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OPTIMUM DESIGNS FOR SELECTING ONE OF TWO TREATMENTS, FIXED SAMPLE SIZE PLAN 6 AND SEQUENTIAL PLAN 3

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Introduction

Our present question is how it is possible to design an optimum clinical trial when a group of patients with a disease are to be treated with one of the two medical treatments of which the efficacious proportions are both unknown to us in this paper (, though only one of the two proportions was unknown to us in our previous papers [6], [7]).

In this paper, the case of the two binomial populations of which the population proportions are both unknown to us will be investigated.

We shall say that an individual (i.e., a patient) is effective for the treatment if he has the preassigned responses by the administration of a treatment. We want to compare the effectiveness of the two medical treatments (denoted by A and B) in the stage of a clinical trial where the effectiveness of each treatment may be measured in terms of the proportion of the effective individuals.

Let $\mathfrak{p}_A$ be the proportion of the effectiveness if treatment A is performed, and $\mathfrak{p}_B$ the proportion of the effectiveness if treatment B is performed, where the values of $\mathfrak{p}_A$ and $\mathfrak{p}_B$ are unknown to us. In other words, $\mathfrak{p}_A$ is the probability by which any one patient treated will be effective if treatment A is performed, and $\mathfrak{p}_B$ is the probability by which any one patient treated will be effective if treatment B is perfomed. We want to select treatment A if $\mathfrak{p}_A>\mathfrak{p}_B$, treatment B if $\mathfrak{p}_A<\mathfrak{p}_B$.

In the first place, the fixed sample size plan will be discussed in Part I. Namely, a clinical trial will be performed on $2n$ of all the patients, on n each of the two treatments, and both efficacious proportions $\mathfrak{p}_A$ and $\mathfrak{p}_B$ of the considered two treatments will be compared by observing the numbers of the effective patients in each group of n individuals. Thus, the treatment that was selected as the better at the conclusion of the abovementioned clinical trial will be performed on the remaining all patients.

As discussed in our previous paper [6], we are concerned to determine the optimum value of a parameter (i.e., a sample size or a sampling proportion for the considered clinical trial) so that the loss based on the consequences of right and wrong decisions is minimized, or the gain maximized, where "the loss" and "the gain" were defined in the previous papers [4]~[8].

Latter in this Part, the optimum values of the sample size and the minimized values of the overall expected loss will be numerically evaluated and the numerical tables for practical use will be given in the cases of the various numerical examples.

In the next place, the sequential plan will be discussed in Part II. Namely, a clinical trial will be sequentially perfomed on each patient chosen at random one by one from the total patients by administrating one of the two treatments of which the efficacious proportions are both unknown, and the both proportions $\mathfrak{p}_A$ and $\mathfrak{p}_B$ will be compared by observing respectively the numbers of the effective patients due to each treatment from the first patient until the n-th in the clinical trial, and a decision for selecting one of the two treatments will be finally determined as the result. Thus, the one treatment that is selected as the better at the conclusion of the abovementioned clinical trial will be perfomed on the remaining all patients. The problem now is to determine the optimum location of the boundaries and the optimum common slope of the two decision lines so that the overall expected loss function constructed on the basis of the proposed procedure is minimized.

The sequential plan has already been investigated by T. Colton [4] in the case of the two normal populations, and by the authors [7] in the case of the two binomial populations of which only one of the population proportions is unknown tc us. In this Part, the authors should like to investigate the case of the double dichotomies. Latter in this Part, the optimum values of the location of the boundaries and the minimized overall expected loss will be numerically evaluatec in the cases of the various numerical examples.

Part I. Fixed Sample Size Plan 6

1.1 Assumption

The assumptions are prepared throughout this Part as follows. These are

(1) There are N patients with a disease who are to be treated with one of th two treatments. Let us denote respectively by $\mathfrak{p}_A$ and $\mathfrak{p}_B$ the effective pro portions of two treatments A and B, where the both values of the proportion are unknown. N is fixed and large.

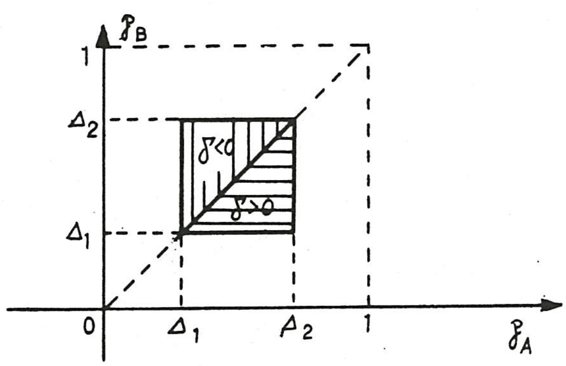
(2) Select at random $2n$ patients from all the N patients for a clinical trial and perform respectively each treatment on the n patients. Then denote by n_j a variate representing the number of the patients with the preassigned effective responses observed by perfoming j-th treatment, where $j=A, B$. It is assumed that n_j is distributed in accordance with a binomial distribution where the population proportion is $\mathfrak{p}_j$ and higher proportion is associated with better (i.e., superior) effect. Now, when $\delta=\mathfrak{p}_A-\mathfrak{p}_B$, we should like to select treatment A for the trial if δ is positive and treatment B if δ is negative.

(3) The only cost involved is the consequence of treating a patient with the superior or the inferior of the two treatments, and all other costs may be disregarded. The cost is directly proportional to the difference δ. Namely, the loss formulation states that if a patient is treated with the inferior treatment a positive loss proportional to δ is scored for him.

(3′) Also the net gain formulation states that if a patient is treated with the superior treatment a positive gain proportional to δ is scored for him, while if treated with the inferior treatment a negative gain proportional to δ is scored for him.

(4) We should like to suppose here upon a uniform probability distribution $f(\mathfrak{p}_j)=\dfrac{1}{\Delta_2-\Delta_1}$ about an *a priori* distribution for each parameter $\mathfrak{p}_j$, where $0\leqq\Delta_1\leqq\mathfrak{p}_j\leqq\Delta_2\leqq1$ ($j=A, B$), and let us suppose that two $\mathfrak{p}_j$s are independently distributed.

Now, the event in which $\delta\geqq0$ is equivalent to the event in which $\mathfrak{p}_A$ variates over the interval $<\Delta_1, \Delta_2>$ and $\mathfrak{p}_B$ variates over the interval $<\Delta_1, \mathfrak{p}_A>$ for a certain value of $\mathfrak{p}_A$ fixed at will in the interval $<\Delta_1, \Delta_2>$. For the same reason, the event in which $\delta\leqq0$ is equivalent to the event in which $\mathfrak{p}_A$ variates over the interval $<\Delta_1, \Delta_2>$ and $\mathfrak{p}_B$ variates over the interval $<\mathfrak{p}_A, \Delta_2>$ for a certain value $\mathfrak{p}_A$ fixed at will in the interval $<\Delta_1, \Delta_2>$. We may denote an



a priori joint probability density function of $\mathfrak{p}_A$ and $\mathfrak{p}_B$ by $g(\mathfrak{p}_A, \mathfrak{p}_B)$ wher

$g(\mathfrak{p}_A, \mathfrak{p}_B)=f(\mathfrak{p}_A)\cdot f(\mathfrak{p}_B)=\frac{1}{(\Delta_2-\Delta_1)^2}$ from the assumption (4).

1.2 Procedure

Perform a clinical trial on $2n$ patients, each treatment on n. Compute th observed difference in the numbers of the patients in whom the preassigned effe tive responses were observed by performing each treatment, $d=n_A-n_B$.

Procedure:

If $d>K$, use treatment A on the remaining $N-2n$;

If $d<-K$, use treatment B on the remaining $N-2n$;

If $-K\leqq d\leqq K$, use half and half two treatments on the remaining $N-2n$

The unknown parameters contained in the above procedure are the number of patients for the clinical trial and the positive boundary value K. The optimur values of the two parameters n and K such that the loss is minimized or the gai is maximized under the above procedure should be determined.

1.3 Construction of Overall Expected Loss Function

From the assumption (3) and the above procedure, if treatment B is inferic to A (i.e., $\delta>0$), then the expected loss L_B due to performing B is obtained as fo lows.

$$(1.\ 1)\qquad L_B=C\delta\left\{n+(N-2n)\cdot Pr(d<-K)+\frac{1}{2}(N-2n)\cdot Pr(-K\leqq d\leqq K)\right\},$$

where C is a proportionality factor.

For the same reason, if treatment A is inferior to B (i.e., $\delta<0$), then the ex pected loss L_A due to performing A is obtained as follows.

$$(1.\ 2)\qquad L_A=-C\delta\left\{n+(N-2n)\cdot Pr(d>K)+\frac{1}{2}(N-2n)\cdot Pr(-K\leqq d\leqq K)\right\}$$

$$=-C\delta N+C\delta\left[n+(N-2n)\cdot Pr(d<-K)+\frac{1}{2}(N-2n)\cdot Pr(-K\leqq d\leqq K)\right].$$

Therefore, from the assumption (4), integrating (1.1) and (1.2) over an *a prior* joint distribution for $\mathfrak{p}_A$ and $\mathfrak{p}_B$, the overall expected loss function $\overline{E\ Loss}$ is ol tained as follows.

$$(1.\ 3)\qquad \overline{E\ Loss}=\int_{\Delta_1}^{\Delta_2}\left\{\int_{\mathfrak{p}_A}^{\Delta_2}L_A g(\mathfrak{p}_A, \mathfrak{p}_B)d\mathfrak{p}_B\right\}d\mathfrak{p}_A+\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\mathfrak{p}_A}L_B g(\mathfrak{p}_A, \mathfrak{p}_B)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=-\frac{NC}{(\Delta_2-\Delta_1)^2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\mathfrak{p}_A}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$+\frac{C}{(\Delta_2-\Delta_1)^2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\Big[n+(N-2n)\cdot Pr(d<-K)\right.$$

$$\left.+\frac{1}{2}(N-2n)\cdot Pr(-K\leqq d\leqq K)\Big]d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\frac{NC(\Delta_2-\Delta_1)}{6}+\frac{C}{(\Delta_2-\Delta_1)^2}\Big[\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)n\,d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$+\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)(N-2n)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$+\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\frac{1}{2}(N-2n)\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A\Big]$$

$$=\frac{NC(\Delta_2-\Delta_1)}{6}+\frac{C(N-2n)}{(\Delta_2-\Delta_1)^2}\Big[\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$+\frac{1}{2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(-K\leqq d\leqq K)\Big]d\mathfrak{p}_B\right\}d\mathfrak{p}_A.$$

