quad R(m,N,a,b) = 0 \quad \text{for } b > 0$$
$$S(m,N,a,b) = 0 \quad \text{for } a > 0$$

$$(f)\quad \left.\begin{aligned} R(m,n,a,b) &= 0 \\ S(m,n,a,b) &= 0 \end{aligned}\right\} \quad \text{when } \left|\frac{S(A)}{N(A)} - \frac{S(B)}{N(B)}\right| \geq \frac{c}{a+b}$$

(3.11)

(g) $0 \le a \le N, \quad 0 \le b \le N, |a-b| \le 1$

Solving (3.10) subject to (3.11), we obtain

$$E(N(B)/R[DPPW]) = \frac{1}{2}\{R(N,N,0,0)+S(N,N,0,0)\}$$

Program B (appendix) was used to evaluate $E(N(B)/R[DPPW])$ for different (P^*, Δ^*) combinations and the results are summarized below:

Table 4

Expected Number of observations under R[DPPW]

E[N(B)] : Expected number of observations on population B.

E[N] : Expected total number of observations.

(P^*,Δ^*)	(.90, .2)[a]		(.95, .2)[b]		(.99, .2)[c]		(.90, .1)[d]
$\frac{p+p'}{2}$ \ Δ	.2	0	.2	0	.2	0	.1
	E[N(B)]	E[N]	E[N(B)]	E[N]	E[N(B)]	E[N]	E[N(B)]
0.1	12.1	40.2	14.3	62.0	22.1	123.0	43.5
0.2	11.5	34.2	15.2	54.0	24.9	109.8	43.6
0.3	11.6	32.8	15.7	51.4	26.1	107.0	44.8
0.4	12.0	33.6	16.8	53.4	28.8	111.2	48.2
0.5	12.6	35.4	18.3	57.6	32.2	118.8	53.4
0.6	12.8	37.4	19.5	62.4	35.4	125.2	58.9
0.7	11.9	38.4	18.8	65.2	34.8	128.6	60.9
0.8	9.0	38.0	14.1	64.8	25.2	126.2	54.1
0.9	2.5	35.2	2.5	60.6	2.5	119.2	32.5

a. $(N,c)=(24,4)$ required for $P^*=.90$ and $\Delta^*=.2$

b. $(N,c)=(39,5)$ required for $P^*=.95$ and $\Delta^*=.2$

c. $(N,c)=(72,8)$ required for $P^*=.99$ and $\Delta^*=.2$

d. $(N,c)=(89,8)$ required for $P^*=.90$ and $\Delta^*=.1$

Consider the procedure R[MDPPW] obtained by modifying the stopping rule of R[DPPW]. The procedure R[MDPPW] uses PW rule and sampling is terminated whenever either population is sampled completely or when

$$\left| \frac{S(A)}{N(A)} - \frac{S(B)}{N(B)} \right| \geq \frac{c}{F(A)+F(B)} - \left[\frac{S(A)+S(B)}{N} \right]$$

where [.] denotes " largest integer contained in". It was verified numerically when c=5, N=38, the P(CS/R[MDPPW]) to be at least .95 whenever $p - p' \geq .2$. The LF configuration is given by $(p,p') = (.52, .32)$ and the expected sample size on the poorer population (B) is summarised in Table 5. The computations were made using program A and program B listed in the appendix.

It should be noted that R[MDPPW] attains 0.95 probability of correct selection with a smaller N and

Table 5.

Comparison of E(N(B) for the procedures R[DPPW] and R[MDPPW] for $(P^*,\Delta^*) = (.95,.2)$

$\Delta = \Delta^* = .2$		
$\frac{p+p'}{2}$	E(N(B)/R[DPPW] N = 39	E(N(B)/R[MDPPW] n = 38
0.1	14.3	14.3
0.2	15.2	15.2
0.3	15.7	15.7
0.4	16.8	16.7
0.5	18.3	18.0
0.6	19.5	18.2
0.7	18.8	16.2
0.8	14.1	12.0
0.9	2.5	2.5

performs uniformly better than R[DPPW]. The procedure R[MDPPW] has not been investigated thoroughly. In the next chapter, we discuss the unsolved problems regarding R[DPPW]. The performance of R[DPPW] with R[ISPW], R[IFPW],R[DPW],R[DVT],R[H],R[DTS] and R[DT]discussed earlier.