Whence, letting $n/N=a$,

$$\text{(1. 3')}\quad \overline{E\ Loss}/NC=\frac{\Delta_2-\Delta_1}{6}+\frac{1-2a}{(\Delta_2-\Delta_1)^2}\Big[\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$+\frac{1}{2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A\Big].$$

Now, from the assumption (2),

$$Pr\{d=n_A-n_B=-k\}=\sum_{j=0}^{n-k}Pr\{n_A=j \text{ and } n_B=k+j\}$$

$$=\sum_{j=0}^{n-k}Pr\{n_A=j\}\cdot Pr\{n_B=k+j\}$$

$$=\sum_{j=0}^{n-k}\binom{n}{j}\mathfrak{p}_A^j(1-\mathfrak{p}_A)^{n-j}\binom{n}{k+j}\mathfrak{p}_B^{k+j}(1-\mathfrak{p}_B)^{n-(k+j)}.$$

$$(k=0, 1, 2, \cdots, n)$$

On the other hand,

$$Pr\{d=n_A-n_B=k\}=\sum_{j=0}^{n-k}Pr\{n_A=k+j\}\cdot Pr\{n_B=j\}$$

$$=\sum_{j=0}^{n-k}\binom{n}{k+j}\mathfrak{p}_A^{k+j}(1-\mathfrak{p}_A)^{n-(k+j)}\binom{n}{j}\mathfrak{p}_B^{j}(1-\mathfrak{p}_B)^{n-j}.$$

$$(k=0, 1, 2, \cdots, n)$$

Now, the second term in (1.3′) results as follows.

$$(1.\ 4)\quad \int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d\leqq-(K+1))d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot\sum_{k=K+1}^{n}Pr\{d=-k\}\,d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\frac{1}{(n+1)^2(n+2)}\sum_{k=K+1}^{n}\sum_{j=0}^{n-k}\{(j+1)[I_x(j+2,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot$$

$$[I_x(k+j+1,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}$$

$$-(k+j+1)[I_x(j+1,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(k+j+2,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\},$$

where $I_x(p, q)$ denotes an incomplete Beta function

$$\int_0^x t^{p-1}(1-t)^{q-1}dt/B(p,q).$$

On the other hand, the third term in (1.3′) results as follows in the same manner.

$$(1.\ 5)\quad \int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\int_{\Delta_1}^{\Delta_2}\mathfrak{p}_A\left\{\int_{\Delta_1}^{\Delta_2}Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A-\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}\mathfrak{p}_B\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\int_{\Delta_1}^{\Delta_2}\mathfrak{p}_A\left\{\int_{\Delta_1}^{\Delta_2}\Big[\sum_{k=0}^{K}\sum_{j=0}^{n-k}Pr(n_A=j)\cdot Pr(n_B=k+j)\right.$$

$$\left.+\sum_{k=1}^{K}\sum_{j=0}^{n-k}Pr(n_A=k+j)\cdot Pr(n_B=j)\Big]d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$-\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}\mathfrak{p}_B\Big[\sum_{k=0}^{K}\sum_{j=0}^{n-k}Pr(n_A=j)\cdot Pr(n_B=k+j)\right.$$

$$\left.+\sum_{k=1}^{K}\sum_{j=0}^{n-k}Pr(n_A=k+j)\cdot Pr(n_B=j)\Big]d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=\frac{1}{(n+2)(n+1)^2}\Big[\sum_{k=0}^{K}\sum_{j=0}^{n-k}(j+1)\cdot[I_x(j+2,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot$$

$$[I_x(k+j+1,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}$$

$$+\sum_{k=1}^{K}\sum_{j=0}^{n-k}(k+j+1)\cdot[I_x(k+j+2,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(j+1,\ n-j+1)]_{\Delta_1}^{\Delta_2}$$

$$-\sum_{k=0}^{K}\sum_{j=0}^{n-k}(k+j+1)\cdot[I_x(k+j+2,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(j+1,\ n-j+1)]_{\Delta_1}^{\Delta_2}$$

$$-\sum_{k=1}^{K}\sum_{j=0}^{n-k}(j+1)\cdot[I_x(j+2,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(k+j+1,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\Big]$$

$$=0.$$

From (1.4) and (1.5) $\overline{E\ Loss/NC}$ is consequently obtained as follows.

$$(1.\ 6)\quad \overline{E\ Loss/NC}=\frac{\Delta_2-\Delta_1}{6}+\frac{1-2a}{(\Delta_2-\Delta_1)^2(n+1)^2(n+2)}\cdot\sum_{k=K+1}^{n}\sum_{j=0}^{n-k}$$

$$\{(j+1)\cdot[I_x(j+2,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(k+j+1,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}$$

$$-(k+j+1)\cdot[I_x(j+1,\ n-j+1)]_{\Delta_1}^{\Delta_2}\cdot$$

$$[I_x(k+j+2,\ n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\}.$$

1.4 Construction of Overall Expected Net Gain Function

The expected net gain formulations based on the assumption (3′) are identical, when treatment A is superior (i.e., $\delta>0$) or treatment B is superior (i.e., $\delta<0$). Therefore, without loss of generality we can take δ as positive.

From the assumption (3′) and the procedure in **1.2**, then the expected net gain *E Net Gain* then is obtained for all of the N individuals.

$$(1.\ 7)\qquad E\ Net\ Gain=G\delta(N-2n)\{Pr(\text{Select only }A)-Pr(\text{Select only }B)\}$$

$$=G\delta(N-2n)\{1-2Pr(\text{Select only }B)$$

$$-Pr(\text{Select equally }A\text{ and }B)\}$$

$$=G\delta(N-2n)\{1-2Pr(d<-K)-Pr(-K\leq d\leq K)\},$$

where G is a positive proportionality factor.

From the assumption (4), integrating (1.7) over an *a priori* joint distribution for p_A and p_B, the overall expected net gain function $\overline{E\ Net\ Gain}$ is obtained as follows.

$$(1.\ 8)\qquad \overline{E\ Net\ Gain}=\int_{\Delta_1}^{\Delta_2}\Big\{\int_{\Delta_1}^{p_A}[E\ Net\ Gain]\cdot g(p_A,\ p_B)dp_B\Big\}dp_A$$

$$+\int_{\Delta_1}^{\Delta_2}\Big\{\int_{p_A}^{\Delta_2}[E\ Net\ Gain]\cdot g(p_A,\ p_B)dp_B\Big\}dp_A$$

$$=\int_{\Delta_1}^{\Delta_2}\Big\{\int_{\Delta_1}^{\Delta_2}[E\ Net\ Gain]\cdot g(p_A,\ p_B)dp_B\Big\}dp_A$$

$$=G(N-2n)\int_{\Delta_1}^{\Delta_2}\Big\{\int_{\Delta_1}^{\Delta_2}(p_A-p_B)\{1-2Pr(d<-K)$$

$$-Pr(-K\leq d\leq K)\cdot g(p_A,\ p_B)dp_B\Big\}dp_A.$$

Therefore, letting $n/N=a$,

$$(1.9)\quad \overline{E\ Net\ Gain}/NG=\frac{1-2a}{(\Delta_2-\Delta_1)^2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\{1-2Pr(d<-K)-Pr(-K\leqq d\leqq K)\}\,d\mathfrak{p}_B\right\}d\mathfrak{p}_A$$

$$=-\frac{2(1-2a)}{(\Delta_2-\Delta_1)^2}\left[\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A+\frac{1}{2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A\right].$$

From (1.3′)

$$(1.10)\quad \frac{1-2a}{(\Delta_2-\Delta_1)^2}\left[\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(d<-K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A+\frac{1}{2}\int_{\Delta_1}^{\Delta_2}\left\{\int_{\Delta_1}^{\Delta_2}(\mathfrak{p}_A-\mathfrak{p}_B)\cdot Pr(-K\leqq d\leqq K)d\mathfrak{p}_B\right\}d\mathfrak{p}_A\right]$$

$$=\overline{E\ Loss}/NC-\frac{\Delta_2-\Delta_1}{6}.$$

Substituting (1.10) into (1.9), the connection between $\overline{E\ Loss}/NC$ and $\overline{E\ Net\ Gain}/NG$ is obtained as follows.

$$(1.11)\quad \overline{E\ Net\ Gain}/NG=\frac{\Delta_2-\Delta_1}{3}-2\cdot\overline{E\ Loss}/NC.$$

1.5 Numerical Examples and Numerical Tables

For each type of the given *a priori* distributions for $\mathfrak{p}_j$, the numerical values of $\overline{E\ Loss}/NC$ (1.6) may be evaluated in cases when $N=100$, $a=0.03, 0.04, 0.05, \cdots, 0.50$ (, that is, $n=3, 4, \cdots, 50$), and $K=0, 1, 2, 3, \cdots, 10$. We should like to find numerically such an optimum pair (a, K) in which $\overline{E\ Loss}/NC$ will be minimized for each type of the given *a priori* distributions.

If $K>n=\max.(d)$ (, that is, $-K<-n=\min.(d)$), then the consequence of decision results as follows. "Use always half and half the two treatments on the remaining $N-2n$". Whence, it may be nonsense to consider the case of $K>n$ in numerical examples.

Even if $K\leqq n$, the probability of making the decision "Use half and half the two treatments on the remaining" may increase as K approaches n. In such a case, on the other hand a part of $\overline{E\ Loss}$ based on making the decision "Use only one treatment on the remaining" then may decrease, but it may be that the other part of $\overline{E\ Loss}$ based on making the decision "Use half and half the two treatments on the remaining "then may increase more than the amount of the above decrease of $\overline{E\ Loss}$. Whence $\overline{E\ Loss}$ may consequently increase as K approaches n, even if $K \leqq n$. This matter may numerically be proved by the next numerical examples.

Numerical example (1°): In the case when $<\Delta_1, \Delta_2> = <0, 1>$, that is, when there is no information with respect to the defined interval of $\mathfrak{p}_j (j=A, B)$, $\overline{E\ Loss/NC}$ are evaluated numerically at the below Table 1.1. In this special case the form of $\overline{E\ Loss/NC}$ results.