CHAPTER IV

COMPARISON OF R[DPPW] WITH OTHER PROCEDURES

Procedure R is said to be uniformly better than procedure R' if $E[N(B)/R] < E[N(B)/R']$. In this chapter we use this criterion to compare the different procedures described in the previous chapters. Later we state some open questions concerning the procedure R[DPPW] and some open problems in selecting better of two binomial populations.

R[DPPW] is a truncated sampling procedure with the selection based on the difference in the proportion of successes at termination. Tables 6, 7, 8 and 9 give the expected number of observations on the poorer population for various procedures. Let $\bar{p} = (p+p')/2$.

Table 6.

Expected number of observations on the poorer population.

$P^* = .95$ $\Delta = \Delta^* = .2$

$\bar{p}$	R[ISPW] r=20.042	R[IFPW] r=20.042	R[DPW] r=11	R[DVT] s=4	R[H] r=33.4	R[DTS] N=5,k=3	R[DPPW] N=39 c=5	R[IT] r=c=20.24
0.1	80.7	20.0	44.5	20.0	26.8	20.4	14.3	20.2
0.2	52.5	22.3	39.3	19.8	26.1	21.0	15.2	22.5
0.3	38.1	25.1	34.0	19.2	25.2	21.5	15.7	24.9
0.4	29.1	28.6	28.6	18.9	24.1	21.2	16.8	25.7
0.5	22.8	33.4	23.1	18.4	22.6	19.5	18.3	22.7
0.6	17.8	40.1	17.6	18.9	20.5	16.5	19.5	18.0
0.7	13.4	50.1	11.9	19.2	17.5	13.0	18.8	13.6
0.8	8.8	66.8	7.1	19.8	12.5	9.4	14.1	8.9
0.9	2.5	100.2	2.3	20.0	2.5	5.7	2.5	2.5

Table 7.

Expected number of observations on the poorer population.

$P^* = .99 \quad \Delta = \Delta^* = .2$

$\bar{p}$	R[ISPW] r=40	R[IFPW] r=40	R[DPW] r=18	R[DVT] s=6	R[H] r=67	R[DTS] N=5,k=3	R[DPPW] N=72,c=8	R[IT] r=c=40 .05
0.1	160.5	40.0	72.5	30.0	53.7	-	22.1	40.0
0.2	104.3	44.4	63.8	30.0	52.3	31.2	24.1	44.5
0.3	75.6	50.0	55.0	29.8	50.1	33.1	26.1	50.0
0.4	57.8	57.1	46.3	29.6	48.2	35.2	28.8	52.4
0.5	45.2	66.7	37.5	29.5	45.1	35.4	32.2	45.3
0.6	35.2	80.0	28.7	29.6	40.9	32.6	35.4	35.2
0.7	26.2	100.0	19.8	29.8	34.5	27.1	34.8	26.2
0.8	16.4	133.3	11.1	30.0	23.9	20.2	25.2	16.5
0.9	2.5	200.0	2.5	30.0	2.5	13.1	2.5	2.5

Table 8.

Expected number of observations on the poorer population.

$P^* = .90$ $\Delta = \Delta^* = .2$

p	R[ISPW] r=12.167	R[IFPW] r=12.167	R[DPW] r=8	R[H] r=21	R[DPPW] N=24 c=4	R[DVT] s=3	R[IT] r=c=12.47
0.1	48.5	12.2	32.5	16.9	12.1	15.0	12.5
0.2	31.7	13.5	28.8	16.4	11.5	14.4	13.8
0.3	23.0	15.2	24.8	15.8	11.6	13.6	15.1
0.4	17.5	17.4	20.6	15.1	12.0	12.8	15.3
0.5	13.7	20.3	16.4	14.2	12.6	12.5	13.7
0.6	10.7	24.3	12.3	12.9	12.8	12.8	11.1
0.7	8.2	30.4	8.6	11.1	11.9	13.6	8.5
0.8	5.6	40.6	5.2	8.2	9.0	14.4	5.8
0.9	2.3	60.8	2.1	2.5	2.5	15.0	2.3

Table 9.

Expected number of observations on the poorer population.