(1.12) $$\overline{E\ Loss/NC} = \frac{1}{6} + \frac{(1-2a)}{(n+1)^2(n+2)}\Big[-\Big\{\frac{n(n+1)^2}{2} + \frac{1}{6}K(K+1)(2K+1)\Big\} + \Big\{\frac{1}{6}n(n+1)(2n+1) + \frac{1}{2}(n+1)K(K+1)\Big\}\Big].$$

In Tab. 1.1, the numerical values of $\overline{E\ Loss/NC}$ of (1.6) or (1.12) are evaluated in various cases when $N=100$, $a=0.03, 0.04, \cdots, 0.50$ (, that is, $n=3, 4, \cdots, 50$), and $K=0, 1, 2, \cdots, 10$.

Now, the next three conclusions may be numerically derived from Tab. 1.1.

Conclusions: (1) For each fixed n, $\overline{E\ Loss}$ also increases as K increases. Moreover, the degree of the increase of $\overline{E\ Loss}$ corresponding to the increase of K grows flat as n increases, and $\overline{E\ Loss}$ for any one K are all equal to 0.1666666 maximally in the case of $n=50$ (, that is, $a=$ 0.50).

(2) For each K, $\overline{E\ Loss}$ decreases for some time as n increases and inversely increases as n reaches a certain point. Moreover, the minimum value of $\overline{E\ Loss}$ for each K appears in larger values of n as K increases.

(3) It may be that an optimum pair of parameter pairs (a, K) of $\overline{E\ Loss/NC}$ is nearly equal to (0.06, 0) in the case of $N=100$. Namely, such an optimum designs that $\overline{E\ Loss/NC}$ can be minimized may be numerically stated as follows.

"In the case of $N=100$, perform a clinical trial on 12 patients, each treatment on 6. Compute the observed difference $d=n_A-n_B$.

If $d>0$, use treatment A on the remaining 88 patients;

If $d<0$, use treatment B on the remaining 88 patients;

If $d=0$, use half and half the two treatments on the remainder."

Numerical example (2°): Let us consider the next various types for *a priori* uniform distribution of $(\mathfrak{p}_A, \mathfrak{p}_B)$, that is,

Type I (such a type that the center of distribution is 0.5):

$<\Delta_1, \Delta_2> =$ (1) $<0.4, 0.6>$, (2) $<0.3, 0.7>$, (3) $<0.25, 0.75>$, (4) $<0.2, 0.8>$, and (5) $<0, 1>$ (i.e., the case of numerical example (1°)).

Table 1.1.

n \ K	0	1	2	3	4
3	0.0491666	0.0844166	0.1314166	0.1666666	
4	0.0439999	0.0685333	0.1053333	0.1421333	0.1666666
5	0.0416666	0.0595238	0.0880952	0.1202380	0.1488095
6	0.0409523	0.0544217	0.0768707	0.1038095	0.1307483
7	0.0412499	0.0517013	0.0696180	0.0920138	0.1159027
8	0.0422222	0.0505185	0.0650370	0.0837037	0.1044444
9	0.0436666	0.0503757	0.0623030	0.0779575	0.0958484
10	0.0454545	0.0509641	0.0608815	0.0741046	0.0895316
11	0.0475000	0.0520833	0.0604166	0.0716666	0.0850000
12	0.0497435	0.0535981	0.0606649	0.0703014	0.0818653
13	0.0521428	0.0554149	0.0614557	0.0697619	0.0798299
14	0.0546666	0.0574666	0.0626666	0.0698666	0.0786666
15	0.0572916	0.0597043	0.0642080	0.0704810	0.0782015
16	0.0600000	0.0620915	0.0660130	0.0715032	0.0783006
17	0.0627777	0.0646003	0.0680311	0.0728557	0.0788596
18	0.0656140	0.0672096	0.0702234	0.0744783	0.0797968
19	0.0685000	0.0699023	0.0725595	0.0763238	0.0810476
20	0.0714285	0.0726654	0.0750154	0.0783549	0.0825602
21	0.0743939	0.0754880	0.0775721	0.0805419	0.0842933
22	0.0773913	0.0783616	0.0802142	0.0828607	0.0862129
23	0.0804166	0.0812791	0.0829291	0.0852916	0.0882916
24	0.0834666	0.0842346	0.0857066	0.0878186	0.0905066
25	0.0865384	0.0872233	0.0885382	0.0904284	0.0928391
26	0.0896296	0.0902410	0.0914168	0.0931099	0.0952733
27	0.0927380	0.0932843	0.0943364	0.0958538	0.0977961
28	0.0958620	0.0963503	0.0972921	0.0986523	0.1003963
29	0.0990000	0.0994365	0.1002795	0.1014989	0.1030645
30	0.1021505	0.1025407	0.1032951	0.1043877	0.1057925
31	0.1053124	0.1056611	0.1063358	0.1073141	0.1085736
32	0.1084848	0.1087959	0.1093988	0.1102738	0.1114017
33	0.1116666	0.1119439	0.1124817	0.1132633	0.1142717
34	0.1148571	0.1151038	0.1155827	0.1162793	0.1171791
35	0.1180555	0.1182745	0.1186999	0.1193193	0.1201201
36	0.1212612	0.1214550	0.1218317	0.1223807	0.1230912
37	0.1244736	0.1246445	0.1249769	0.1254616	0.1260895
38	0.1276923	0.1278422	0.1281341	0.1285601	0.1291124
39	0.1309166	0.1310474	0.1313023	0.1316745	0.1321575
40	0.1341463	0.1342596	0.1344806	0.1348035	0.1352227
41	0.1373809	0.1374782	0.1376680	0.1379457	0.1383064
42	0.1406201	0.1407027	0.1408640	0.1411000	0.1414068
43	0.1438636	0.1439327	0.1440677	0.1442653	0.1445224
44	0.1471111	0.1471677	0.1472785	0.1474409	0.1476521
45	0.1503623	0.1504075	0.1504960	0.1506257	0.1507946
46	0.1536170	0.1536517	0.1537196	0.1538192	0.1539489
47	0.1568749	0.1568999	0.1569488	0.1570206	0.1571141
48	0.1601360	0.1601520	0.1601833	0.1602293	0.1602893
49	0.1633999	0.1634076	0.1634227	0.1634448	0.1634737
50	0.1666666	0.1666666	0.1666666	0.1666666	0.1666666

$\overline{E\ Loss}/NC$.

5	6	7	8	9	10
0. 1666666					
0. 1531972	0. 1666666				
0. 1382986	0. 1562152	0. 1666666			
0. 1251851	0. 1438518	0. 1583703	0. 1666666		
0. 1144848	0. 1323757	0. 1480303	0. 1599575	0. 1666666	
0. 1060606	0. 1225895	0. 1380165	0. 1512396	0. 1611570	0. 1666666
0. 0995833	0. 1145833	0. 1291666	0. 1425000	0. 1537500	0. 1620833
0. 0947140	0. 1082051	0. 1216962	0. 1345449	0. 1461087	0. 1557452
0. 0911564	0. 1032380	0. 1155714	0. 1276530	0. 1389795	0. 1490476
0. 0886666	0. 0994666	0. 1106666	0. 1218666	0. 1326666	0. 1426666
0. 0870481	0. 0966988	0. 1068321	0. 1171262	0. 1272594	0. 1369102
0. 0861437	0. 0947712	0. 1039215	0. 1133333	0. 1227450	0. 1318954
0. 0858284	0. 0935477	0. 1018031	0. 1103801	0. 1190643	0. 1276413
0. 0860018	0. 0929159	0. 1003619	0. 1081625	0. 1161403	0. 1241181
0. 0865833	**0. 0927833**	0. 0995000	0. 1065857	0. 1138928	0. 1212738
0. 0875077	0. 0930735	**0. 0991342**	0. 1055658	0. 1122448	0. 1190476
0. 0887220	0. 0937238	0. 0991945	0. 1050299	0. 1111258	0. 1173781
0. 0901827	0. 0946817	0. 0996219	**0. 1049149**	0. 1104725	0. 1162066
0. 0918541	0. 0959041	0. 1003666	0. 1051666	**0. 1102291**	0. 1154791
0. 0937066	0. 0973546	0. 1013866	0. 1057386	0. 1103466	**0. 1151466**
0. 0957155	0. 0990028	0. 1026462	0. 1065910	0. 1107823	0. 1151654
0. 0978600	0. 1008230	0. 1041152	0. 1076895	0. 1114991	0. 1154967
0. 1001228	0. 1027935	0. 1057676	0. 1090048	0. 1124645	0. 1161063
0. 1024891	0. 1048957	0. 1075814	0. 1105112	0. 1136504	0. 1160639
0. 1049462	0. 1071139	0. 1095376	0. 1121870	0. 1150322	0. 1180430
0. 1074835	0. 1094346	0. 1116198	0. 1140131	0. 1165886	0. 1193201
0. 1100917	0. 1118459	0. 1138139	0. 1159730	0. 1183007	0. 1207747
0. 1127629	0. 1143380	0. 1161075	0. 1180521	0. 1201523	0. 1223885
0. 1154901	0. 1169019	0. 1184901	0. 1202380	0. 1221288	0. 1241456
0. 1182675	0. 1195301	0. 1209523	0. 1225197	0. 1242176	0. 1260317
0. 1210898	0. 1222159	0. 1234859	0. 1248873	0. 1264076	0. 1280342
0. 1239524	0. 1249535	0. 1260838	0. 1273325	0. 1286888	0. 1301421
0. 1268513	0. 1277377	0. 1287396	0. 1298476	0. 1310526	0. 1323453
0. 1297830	0. 1305641	0. 1314477	0. 1324260	0. 1334911	0. 1346351
0. 1327444	0. 1334285	0. 1342032	0. 1350617	0. 1359974	0. 1370035
0. 1357326	0. 1363275	0. 1370017	0. 1377496	0. 1385654	0. 1394436
0. 1387454	0. 1392580	0. 1398394	0. 1404848	0. 1411896	0. 1419490
0. 1417804	0. 1422170	0. 1427126	0. 1432633	0. 1438651	0. 1445141
0. 1448358	0. 1452022	0. 1456184	0. 1460812	0. 1465874	0. 1471338
0. 1479098	0. 1482112	0. 1485539	0. 1489352	0. 1493526	0. 1498035
0. 1510008	0. 1512421	0. 1515166	0. 1518223	0. 1521571	0. 1525191
0. 1541074	0. 1542930	0. 1545043	0. 1547397	0. 1549977	0. 1552768
0. 1572284	0. 1573623	0. 1575148	0. 1576849	0. 1578714	0. 1580734
0. 1603626	0. 1604485	0. 1605465	0. 1606558	0. 1607757	0. 1609057
0. 1635090	0. 1635504	0. 1635976	0. 1636503	0. 1637082	0. 1637709
0. 1666666	0. 1666666	0. 1666666	0. 1666666	0. 1666666	0. 1666666