$p^* = .90 \qquad \Delta = \Delta^* = .1$

$\bar{p}$	R[ISPW] r=49	R[IFPW] r=49	R[DPW] r=16	R[DVT] s=6	R[H] r=82	R[DPPW] N=89 c=8
0.1	292.8	51.6	136.8	59.9	73.4	43.5
0.2	174.1	57.7	121.2	57.4	72.3	43.6
0.3	124.0	65.3	104.8	53.6	71.0	44.9
0.4	95.7	75.4	87.3	51.0	69.2	48.2
0.5	76.8	89.1	69.5	50.1	67.0	53.4
0.6	62.6	108.9	52.4	51.0	63.8	58.9
0.7	51.4	140.0	36.7	53.6	59.0	60.9
0.8	39.1	196.0	22.7	57.4	50.3	54.1
0.9	22.2	326.7	10.1	59.9	30.3	32.6

Table 10.

Expected number of observations on the poorer population: $(P^*, \Delta^*) = (.95, .2)$

$\Delta > \Delta^*$

$\bar{p}$	Δ	R[H] r=34	R[DPW] r=11	R[DVT] s=4	R[DPPW] N=39 c=5
0.25	0.3	22.9	22.7	13.3	10.6
0.50	0.3	18.8	13.9	13.1	13.1
0.75	0.3	9.6	5.1	13.3	10.4
0.30	0.4	19.2	14.4	10.0	8.0
0.50	0.4	15.1	9.1	10.0	9.6
0.70	0.4	7.7	3.9	10.0	8.0

The following conclusions are made from the numerical results in Tables 6,7,8 and 9.

(a) We observe that whenever $\bar{p} < 0.5$, the procedure R[DPPW] is uniformly better than any other procedure currently known; R[DPPW] results in a substantial (more than 25%) savings in the expected number of observations on the poorer population.

(b) We conclude that for $\bar{p} > 0.7$, R[DPW] is uniformly better than any other procedure.

(c) When $0.5 \leq \bar{p} \leq 0.7$, none of the procedures is uniformly better. However, if the experimenter knows apriori that $\bar{p} = 0.6$, then for $P^* = 0.90$, $\Delta = \Delta^* = 0.2$, R[DTS] is recommended.

Table 10 gives the expected number of observations on the poorer population when $\Delta \geq \Delta^*$. The performance of R[DPPW] is compared with R[H], R[DPW] and R[DVT]. As expected for $\bar{p} < 0.5$, the performance of R[DPPW] is better than any other procedure.

The better performance of R[DPPW], when $\bar{p}$ is small, can be intutively justified for the following reasons. Since the maximum sample size, N, is specified in advance R[DPPW] prevents unduly long continuation of trials. The critical value, $\frac{c}{F(A)+F(B)}$, is based on the critical

parameter,c, and the total number of failures at each stage. The critical value decreases whenever a failure occurs, which is contrary to the constant critical value specified by the other procedures. If $p < 0.5$, the result is frequent occurence of failures, and termination will occur when the difference in the sample proportion of successes exceeds the gradually decreasing critical value when N is large. However if N is small, we terminate the trials by sampling either population completely. In either case, we expect R[DPPW] to terminate the trials quicker than other procedures, due to the decreasing characteristic of the critical value. Consequently, we expect R[DPPW] to discontinue sampling with a smaller total number of failures. The procedure is specified such that fewer failures are needed to distinguish a large difference in the sample proportion of successes.For example when $P^*=0.95$, c=5 and $\Delta = \Delta^* = 0.2$, R[DPPW] requires only 13(26) failures to terminate the trials when the difference in the sample proportion of successes is 0.2(0.1). Further the critical parameter prevents us from terminating trials at a very early stage, thereby reducing the probability of making a wrong selection by chance at a very early stage. If $p > 0.5$ the result is frequent occurence of successes and the critical value does not decrease quickly and hence we terminate the trials by sampling either population completely.

Consequently, in this situation the performance of R[DPPW] is not better than some procedures.

The principal shortcomings of the procedures described above are the assumptions of dichotomous and instantaneous response to treatment. So far, no analogue has been proposed for the continuous case in which the response is continuous - a very important consideration in testing anti-cancer treatments for which a natural measure of effectiveness is life time. Further this problem has not been analysed when the response is at some random time after the administration of the treatment. The selection problem under the present formulation has not been studied when several patients are assigned to any treatment at each stage. In fact, any enumeration of practical difficulties associated with clinical trials is a good source for future investigation. Most of the stopping rules excepting the inverse sampling lead to mathematical difficulties.

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Appendix
Program A

```
      DIMENSION U(66,66,3),U1(66,66,3),V(66,66,3),V1(66,66,3)
C     THIS PROGRAM CALCULATES THE PROBABILITY OF CORRECT
C     SELECTION. IN THIS PROGRAM
C              MP1=(M+1)
C              NP1=(N+1)
C              IFAP1=A+1(#FAILURES ON POPULATION A + 1)
C              IFBP1=B+1(#FAILURES ON POPULATION B + 1)
C           IFAPFB= TOTAL NUMBER OF FAILURES
C      WHERE (M,N,A,B) ARE DEFINED BY (3.4). P(P1) IS THE
C      PROBABILITY OF SUCCESS IN A SINGLE TRIAL ON POPULATION
C      A(B).  DEL IS THE DIFFERENCE IN SUCCESS PROBABILITIES.
C      IR IS THE MAXIMUM SAMPLE SIZE ON EACH POPULATION,
C      THE PROBABILITY OF CORRECT SELECTION IS GIVEN BY (3.8).
C       FOR THIS WE CALCULATE U(N,N,0,0) AND V(N,N,0,0).
C      FIRST WE FIX MP1; AND THEN ALLOW NP1 TO VARY. NOW FOR
C      FIXED NP1, WE LET IFAP1 TO VARY; SINCE PW SAMPLING IS
C      IS USED IFAP1 AND IFBP1 DIFFER BY AT MOST 1. IFBP1 IS
C      DEFINED IN TERMS OF J3 WHERE J3=IFBP1-IFAP1+2.
C      IN THIS PROGRAM EACH U(M,N,A,B) AND V(M,N,A,B) IS
C      ASSOCIATED WITH A PARTICULAR VALUE OF MP1 AND
C      U(NP1,IFAP1,J3) AND V(NP1,IFAP1,J3) RESPECTIVELY;
C      BY FIXING MP1 FIRST, WE NEED TO USE ONLY THREE DIMENSIONS
C      IN THE PROGRAM, THEREBY MAKING A SUBSTANTIAL SAVING OF
C       VIRTUAL MEMORY STORAGE. THE VALUE OF U(M-1,N,A,B)
C      NEEDED FOR CALCUATING U(M,N,A,B) IS STORED BY SETTING
C      U1(NP1,IFAP1,J3) = U(NP1,IFAP1,J3).
C      WE FIRST LET U(M,N,A,B)=0, V(M,N,A,B)=0; LATER WE
C      CHECK THE BOUNDARY CONDITIONS AND TERMINATION
C      CRITERION.
C        IF REQUIRED, U(M,N,A,B) AND V(M,N,A,B) ARE CALCUALTED
C     BY USING THE DIFFERENCE EQUATIONS.
999   READ(5,14) P,DEL,IR
14    FORMAT(F10.6/F10.6/I2)
      Q=1.-P
```

```
      Q1=1.-P1
      IRP1=IR+1
      DO 15 MP1=1,IRP1
      DO 15 NP1=1,IRP1
      NAP1=IR+2.-MP1
      DO 15 IFAP1=1,NAP1
      NBP1=IR+2-NP1
C      WHEN J3=1, A=B+1; WHEN J3=2, A=B;  WHEN J3=3, B=A+1.
      DO 15 J3=1,3
      IFBP1=IFAP1+J3-2
      U(NP1,IFAP1,J3)=0
      V(NP1,IFAP1,J3)=0
C     WE CHECK THE BOUNDARY CONDITIONS AND TERMINATION
C     CRITERION
      IF(MP1.NE.1) GO TO 44
C     MP1=NP1=1 MEANS THAT BOTH THE POPULATIONS ARE SIMULTANEOUSLY
C     SAMPLED COMPLETELY, WHICH IS NOT POSSIBLE IN PW SAMPLING.
      IF(NP1.EQ.1)GO TO 16
C     NUMBER OF FAILURES ON POPULATION B CANNOT EXCEED THE NUMBER
C     TRIALS ON THAT POPULATION.
      IF(IFBP1.GT.NBP1) GO TO 16
C     J3=1 MEANS A=B+1; THE NUMBER OF FAILURES ON POPULATION B
C     IS ONE LESS THAN THE NUMBER OF FAILURES ON POPULATION A.
C     SINCE THE NUMBER OF FAILURES IN PW SAMPLING DIFFER BY
C     AT MOST 1, THE NEXT TRIAL CANNOT BE ON POPULATION A.