(Table 1.1 FACOM 270-20/30 FORTRAN LIST

```
      DO 1 K=1, 11
      L=K-1
      DO 1 N=3, 50
      CN=N
      CK=K-1
      A=0.01*CN
      T2=CN*(CN+1.)**2+CK*(CK+1.0)*(2.0*CK+1.0)/3.0
      T3=CN*(CN+1.0)*(2.0*CN+1.0)/3.0+(CN+1.0)*CK*(CK+1.0)
      CD=2.0*(CN+2.0)*(CN+1.0)**2
      C=(1.0-2.0*A)/CD
***   ANS=C*(T3-T2)+1.0/6.0
      WRITE (50, 200), N, ANS, L
  200 FORMAT (13, F14, 7, 18)
    1 CONTINUE
      STOP
      END
```

)

Type II (such a type that the center of distribution is biased in the left side for 0.5)

Type II_1 (the type with center 0.45): $<\Delta_1, \Delta_2> = <0.3, 0.6>$,

Type II_2 (the types with center 0.4): $<\Delta_1, \Delta_2> =$ (1) $<0.3, 0.5>$, (2) $<0.2, 0.6>$, and (3) $<0.15, 0.65>$

Type II_3 (the type with center 0.35): $<\Delta_1, \Delta_2> = <0.2, 0.5>$,

Type II_4 (the type with center 0.3): $<\Delta_1, \Delta_2> = <0, 0.6>$,

Type II_5 (the type with center 0.25): $<\Delta_1, \Delta_2> = <0, 0.5>$.

Type III (such a type that the center of distribution is biased in the right side for 0.5)

Type III_1 (the type with center 0.55): $<\Delta_1, \Delta_2> = <0.4, 0.7>$,

Type III_2 (the type with center 0.6): $<\Delta_1, \Delta_2> =$ (1) $<0.5, 0.7>$, (2) $<0.4, 0.8>$, (3) $<0.35, 0.85>$, and (4) $<0.3, 0.9>$,

Type III_3 (the type with center 0.65): $<\Delta_1, \Delta_2> = <0.5, 0.8>$,

Type III_4 (the type with center 0.7): $<\Delta_1, \Delta_2> =$ (1) $<0.6, 0.8>$, (2) $<0.5, 0.9>$, (3) $<0.45, 0.95>$, and (4) $<0.4, 1>$,

Type III_5 (the type with center 0.75): $<\Delta_1, \Delta_2> =$ (1) $<0.6, 0.9>$, and (2) $<0.5, 1>$,

Type III_6 (the type with center 0.8): $<\Delta_1, \Delta_2> = <0.6. 1>$,

Type III_7 (the type with center 0.85): $<\Delta_1, \Delta_2> = <0.7, 1>$.

(Remark) We here should like to note the next, that is, the two types in next each bracket have such distributions that two centers are mutually symmetric for 0.5 and range of distribution is similar.

(II_1, III_1): centers 0.45, 0.55 and range 0.3,

(II_2-(1), III_2-(1)): centers 0.4, 0.6 and range 0.2,

(II_2-(2), III_2-(2)): centers 0.4, 0.6 and range 0.4,
(II_2-(3), III_2-(3)): centers 0.4, 0.6 and range 0.5,
(II_3, III_3): centers 0.35, 0.65 and range 0.3,
(II_4, III_4-(4)): centers 0.3, 0.7 and range 0.6,
(II_5, III_5-(2)): centers 0.25, 0.75 and range 0.5.

In this case the form of $\overline{E\ Loss}/NC$ ersults.

$$(1.13)\quad \overline{E\ Loss}/NC=\frac{\Delta_2-\Delta_1}{6}+\frac{50-n}{50(\Delta_2-\Delta_1)^2(n+1)^2(n+2)}\cdot\sum_{k=K+1}^{n}\sum_{j=0}^{n-k}$$
$$\{(j+1)[I_x(j+2,n-j+1)]_{\Delta_1}^{\Delta_2}\cdot[I_x(k+j+1,n-(k+j)+1)]_{\Delta_1}^{\Delta_2}$$
$$-(k+j+1)\cdot[I_x(j+1,n-j+1)]_{\Delta_1}^{\Delta_2}$$
$$\cdot[I_x(k+j+2,n-(k+j)+1)]_{\Delta_1}^{\Delta_2}\}.$$

Thus the values of $\overline{E\ Loss}/NC$ are given at the belows Table 1.2.

Now, the next conclusions may be numerically derived from Tab. 1.2.

Conclusions: (1) For each fixed n, $\overline{E\ Loss}$ also increases as K increases, in each type of *a priori* distribution. Moreover, the degree of the increase of $\overline{E\ Loss}$ corresponding to the increase of K grows flat as n increases.

(2) When K is not so large, $\overline{E\ Loss}$ decreases for some time as n increases and inversely increases as n reaches a certain point. But, for each large value of K it seems that $\overline{E\ Loss}$ decreases monotonously as n increases in the range $5\leq n\leq 20$ and that the minimum value of $\overline{E\ Loss}$ for such value of K appears in larger values than 21 of n. Moreover, the minimum value of $\overline{E\ Loss}$ for each K appears in larger values of n as K increases.

(3) For each type of *a priori* distribution, the $\overline{E\ Loss}/NC$ in the neighborhood of the minimum and the optimum pair (a, K) (i.e., (n, K)) of giving the minimum value of $\overline{E\ Loss}/NC$ are given below.

It follows that the two types in the bracket noted in the abovementioned (Remark) have exactly the same values of $\overline{E\ Loss}/NC$.

(4) It seems that the optimum value of n is less as the range of distribution grows larger, and the optimum value of K is always equal to zero, for eahc type.

Thus, such an optimum designs that $\overline{E\ Loss}/NC$ can be minimized may be numerically stated as follows.

"In the case of $N=100$, perform a clinical trial on $2n^*$ patients (where n^* is each value of the second column in Tab. 1.3 for each type given in the first column of Tab. 1.3), each treatment on n^*. Compute the observed difference $d=n_A-n_B$.

If $d>0$, use treatment A on the remaining $N-2n^*$ patients;

If $d<0$, use treatment B on the remaining $N-2n^*$;

If $d=0$, use half and half the two treatments on the remainder."

(5) In the cases when the center of distribution= 0.5, 0.4 (i.e., 0.6) and 0.3 (i.e., 0.7), the curves of points ($\Delta_2-\Delta_1$, minimum $\overline{E\ Loss}/NC$) and the curves of points ($\Delta_2-\Delta_1$, n^*) are given in Figures 1.1~1.3.

Table 1.2.

Type I-(1). *a priori* distribution <0. 4, 0. 6>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0260964	0. 0255897	0. 0251770	0. 0248411	0. 0245697	0. 0243538	0. 0241863	0. 0240618
1	0. 0284133	0. 0276924	0. 0270947	0. 0265975	0. 0261841	0. 0258421	0. 0255617	0. 0253356
2	0. 0311408	0. 0304003	0. 0297291	0. 0291310	0. 0286033	0. 0281419	0. 0277415	0. 0273973
3	0. 0327524	0. 0322969	0. 0318051	0. 0313088	0. 0308272	0. 0303719	0. 0299491	0. 0295623
4	0. 0332636	0. 0331094	0. 0328832	0. 0326047	0. 0322928	0. 0319637	0. 0316297	0. 0313002

Type I-(2). *a priori* distribution <0. 3, 0. 7>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0393407	0. 0378296	0. 0366959	0. 0358609	0. 0352686	0. 0348779	0. 0346571	[0. 0345812]
1	0. 0470901	0. 0445611	0. 0425794	0. 0410316	0. 0398349	0. 0389275	0. 0382617	0. 0378001
2	0. 0569909	0. 0539539	0. 0513203	0. 0490815	0. 0472053	0. 0456537	0. 0443891	0. 0433772
3	0. 0636811	0. 0614572	0. 0591524	0. 0569249	0. 0548597	0. 0529977	0. 0513539	0. 0499287
4	0. 0662303	0. 0653032	0. 0639991	0. 0624629	0. 0608200	0. 0591653	0. 0575651	0. 0560632

Type I-(3). *a priori* distribution <0. 25, 0. 75>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0423521	0. 0404678	0. 0391466	0. 0382590	0. 0377145	0. 0374471	[0. 0374073]	0. 0375568
1	0. 0529726	0. 0494278	0. 0467679	0. 0447899	0. 0433483	0. 0423359	0. 0416721	0. 0412949
2	0. 0672925	0. 0625803	0. 0586413	0. 0554186	0. 0528256	0. 0507745	0. 0491855	0. 0479898
3	0. 0778721	0. 0740082	0. 0701536	0. 0665688	0. 0633719	0. 0606018	0. 0582550	0. 0563075
4	0. 0824270	0. 0805825	0. 0780973	0. 0752915	0. 0724146	0. 0690355	0. 0670577	0. 0647378

Type I-(4). *a priori* distribution <0. 2, 0. 8>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0437266	0. 0416808	0. 0403760	0. 0396234	[0. 0392945]	0. 0392982	0. 0395679	0. 0400537
1	0. 0568222	0. 0523939	0. 0492425	0. 0470393	0. 0455556	0. 0446287	0. 0441400	[0. 0440013]
2	0. 0755057	0. 0689366	0. 0636944	0. 0596032	0. 0564710	0. 0541261	0. 0524248	0. 0512506
3	0. 0907181	0. 0846233	0. 0788491	0. 0737404	0. 0694016	0. 0658205	0. 0269347	0. 0606646
4	0. 0982271	0. 0948428	0. 0905533	0. 0859845	0. 0815528	0. 0774935	0. 0739176	0. 0708593

Type I-(5). *a priori* distribution <0, 1. 0>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0416666	[0. 0409523]	0. 0412499	0. 0422222	0. 0436666	0. 0454545	0. 0474999	0. 0497435
1	0. 0595238	0. 0544217	0. 0517013	0. 0505185	[0. 0503757]	0. 0509641	0. 0520833	0. 0535981
2	0. 0880952	0. 0768707	0. 0696180	0. 0650370	0. 0623030	0. 0608815	[0. 0604166]	0. 0606649
3	0. 1202380	0. 1038095	0. 0920138	0. 0837037	0. 0779575	0. 0741046	0. 0716666	0. 0703014
4	0. 1488095	0. 1307482	0. 1159027	0. 1044444	0. 0958484	0. 0895316	0. 0849999	0. 0818653

From Fig. 1.1~1.3, it follows that in each distribution $\overline{E\ Loss}/NC$ increases and inversely n^* decreases as the width $(\Delta_2-\Delta_1)$ of the distribution increases. It seems that the degree of the increase of $\overline{E\ Loss}/NC$ is rather flat as $(\Delta_2-\Delta_1)$ increases.

$\overline{E\ Loss}/NC$. Table 1.2-1

13	14	15	16	17	18	19	20
0. 0239759	0. 0239247	**0. 0239052**	0. 0239148	0. 0239512	0. 0240122	0. 0240964	0. 0242020
0. 0251575	0. 0250224	0. 0249261	0. 0248650	**0. 0248362**	0. 0248369	0. 0248651	0. 0249186
0. 0271046	0. 0268591	0. 0266572	0. 0264953	0. 0263704	0. 0262799	0. 0262212	0. 0261922
0. 0292128	0. 0289006	0. 0286254	0. 0283860	0. 0281812	0. 0280094	0. 0278694	0. 0277596
0. 0309819	0. 0306800	0. 0303978	0. 0301377	0. 0299013	0. 0296993	0. 0295023	0. 0293402

13	14	15	16	17	18	19	20
0. 0346302	0. 0347880	0. 0350411	0. 0353782	0. 0357898	0. 0362678	0. 0368052	0. 0373962
0. 0375130	0. 0373763	**0. 0373700**	0. 0374777	0. 0376858	0. 0379825	0. 0383579	0. 0388036
0. 0425876	0. 0419937	0. 0415724	0. 0413037	0. 0411703	**0. 0411572**	0. 0412513	0. 0414414
0. 0487142	0. 0476982	0. 0468668	0. 0462054	0. 0456998	0. 0453364	0. 0451026	0. 0449867
0. 0546866	0. 0534499	0. 0523598	0. 0514168	0. 0506182	0. 0499584	0. 0494307	0. 0490275

13	14	15	16	17	18	19	20
0. 0378658	0. 0383103	0. 0388710	0. 0395320	0. 0402804	0. 0411051	0. 0419971	0. 0429486
0. 0411560	0. 0412173	0. 0414481	0. 0418236	0. 0423235	0. 0429312	0. 0436325	0. 0444159
0. 0471290	0. 0465539	0. 0462235	**0. 0461036**	0. 0461652	0. 0463844	0. 0467406	0. 0472167
0. 0547259	0. 0534743	0. 0525172	0. 0518216	0. 0513575	0. 0510980	**0. 0510195**	0. 0511011
0. 0627009	0. 0609516	0. 0594822	0. 0582782	0. 0573211	0. 0565912	0. 0560687	0. 0557345

13	14	15	16	17	18	19	20
0. 0407175	0. 0415296	0. 0424666	0. 0435098	0. 0446439	0. 0458566	0. 0471375	0. 0484781
0. 0441459	0. 0445227	0. 0450918	0. 0458218	0. 0466875	0. 0476687	0. 0487490	0. 0499147
0. 0505099	C. 0501275	**0. 0500434**	0. 0502091	0. 0505853	0. 0511402	0. 0518475	0. 0526859
0. 0589300	0. 0576564	0. 0567780	0. 0562382	0. 0559885	**0. 0559880**	0. 0562020	0. 0566015
0. 0683092	0. 0662350	0. 0645948	0. 0633435	0. 0624376	0. 0618364	0. 0615034	0. 0614061

13	14	15	16	17	18	19	20
0. 0521428	0. 0546666	0. 0572916	0. 0599999	0. 0627777	0. 0656140	0. 0684999	0. 0714285
0. 0554149	0. 0574666	0. 0597043	0. 0620915	0. 0646003	0. 0672096	0. 0699023	0. 0726654
0. 0614557	0. 0626666	0. 0642080	0. 0660130	0. 0680311	0. 0702234	0. 0725595	0. 0750154
0. 0697619	0. 0698666	0. 0704810	0. 0715032	0. 0728557	0. 0744783	0. 0763238	0. 0783549
0. 0798299	0. 0786666	**0. 0782015**	0. 0783006	0. 0788596	0. 0797968	0. 0810476	0. 0825602

Type II_1. *a priori* distribution $<0.3, 0.6>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0340416	0.0330275	0.0322293	0.0316051	0.0311253	0.0307578	0.0305157	0.0303555
1	0.0389429	0.0373924	0.0361366	0.0351185	0.0342968	0.0336402	0.0331245	0.0327305
2	0.0448836	0.0431862	0.0416719	0.0403457	0.0391990	0.0382177	0.0373871	0.0366927
3	0.0485667	0.0474512	0.0462599	0.0450737	0.0439404	0.0428868	0.0419266	0.0410656
4	0.0498150	0.0494071	0.0488130	0.0480894	0.0472900	0.0464585	0.0456282	0.0448232

Type II_2-(1). *a priori* distribution $<0.3, 0.5>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0259666	0.0254491	0.0250281	0.0246858	0.0244099	0.0241906	0.0240209	0.0238952
1	0.0284124	0.0276704	0.0270545	0.0265419	0.0261157	0.0257628	0.0254735	0.0252400
2	0.0312148	0.0304696	0.0297888	0.0291787	0.0286385	0.0281646	0.0277522	0.0273969
3	0.0327994	0.0323619	0.0318809	0.0313893	0.0309080	0.0304496	0.0300216	0.0296281
4	0.0332732	0.0331343	0.0329242	0.0326599	0.0323594	0.0320382	0.0317091	0.0313819

Type II_2-(2). *a priori* distribution $<0.2, 0.6>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0388750	0.0373468	0.0362066	0.0353723	0.0347860	0.0344048	0.0341960	0.0341340
1	0.0470548	0.0444453	0.0424021	0.0408085	0.0395786	0.0386479	0.0379665	0.0374956
2	0.0572471	0.0541648	0.0514725	0.0491736	0.0472418	0.0456412	0.0443350	0.0432886
3	0.0638764	0.0617042	0.0594136	0.0571740	0.0550806	0.0531822	0.0514990	0.0500347
4	0.0662798	0.0654210	0.0641772	0.0626820	0.0610595	0.0594075	0.0577969	0.0562756

Type II_2-(3). *a priori* distribution $<0.15, 0.65>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0415572	0.0397908	0.0384799	0.0376112	0.0370905	0.0368496	0.0368376	0.0370153
1	0.0527965	0.0492297	0.0464887	0.0444567	0.0429810	0.0419491	0.0412764	0.0408979
2	0.0675901	0.0628425	0.0588009	0.0554835	0.0528102	0.0506943	0.0490549	0.0478211
3	0.0781578	0.0743713	0.0705080	0.0668776	0.0636181	0.0607813	0.0583711	0.0563667
4	0.0825139	0.0807852	0.0783815	0.0756152	0.0727410	0.0699389	0.0673228	0.0649574

Type II_3. *a priori* distribution $<0.2, 0.5>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0334602	0.0324086	0.0315861	0.0309474	0.0304606	0.0301020	0.0298533	0.0297002
1	0.0389389	0.0372891	0.0359512	0.0348670	0.0339927	0.0332947	0.0327471	0.0323292
2	0.0452126	0.0434855	0.0419179	0.0405294	0.0393193	0.0382776	0.0373914	0.0366475
3	0.0487784	0.0477408	0.0465903	0.0454146	0.0442698	0.0431900	0.0421946	0.0412937
4	0.0498597	0.0495225	0.0490014	0.0483388	0.0475829	0.0467771	0.0459564	0.0451480

Type II_4. *a priori* distribution $<0, 0.6>$.

K \ n	5	6	7	8	9	10	11	12
0	0.0398230	0.0378712	0.0367394	0.0361929	0.0360794	0.0362956	0.0367689	0.0374466
1	0.0564882	0.0513847	0.0477975	0.0453345	0.0437126	0.0427289	0.0422370	0.0421297
2	0.0774264	0.0702579	0.0643927	0.0597687	0.0562212	0.0535702	0.0516529	0.0503327
3	0.0924675	0.0865841	0.0806309	0.0751540	0.0703980	0.0664258	0.0632061	0.0606665
4	0.0987946	0.0960607	0.0921716	0.0877001	0.0831415	0.0788321	0.0749614	0.0716123

Table 1.2-2

13	14	15	16	17	18	19	20
0. 0302763	0. 0302690	0. 0303261	0. 0304411	0. 0306086	0. 0308238	0. 0310825	0. 0313811
0. 0324429	0. 0322488	0. 0321379	0. 0321011	0. 0321311	0. 0322212	0. 0323659	0. 0325603
0. 0361213	0. 0356610	0. 0353011	0. 0350322	0. 0348459	0. 0347349	0. 0346925	0. 0347129
0. 0403048	0. 0396421	0. 0390738	0. 0385954	0. 0382021	0. 0378886	0. 0376500	0. 0374813
0. 0440602	0. 0433505	0. 0427019	0. 0421178	0. 0416005	0. 0411504	0. 0407668	0. 0404481

13	14	15	16	17	18	19	20
0. 0238088	0. 0237579	0. 0237395	0. 0237505	0. 0237889	0. 0238524	0. 0239393	0. 0240480
0. 0250558	0. 0249158	0. 0248159	0. 0247519	0. 0247212	0. 0247207	0. 0247484	0. 0248019
0. 0270939	0. 0268391	0. 0266289	0. 0264596	0. 0263284	0. 0262322	0. 0261688	0. 0261357
0. 0292709	0. 0289508	0. 0286675	0. 0284200	0. 0282074	0. 0280283	0. 0278814	0. 0277651
0. 0310637	0. 0307600	0. 0304748	0. 0302105	0. 0299692	0. 0297518	0. 0295591	0. 0293912