      IF(J3.EQ.1) GO TO 18
      IF(NP1.EQ.IRP1) GO TO 20
      IF(IFBP1.EQ.1) GO TO 18
20    U(NP1,IFAP1,J3)=1
18    IF(IFAP1.EQ.1) GO TO 16
C     WHEN J3=3, B=A+1; SINCE THE NUMBER OF FAILURES IN PW SAMPLING
C     DIFFER BY AT MOST 1, THE NEXT TRIAL CANNOT BE ON POPULATION B.
      IF(J3.EQ.3) GO TO 16
      IF(NP1.EQ.IRP1) GO TO 21
      IF( IFBP1.EQ.1) GO TO 16
21    V(NP1,IFAP1,J3) =1
      GO TO 16
```

```
44    IF(IFBP1.GT.NBP1) GO TO 16
      IF(NP1.EQ.1) GO TO 16
C     IFAPFB DENOTES THE TOTAL NUMBER OF FAILURES.
      IFAPFB=IFAP1+IFBP1-2.
      IF(IFAPFB.LE.1) GO TO 24
C     RULE IS BASED ON THE TOTAL NUMBER OF FAILURES AND THE CRITICAL
C     PARAMETER C; IT SPECIFIES THE CUTOFF POINT FOR THE TERMINATION
C     CRITERION.
      RULE=5./IFAPFB
C      DIFPRO IS THE DIFFERENCE IN THE PROPORTION OF SUCCESSES.
      DIFPRO=((IFBP1-1.)/(NBP1-1))-((IFAP1-1.)/(NAP1-1))
      DIFNEG=-DIFPRO
24    IF(J3.EQ.1) GO TO 23
      IF(NP1.EQ.IRP1) GO TO 26
      IF(IFAPFB.LE.1) GO TO 26
C      WE TERMINATE AND MAKE THE CORRECT SELECTION IF
C      THE DIFFERENCE IN THE PROPORTION OF SUCCESSES
C      IS GREATER THAN OR EQUAL TO THE CRITICAL VALUE
C      (RULE); OTHERWISE P(CS/T=(M,N,A,B) IS CALCULATED
C      BY USING THE DIFFERENCE EQUATIONS.
      IF(DIFPRO.LT.RULE) GO TO 31
      U(NP1,IFAP1,J3)=1
      GO TO 23
C     WE TERMINATE AND MAKE A CORRECT SELECTION IF DIFNEG IS LESS
C     IS LESS THAN OR EQUAL TO RULE.
31    IF(DIFNEG.GT.RULE) GO TO 23
C       CALCULATING P(CS/T=(M,N,A,B) NT=A) BY  USING THE DIFFERENCE EQUATION.
26    U(NP1,IFAP1,J3)=P*U1(NP1,IFAP1,J3) +Q*V1(NP1,IFAP1+1,J3-1)
      IF(U(NP1,IFAP1,J3).LT.10E-10) U(NP1,IFAP1,J3)=0
23    IF(J3.EQ.3) GO TO 16
      IF(NP1.EQ.IRP1) GO TO 27
      IF(IFAP1.EQ.1) GO TO 16
      IF(IFAPFB.LE.1) GO TO 27
      IF(DIFPRO.LT.RULE) GO TO 33
      V(NP1,IFAP1,J3)=1
      GO TO 16
C     CHECKING THE DIFFERENCE OF PROPORTION CONDITION.
```

```
33    IF(DIFNEG.GT.RULE) GO TO 16
C       CALCULATING P(CS/T=(M,N,A,B) NT=B) BY  USING THE DIFFERENCE EQUATION.
27    V(NP1,IFAP1,J3)=P1*V1(NP1-1,IFAP1,J3)+Q1*U1(NP1-1,IFAP1,J3+1)
      IF(V(NP1,IFAP1,J3).LT.10E-10) V(NP1,IFAP1,J3)=0
C     VALUE OF U(M-1,N-1,A,B) IS STORED FOR CALCULATING
C      U(M,N,A,B) BY SETTING U1(NP1,IFAP1,J3)=U(NP1,IFAP1,J3)
16    U1(NP1,IFAP1,J3)=U(NP1,IFAP1,J3)
      V1(NP1,IFAP1,J3)=V(NP1,IFAP1,J3)
15    CONTINUE
C      CALCULATION OF PROBABILITY OF CORRECT SELECTION.
      PCS=(U1(IRP1,1,2)+V1(IRP1,1,2))/2
      WRITE(5,210) IR,U1(IRP1,1,2),V1(IRP1,1,2),PCS
210   FORMAT(' ','MAXIMUM SAMPLE SIZE',I5,2X,'U =',F12.6,
      G2X,'V=',F12.6,'PROBABILITY CORRECT SELECTION',F12.6)
998   CONTINUE
      STOP
      END
```