13	14	15	16	17	18	19	20
0. 0351982	0. 0343718	0. 0346413	0. 0349950	0. 0354232	0. 0359178	0. 0364716	0. 0370786
0. 0372039	0. 0370664	0. 0370623	0. 0371746	0. 0373889	0. 0376933	0. 0380775	0. 0385327
0. 0424710	0. 0418550	0. 0414166	0. 0411351	0. 0409926	0. 0409735	0. 0410643	0. 0412531
0. 0487833	0. 0477338	0. 0468727	0. 0461855	0. 0456580	0. 0452763	0. 0450275	0. 0448995
0. 0548740	0. 0536098	0. 0524913	0. 0515206	0. 0506958	0. 0500119	0. 0494625	0. 0490400

13	14	15	16	17	18	19	20
0. 0373523	0. 0378242	0. 0384115	0. 0390983	0. 0398708	0. 0407193	0. 0416338	0. 0426066
0. 0407633	0. 0408328	0. 0410744	0. 0414627	0. 0419761	0. 0425985	0. 0433149	0. 0441134
0. 0469325	0. 0463380	0. 0459950	0. 0458678	0. 0459260	0. 0461454	0. 0465042	0. 0469849
0. 0547364	0. 0534441	0. 0524540	0. 0517324	0. 0512478	0. 0509733	0. 0508839	0. 0509581
0. 0628733	0. 0610786	0. 0595678	0. 0583272	0. 0573382	0. 0565818	0. 0560372	0. 0556852

13	14	15	16	17	18	19	20
0. 0296310	0. 0296360	0. 0297075	0. 0298383	0. 0300229	0. 0302560	0. 0305335	0. 0308513
0. 0320241	0. 0318183	0. 0317003	0. 0316603	0. 0316905	0. 0317836	0. 0319336	0. 0321353
0. 0260327	0. 0355349	0. 0351432	0. 0348478	0. 0346397	0. 0345112	0. 0344551	0. 0344653
0. 0404912	0. 0397871	0. 0391792	0. 0386636	0. 0382361	0. 0378917	0. 0375254	0. 0374324
0. 0443718	0. 0436413	0. 0429677	0. 0423553	0. 0418083	0. 0413282	0. 0409151	0. 0405681

13	14	15	16	17	18	19	20
0. 0382898	0. 0392688	0. 0403606	0. 0415474	0. 0428147	0. 0441510	0. 0455469	0. 0469945
0. 0423277	0. 0427713	0. 0434149	0. 0442233	0. 0451689	0. 0462297	0. 0473881	0. 0486300
0. 0494987	0. 0490624	0. 0489530	0. 0491143	0. 0495013	0. 0500778	0. 0508144	0. 0516874
0. 0587221	0. 0572901	0. 0562953	0. 0556725	0. 0553661	0. 0553294	0. 0555232	0. 0559146
0. 0688004	0. 0665034	0. 0646801	0. 0632824	0. 0622619	0. 0615729	0. 0611740	0. 0610286

Type II_5. *a priori* distribution <0, 0.5>.

K \ n	5	6	7	8	9	10	11	12
0	0.0373860	0.0354462	0.0342079	0.0334810	0.0331390	0.0330943	0.0332841	0.0336626
1	0.0530459	0.0485933	0.0452583	0.0428092	0.0410581	0.0398579	0.0390957	0.0386847
2	0.0698936	0.0647312	0.0601513	0.0562730	0.0530920	0.0505500	0.0485706	0.0470757
3	0.0797026	0.0763624	0.0726131	0.0688326	0.0652702	0.0620657	0.0592813	0.0569299
4	0.0828834	0.0817094	0.0798144	0.0773732	0.0746163	0.0717585	0.0689680	0.0663612

Type III_1. *a priori* distribution <0.4, 0.7>.

K \ n	5	6	7	8	9	10	11	12
0	0.0340416	0.0330276	0.0322292	0.0316051	0.0311252	0.0307678	0.0305157	0.0303556
1	0.0389429	0.0373925	0.0361365	0.0351185	0.0342968	0.0336402	0.0331245	0.0327306
2	0.0448836	0.0431863	0.0416718	0.0403457	0.0391989	0.0382177	0.0373871	0.0366927
3	0.0485667	0.0474512	0.0462598	0.0450737	0.0439404	0.0428868	0.0419266	0.0410657
4	0.0498150	0.0494071	0.0488130	0.0480894	0.0472899	0.0464585	0.0456282	0.0448232

Type III_2-(1). *a priori* distribution <0.5, 0.7>.

K \ n	5	6	7	8	9	10	11	12
0	0.0259666	0.0254490	0.0250281	0.0246860	0.0244098	0.0241905	0.0240210	0.0238952
1	0.0284124	0.0276703	0.0270545	0.0265420	0.0261156	0.0257628	0.0254736	0.0252399
2	0.0312148	0.0304695	0.0297888	0.0291788	0.0286385	0.0281645	0.0277523	0.0273968
3	0.0327994	0.0323619	0.0318809	0.0313893	0.0309080	0.0304496	0.0300216	0.0296280
4	0.0332732	0.0331343	0.0329242	0.0326599	0.0323593	0.0320382	0.0327092	0.0313818

Type III_2-(2). *a priori* distribution <0.4, 0.8>.

K \ n	5	6	7	8	9	10	11	12
0	0.0388750	0.0373468	0.0362066	0.0353723	0.0347860	0.0344048	0.0341960	0.0341340
1	0.0470548	0.0444453	0.0424021	0.0408085	0.0395786	0.0386478	0.0379665	0.0374956
2	0.0572471	0.0541648	0.0514725	0.0491736	0.0472418	0.0456412	0.0443350	0.0432886
3	0.0638764	0.0617042	0.0594136	0.0571740	0.0550806	0.0531822	0.0514990	0.0500347
4	0.0662798	0.0654210	0.0641772	0.0626820	0.0610595	0.0594075	0.0577969	0.0562756

Type III_2-(3). *a priori* distribution <0.35, 0.85>.

K \ n	5	6	7	8	9	10	11	12
0	0.0418484	0.0397908	0.0384799	0.0376112	0.0370905	0.0368496	0.0368376	0.0370153
1	0.0530040	0.0492297	0.0464887	0.0444567	0.0429810	0.0419491	0.0412764	0.0408980
2	0.0677049	0.0628426	0.0588009	0.0554835	0.0528102	0.0506943	0.0490549	0.0478211
3	0.0792016	0.0743713	0.0705080	0.0668775	0.0636181	0.0607813	0.0583711	0.0563668
4	0.0825223	0.0807852	0.0783813	0.0756152	0.0727410	0.0699389	0.0673228	0.0649574

Type III_2-(4). *a priori* distribution <0.3, 0.9>.

K \ n	5	6	7	8	9	10	11	12
0	0.0428405	0.0408178	0.0395511	0.0388430	0.0385605	0.0386103	0.0389244	0.0394524
1	0.0566740	0.0520993	0.0488569	0.0466013	0.0450915	0.0441558	0.0436697	0.0435409
2	0.0759372	0.0692124	0.0638207	0.0596061	0.0563793	0.0539653	0.0522157	0.0510092
3	0.0911616	0.0850953	0.0792627	0.0740592	0.0696194	0.0659460	0.0629820	0.0606491
4	0.0983864	0.0951611	0.0909559	0.0863975	0.0819270	0.0778041	0.0741569	0.0710297

Table 1.2-3

13	14	15	16	17	18	19	20
0. 0341950	0. 0348549	0. 0356215	0. 0364783	0. 0374123	0. 0384127	0. 0394706	0. 0405789
0. 0385580	0. 0386637	0. 0389612	0. 0394185	0. 0400098	0. 0407148	0. 0415166	0. 0424017
0. 0459933	0. 0452607	0. 0448241	0. 0446384	0. 0446660	0. 0448756	0. 0452411	0. 0457408
0. 0549953	0. 0534468	0. 0522473	0. 0513588	0. 0507450	0. 0503725	0. 0502116	0. 0502359
0. 0640090	0. 0619472	0. 0601870	0. 0587235	0. 0575420	0. 0566229	0. 0559441	0. 0554833

13	14	15	16	17	18	19	20
0. 0302763	0. 0302690	0. 0303261	0. 0304411	0. 0306086	0. 0308238	0. 0310825	0. 0313811
0. 0324429	0. 0322488	0. 0321379	0. 0321012	0. 0321311	0. 0322212	0. 0323659	0. 0325604
0. 0361213	0. 0356609	0. 0353011	0. 0350322	0. 0348459	0. 0347349	0. 0346925	0. 0347129
0. 0403048	0. 0396420	0. 0390738	0. 0385955	0. 0382021	0. 0378886	0. 0376500	0. 0374814
0. 0440602	0. 0433507	0. 0427019	0. 0421178	0. 0416005	0. 0411504	0. 0407668	0. 0404481

13	14	15	16	17	18	19	20
0. 0238088	0. 0237580	0. 0237394	0. 0237505	0. 0237889	0. 0238524	0. 0239393	0. 0240481
0. 0250558	0. 0249159	0. 0248158	0. 0247520	0. 0247212	0. 0247208	0. 0247484	0. 0248019
0. 0270939	0. 0268392	0. 0266289	0. 0264597	0. 0263284	0. 0262322	0. 0261688	0. 0261358
0. 0292709	0. 0289508	0. 0286674	0. 0284200	0. 0282074	0. 0280284	0. 0278814	0. 0277652
0. 0310637	0. 0307601	0. 0304747	0. 0302106	0. 0299692	0. 0297519	0. 0295591	0. 0293912

13	14	15	16	17	18	19	20
0. 0341981	0. 0343718	0. 0346413	0. 0349950	0. 0354232	0. 0359178	0. 0364716	0. 0370787
0. 0372039	0. 0370664	0. 0370623	0. 0371746	0. 0373889	0. 0376933	0. 0380775	0. 0385327
0. 0424710	0. 0418550	0. 0414165	0. 0411351	0. 0409926	0. 0409735	0. 0410643	0. 0412531
0. 0487833	0. 0477338	0. 0468727	0. 0461855	0. 0456580	0. 0452763	0. 0450275	0. 0448995
0. 0548740	0. 0536098	0. 0524913	0. 0515206	0. 0506958	0. 0500119	0. 0494625	0. 0490401

13	14	15	16	17	18	19	20
0. 0373523	0. 0378242	0. 0384115	0. 0390976	0. 0398712	0. 0407194	0. 0416338	0. 0426067
0. 0407633	0. 0408328	0. 0410744	0. 0414621	0. 0419765	0. 0425986	0. 0433149	0. 0441135
0. 0469325	0. 0463380	0. 0459950	0. 0458672	0. 0459263	0. 0461455	0. 0465043	0. 0469849
0. 0547364	0. 0534441	0. 0524540	0. 0517319	0. 0512481	0. 0509734	0. 0508840	0. 0509581
0. 0628733	0. 0610786	0. 0595678	0. 0583268	0. 0573384	0. 0565818	0. 0560373	0. 0556852

13	14	15	16	17	18	19	20
0. 0401559	0. 0410052	0. 0419770	0. 0430525	0. 0442167	0. 0454575	0. 0467647	0. 0481298
0. 0437002	0. 0440943	0. 0446823	0. 0454319	0. 0463175	0. 0473184	0. 0484179	0. 0496023
0. 0502481	0. 0498545	0. 0497657	0. 0499316	0. 0503115	0. 0508726	0. 0515879	0. 0524354
0. 0588655	0. 0575548	0. 0566492	0. 0560900	0. 0558271	0. 0558184	0. 0560280	0. 0564261
0. 0684179	0. 0662912	0. 0646076	0. 0633215	0. 0623882	0. 0617660	0. 0614171	0. 0613083

Type III_3. *a priori* distribution <0.5, 0.8>.

K \ n	5	6	7	8	9	10	11	12
0	0.0334602	0.0324085	0.0315862	0.0309475	0.0304606	0.0301020	0.0298533	0.0297002
1	0.0389389	0.0372889	0.0359513	0.0348671	0.0339927	0.0332947	0.0327471	0.0323291
2	0.0452126	0.0434855	0.0419179	0.0405295	0.0393193	0.0382775	0.0373915	0.0366475
3	0.0487784	0.0477407	0.0465904	0.0454147	0.0442698	0.0431899	0.0421946	0.0412937
4	0.0498597	0.0495225	0.0490014	0.0483388	0.0475829	0.0467770	0.0459564	0.0451480

Type III_4-(1). *a priori* distribution <0.6, 0.8>.

K \ n	5	6	7	8	9	10	11	12
0	0.0255318	0.0249757	0.0245259	0.0241621	0.0238703	0.0236399	0.0234631	0.0233336
1	0.0284437	0.0276294	0.0269505	0.0263837	0.0259115	0.0255200	0.0251984	0.0249382
2	0.0314627	0.0307152	0.0300114	0.0293672	0.0287879	0.0282734	0.0278212	0.0274280
3	0.0329321	0.0325577	0.0321205	0.0316538	0.0311815	0.0307198	0.0302797	0.0298679
4	0.0332961	0.0331988	0.0330377	0.0328207	0.0325606	0.0322707	0.0319635	0.0316492

Type III_4-(2). *a priori* distribution <0.5, 0.9>.

K \ n	5	6	7	8	9	10	11	12
0	0.0373068	0.0357170	0.0345563	0.0337288	0.0331674	0.0328237	0.0326609	0.0326504
1	0.0470725	0.0441791	0.0419124	0.0401497	0.0387957	0.0377772	0.0370368	0.0365294
2	0.0581165	0.0549320	0.0520687	0.0495785	0.0474606	0.0456917	0.0442398	0.0430711
3	0.0644356	0.0624622	0.0602568	0.0580103	0.0558478	0.0538439	0.0520382	0.0504472
4	0.0664017	0.0657381	0.0646889	0.0633429	0.0618091	0.0601884	0.0585621	0.0569911

Type III_4-(3). *a priori* distribution <0.45, 0.95>.

K \ n	5	6	7	8	9	10	11	12
0	0.0602557	0.0374961	0.0362253	0.0354289	0.0349982	0.0348562	0.0349462	0.0352260
1	0.0727794	0.0487518	0.0457088	0.0434700	0.0418609	0.0407501	0.0400379	0.0396487
2	0.0862031	0.0638145	0.0594591	0.0558314	0.0528849	0.0505437	0.0487263	0.0473568
3	0.0916009	0.0754997	0.0716660	0.0679273	0.0644864	0.0614415	0.0588254	0.0566329
4	0.0887024	0.0813435	0.0792176	0.0766131	0.0737829	0.0709331	0.0682100	0.0657062

Type III_4-(4). *a priori* distribution <0.4, 1.0>.

K \ n	5	6	7	8	9	10	11	12
0	0.0398230	0.0378712	0.0367394	0.0361929	0.0360794	0.0362956	0.0367689	0.0374466
1	0.0564882	0.0513847	0.0477975	0.0453345	0.0437126	0.0427289	0.0422370	0.0421297
2	0.0774264	0.0702579	0.0643927	0.0597687	0.0562212	0.0535702	0.0516529	0.0503327
3	0.0924675	0.0865842	0.0806309	0.0751540	0.0703980	0.0664258	0.0632061	0.0606665
4	0.0987946	0.0960607	0.0921716	0.0877001	0.0831415	0.0788321	0.0749614	0.0716123

Type III_5-(1). *a priori* distribution <0.6, 0.9>.

K \ n	5	6	7	8	9	10	11	12
0	0.0320752	0.0309226	0.0300381	0.0293653	0.0288646	0.0285074	0.0282720	0.0281412
1	0.0391111	0.0372198	0.0356714	0.0344118	0.0333950	0.0325837	0.0319478	0.0314628
2	0.0459802	0.0442531	0.0426070	0.0410984	0.0397503	0.0385679	0.0375472	0.0366793
3	0.0491599	0.0483181	0.0473022	0.0461955	0.0405634	0.0439536	0.0428986	0.0419192
4	0.0499232	0.0497089	0.0493364	0.0488170	0.0481792	0.0474577	0.0466866	0.0458960

Table 1.2-4

13	14	15	16	17	18	19	20
0. 0296310	0. 0296361	0. 0297074	0. 0298383	0. 0300228	0. 0302560	0. 0305335	0. 0308514
0. 0320241	0. 0318183	0. 0317002	0. 0316604	0. 0316905	0. 0317836	0. 0319336	0. 0321354
0. 0360327	0. 0355349	0. 0351432	0. 0348478	0. 0346397	0. 0345112	0. 0344551	0. 0344653
0. 0404912	0. 0397871	0. 0391791	0. 0386636	0. 0382361	0. 0378917	0. 0376254	0. 0374325
0. 0443718	0. 0436418	0. 0429676	0. 0423553	0. 0418083	0. 0413282	0. 0409151	0. 0405681

13	14	15	16	17	18	19	20
0. 0232463	0. 0231970	0. 0231822	0. 0231988	0. 0232443	0. 0233165	0. 0234134	0. 0235332
0. 0247322	0. 0245748	0. 0244610	0. 0243867	0. 0243484	0. 0243432	0. 0243684	0. 0244215
0. 0270898	0. 0268028	0. 0275633	0. 0263680	0. 0262136	0. 0260973	0. 0260164	0. 0259686
0. 0294885	0. 0291437	0. 0288344	0. 0285608	0. 0283224	0. 0281184	0. 0279477	0. 0278092
0. 0313363	0. 0310314	0. 0307397	0. 0304649	0. 0302098	0. 0299765	0. 0297663	0. 0295800

13	14	15	16	17	18	19	20
0. 0327699	0. 0330009	0. 0333286	0. 0337408	0. 0342272	0. 0347791	0. 0353892	0. 0360511
0. 0362190	0. 0360764	0. 0360770	0. 0362042	0. 0364388	0. 0367682	0. 0371810	0. 0376674
0. 0421535	0. 0414576	0. 0409569	0. 0406286	0. 0404522	0. 0404102	0. 0404872	0. 0406699
0. 0490736	0. 0479110	0. 0469486	0. 0461728	0. 0455694	0. 0451239	0. 0448224	0. 0446520
0. 0555174	0. 0541684	0. 0529598	0. 0518992	0. 0509881	0. 0502240	0. 0496017	0. 0491143

13	14	15	16	17	18	19	20
0. 0356630	0. 0362316	0. 0369116	0. 0376868	0. 0120654	0. 0757781	0. 0178594	0. 0524308
0. 0395234	0. 0396165	0. 0398915	0. 0403197	0. 0157724	0. 0763497	0. 0207016	0. 0538292
0. 0463681	0. 0457028	0. 0453124	0. 0451563	0. 0225895	0. 0773870	0. 0259940	0. 0564416
0. 0548390	0. 0534095	0. 0523076	0. 0514968	0. 0315689	0. 0787017	0. 0330992	0. 0599541
0. 0634729	0. 0615318	0. 0598854	0. 0585240	0. 0416864	0. 0800176	0. 0413049	0. 0639800

13	14	15	16	17	18	19	20
0. 0382898	0. 0392688	0. 0403606	0. 0415474	0. 0428147	0. 0441510	0. 0455469	0. 0469945
0. 0423277	0. 0427713	0. 0434149	0. 0442233	0. 0451689	0. 0462297	0. 0473881	0. 0486301
0. 0494987	0. 0490624	0. 0489530	0. 0491143	0. 0495013	0. 0500778	0. 0508144	0. 0516874
0. 0587221	0. 0572901	0. 0562953	0. 0556725	0. 0553661	0. 0553294	0. 0555232	0. 0559147
0. 0688004	0. 0665034	0. 0646801	0. 0632825	0. 0622619	0. 0615729	0. 0611740	0. 0610286

13	14	15	16	17	18	19	20
0. 0281014	0. 0281414	0. 0282520	0. 0284253	0. 0286547	0. 0289347	0. 0292602	0. 0296270
0. 0311086	0. 0308685	0. 0307287	0. 0306776	0. 0307053	0. 0308033	0. 0309644	0. 0311822
0. 0359534	0. 0353582	0. 0348825	0. 0345159	0. 0342489	0. 0340719	0. 0339775	0. 0339581
0. 0410278	0. 0402307	0. 0395301	0. 0389254	0. 0384141	0. 0379926	0. 0376567	0. 0374016
0. 0451110	0. 0443512	0. 0436317	0. 0429633	0. 0423536	0. 0418073	0. 0413271	0. 040. 142