Program B

```
      DIMENSION R(73,73,3),R1(73,73,3),S(73,73,3),S1(73,73,3)
C     THIS PROGRAM CALCULATES THE EXPECTED NUMBER OF
C     PATIENTS ON THE POORER TREATMENT. IR DENOTES THE
C     MAXIMUM SAMPLE SIZE AND DEL DENOTES THE DIFFERENCE
C     IN SUCCESS PROBABILITIES.
C     THE NOTATIONS AND STRUCTURE OF THIS PROGRAM ARE IDENTICAL
C     TO PROGRAM A. THE BOUNDARY CONDITIONS ARE GIVEN BY (3.11).
999   READ(5,14) P,DEL,IR
14    FORMAT(F10.6/F10.6/I2)
522   FORMAT('0',T45,'MAXIMUM SAMPLE SIZE',T70,I3)
      PRINT522,IR
888   Q=1.-P
      P1=P-DEL
      Q1=1.-P1
      IRP1=IR+1
      DO 15 MP1=1,IRP1
      DO 15 NP1=1,IRP1
      NAP1=IR+2.-MP1
      DO 15 IFAP1=1,NAP1
      NBP1=IR+2-NP1
      DO 15 J3=1,3
      IFBP1=IFAP1+J3-2
      R(NP1,IFAP1,J3)=0.
      S(NP1,IFAP1,J3)=0.
      IF((IFAP1.EQ.1).AND.(J3.EQ.1)) GO TO 16
      IF(MP1.EQ.1)  GO TO 16
19    IF(NP1.EQ.1)  GO TO 16
      IF(IFBP1.GT.NBP1) GO TO 16
      IF(MP1.EQ.IRP1)  GO TO 44
      IF(NP1.EQ.IRP1) GO TO 44
      IF(IFAP1.NE.1)  GO TO 44
      IF(IFBP1.EQ.IFAP1)  GO TO 16
44    IF(IFBP1.GT.NBP1) GO TO 16
      IFAPFB=IFAP1+IFBP1-2.
      IF(IFAPFB.LE.1) GO TO 24
```

```
      RULE = 8./IFAPFB
      DIFPRO=((IFBP1-1.)/(NBP1-1))-((IFAP1-1.)/(NAP1-1))
      DIFNEG=-DIFPRO
24    IF(J3.EQ.1) GO TO 23
      IF(NP1.EQ.IRP1) GO TO 26
      IF(IFBP1.EQ.1) GO TO 23
      IF(IFAPFB.LE.1) GO TO 26
      IF(DIFPRO.LT.RULE) GO TO 31
      R(NP1,IFAP1,J3)=0.
      GO TO 23
31    IF(DIFNEG.GT.RULE) GO TO 23
26    R(NP1,IFAP1,J3)=P*R1(NP1,IFAP1,J3)+Q*S1(NP1,IFAP1+1,J3-1)
      IF(R(NP1,IFAP1,J3).LT.10E-10) R(NP1,IFAP1,J3)=0.
23    IF(J3.EQ.3) GO TO 16
      IF(MP1.EQ.IRP1) GO TO 27
      IF(IFAP1.EQ.1) GO TO 16
      IF(IFAPFB.LE.1) GO TO 27
      IF(DIFPRO.LT.RULE) GO TO 33
      S(NP1,IFAP1,J3)=0.
      GO TO 16
33    IF(DIFNEG.GT.RULE) GO TO 16
27    S(NP1,IFAP1,J3)=P1*S1(NP1-1,IFAP1,J3) +
     H       Q1*R1(NP1-1,IFAP1,J3+1) + 1.
      IF(S(NP1,IFAP1,J3).LT.10E-10) S(NP1,IFAP1,J3)=0.
16    R1(NP1,IFAP1,J3)=R(NP1,IFAP1,J3)
      S1(NP1,IFAP1,J3)=S(NP1,IFAP1,J3)
15    CONTINUE
C     ENB GIVES THE EXPECTED NUMBER OF OBSERVATIONS ON THE
C     POORER TREATMENT.
      ENB=(R1(IRP1,1,2)+S1(IRP1,1,2))/2.
      P3=(P+P1)/2.
      WRITE(5,210) P3,ENB
210   FORMAT('0',T52,F8.4,T72,F12.6)
      STOP
      END
```