Type III_5-(2). *a priori* distribution <0. 5, 1. 0>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0373860	0. 0354461	0. 0342079	0. 0334811	0. 0331390	[0. 0330942]	0. 0332841	0. 0336625
1	0. 0530459	0. 0485933	0. 0452583	0. 0428093	0. 0410581	0. 0398579	0. 0390957	0. 0386847
2	0. 0698986	0. 0647312	0. 0601513	0. 0562731	0. 0530920	0. 0505500	0. 0485706	0. 0470756
3	0. 0797026	0. 0763624	0. 0726131	0. 0688327	0. 0652702	0. 0620657	0. 0592813	0. 0569298
4	0. 0828834	0. 0817093	0. 0798144	0. 0773733	0. 0746163	0. 0717584	0. 0689680	0. 0663612

Type III_6. *a priori* distribution <0. 6, 1. 0>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0339470	0. 0321626	0. 0309346	0. 0301231	0. 0296318	0. 0293925	[0. 0293551]	0. 0294821
1	0. 0477783	0. 0442981	0. 0415075	0. 0393144	0. 0376256	0. 0363580	0. 0354408	0. 0348154
2	0. 0598368	0. 0566727	0. 0536177	0. 0508204	0. 0483516	0. 0462333	0. 0444594	0. 0430085
3	0. 0652367	0. 0637007	0. 0617870	0. 0596645	0. 0574808	0. 0553494	0. 0533491	0. 0515292
4	0. 0665344	0. 0661410	0. 0654249	0. 0643937	0. 0631021	0. 0616277	0. 0600523	0. 0584503

Type III_7. *a priori* distribution <0. 7, 1. 0>.

K \ n	5	6	7	8	9	10	11	12
0	0. 0292233	0. 0277538	0. 0266723	0. 0258917	0. 0253496	0. 0249998	0. 0248074	0. 0247457
1	0. 0401611	0. 0378867	0. 0359214	0. 0342608	0. 0328842	0. 0317642	0. 0308726	0. 0301818
2	0. 0473010	0. 0458009	0. 0442147	0. 0426343	0. 0411234	0. 0397231	0. 0384576	0. 0373385
3	0. 0495910	0. 0490809	0. 0483747	0. 0475107	0. 0465357	0. 0454971	0. 0444372	0. 0433917
4	0. 0499734	0. 0498839	0. 0497008	0. 0494065	0. 0489974	0. 0484819	0. 0478767	0. 0472031

Table 1.3. Optimum (n^*, K^*),

Types			Optimum (n^*, K^*)	minimum $\overline{E\ Loss}/NC$
I	(1)	<. 4, . 6>	(15, 0)	. 0239052
	(2)	<. 3, . 7>	(12, 0)	. 0345812
	(3)	<. 25, . 75>	(11, 0)	. 0374073
	(4)	<. 2, . 8>	(9, 0)	. 0392945
	(5)	<0, 1>	(6, 0)	. 0409523
II	II_1	<. 3, . 6>	(14, 0)	. 0302690 ☆
	II_2 (1)	<. 3, . 5>	(15, 0)	. 0237395 ○
	II_2 (2)	<. 2, . 6>	(12, 0)	. 0341340 ◎
	II_2 (3)	<. 15, . 65>	(11, 0)	. 0368376 ⊙
	II_3	<. 2, . 5>	(13, 0)	. 0296310 □
	II_4	<0, . 6>	(9, 0)	. 0360794 ▣
	II_5	<0, . 5>	(10, 0)	. 0330943 ■

Table 1.2-5

13	14	15	16	17	18	19	20
0.0341950	0.0348549	0.0356214	0.0364783	0.0374123	0.0384127	0.0394706	0.0405789
0.0385580	0.0386637	0.0389612	0.0394185	0.0400098	0.0407148	0.0415166	0.0424017
0.0459933	0.0452607	0.0448240	0.0446384	0.0446660	0.0448756	0.0452411	0.0457408
0.0549953	0.0534468	0.0522473	0.0513588	0.0507450	0.0503725	0.0502116	0.0502360
0.0640090	0.0619472	0.0601870	0.0587235	0.0575420	0.0566229	0.0559441	0.0554833

13	14	15	16	17	18	19	20
0.0297450	0.0301215	0.0305940	0.0311483	0.0317732	0.0324591	0.0331984	0.0339845
0.0344336	0.0342563	0.0342513	0.0343925	0.0346584	0.0350311	0.0354962	0.0360411
0.0418527	0.0409614	0.0403052	0.0398563	0.0395897	0.0394832	0.0395172	0.0396746
0.0499166	0.0485217	0.0473438	0.0463751	0.0456035	0.0450148	0.0445940	0.0443261
0.0568833	0.0553986	0.0540297	0.0527981	0.0517161	0.0507886	0.0500150	0.0493912

13	14	15	16	17	18	19	20
0.0247937	0.0249346	0.0251552	0.0254445	0.0257935	0.0261948	0.0266422	0.0271303
0.0296674	0.0293069	0.0290812	0.0289733	0.0289688	0.0290550	0.0292211	0.0294577
0.0363691	0.0355469	0.0348659	0.0343181	0.0338943	0.0335850	0.0333808	0.0332725
0.0423887	0.0414491	0.0405878	0.0398144	0.0391343	0.0385496	0.0380601	0.0376637
0.0464843	0.0457432	0.0450006	0.0442751	0.0435821	0.0429337	0.0423396	0.0418064

Minimum $\overline{E\ Loss}/NC$.

Types			Optimum (n^*, $K*$)	minimum $\overline{E\ Loss}/NC$
III	III_1	<.4, .7>	(14, 0)	.0302690 ☆
	III_2	(1) <.5, .7>	(15, 0)	.0237394 ○
		(2) <.4, .8>	(12, 0)	.0341340 ◎
		(3) <.35, .85>	(11, 0)	.0368376 ⊙
		(4) <.3, .9>	(9, 0)	.0385605
	III_3	<.5, .8>	(13, 0)	.0296310 □
	III_4	(1) <.6, .8>	(15, 0)	.0231822
		(2) <.5, .9>	(12, 0)	.0326504
		(3) <.45, .95>	(10, 0)	.0348562
		(4) <.4, 1>	(9, 0)	.0360794 ⬚
	III_5	(1) <.6, .9>	(13, 0)	.0281014
		(2) <.5, 1>	(10, 0)	.0330942 ■
	III_6	<.6, 1>	(11, 0)	.0293551
	III_7	<.7, 1>	(13, 0)	.0247937

Table 1.3 FACOM 270-20/30 FORTRAN LIST

Program for computation of $\overline{E\ Loss}/NC$ based on (1.13)

```
      COMMON A (4, 25, 21)
      REWIND 0
    6 READ (40, 101), I 1, I 2
  101 FORMAT (I 2, I 2)
      IF (I 1) 9, 8, 10
    8 DO 11 J=1, 21
      DO 11 K=1, 25
   11 A (1, K, J)=0.0
      GO TO 3
   10 DO 2 I=1, I 1
***
    2 READ (80) ((A (1, K, J), K=1, 25), J=1, 21)
      REWIND 0
    3 IF (I 2-20) 12, 13, 9
   13 DO 14 J=1, 21
      DO 14 K=1, 25
   14 A (2, K, J)=1.0
      GO TO 15
   12 DO 4 I=1, I 2
    4 READ (80) ((A (2, K, J), K=1.25), J=1, 21)
      REWIND 0
***
   15 I 3=20-I 1
      I 4=20-I 2
      IF (I 4) 9, 30, 60
   30 DO 31 J=1, 21
      DO 31 K=1, 25
   31 A (4, K, J)=0.0
      GO TO 34
   60 IF (I 4-20) 40, 41, 9
   41 DO 42 J=1, 21
      DO 42 K=1, 25
***
   42 A (4, K, J)=1.0
      GO TO 34
   40 DO 33 I=1, I 4
   33 READ (80) ((A (4, K, J), K=1, 25), J=1, 21)
      REWIND 0
   34 IF (I 3) 9, 35, 61
   35 DO 36 J=1, 21
      DO 36 K=1, 25
   36 A (3, K, J)=0.0
      GO TO 62
***
   61 IF (I 3-20) 43, 44, 9
   44 DO 45 J=1, 21
      DO 45 K=1, 25
   45 A (3, K, J)=1.0
      GO TO 62
   43 DO 39 I=1, I 3
   39 READ (80) ((A(3, K, J), K=1, 25), J=1, 21)
      REWIND 0
```

```
   62 DO 5 N=5, 20
      DO 5 K=1, 5
***
      ST=0.0
      DO 7 IR=K, N
      NR=N-IR+1
      DO 7 J=1, NR
      J1=J+1
      K1=N-J+2
      K2=N-IR-J+2
      J2=IR+J
      J3=J
      J4=J2+1
***
      C1=J3
      C2=J2
      X1=A (1, J1, K1)
      X2=A (2, J1, K1)
      X3=A (1, J2, K2)
      X4=A (2, J2, K2)
      X5=A (1, J3, K1)
      X6=A (2, J3, K1)
      X7=A (1, J4, K2)
      X8=A (2, J4, K2)
***
      IF (J1-K1) 50, 51, 51
   50 X1=1.0-A (3, K1, J1)
      X2=1.0-A (4, K1, J1)
   51 IF (J2-K2) 52, 53, 53
   52 X3=1.0-A (3, K2, J2)
      X4=1.0-A (4, K2, J2)
   53 IF (J3-K1) 54, 55, 55
   54 X5=1.0-A (3, K1, J3)
      X6=1.0-A (4, K1, J3)
   55 IF (J4-K2) 56, 57. 57
***
   56 X7=1.0-A (3, K2, J4)
      X8=1.0-A (4, K2, J4)
   57 SS=C1*(X2-X1)*(X4-X3)-C2*(X6-X5)*(X8-X7)
    7 ST=ST+SS
      CN=N
      CI1=I1
      CI1=0.05*CI1
      CI2=I2
      CI2=0.05*CI2
      D=(1.0-CN/50.0)/(((CI2-CI1)*(CN+1.0))*((CI2-CI1)*(CN+1.0))*(CN+2.
***
     10))
      D=D*ST+(CI2-CI1)/6.0
      WRITE (50, 200) N, K, CI1, CI2, D
  200 FORMAT (2I 5, 3F 14.7)
    5 CONTINUE
      GO TO 6
    9 STOP
      END
```

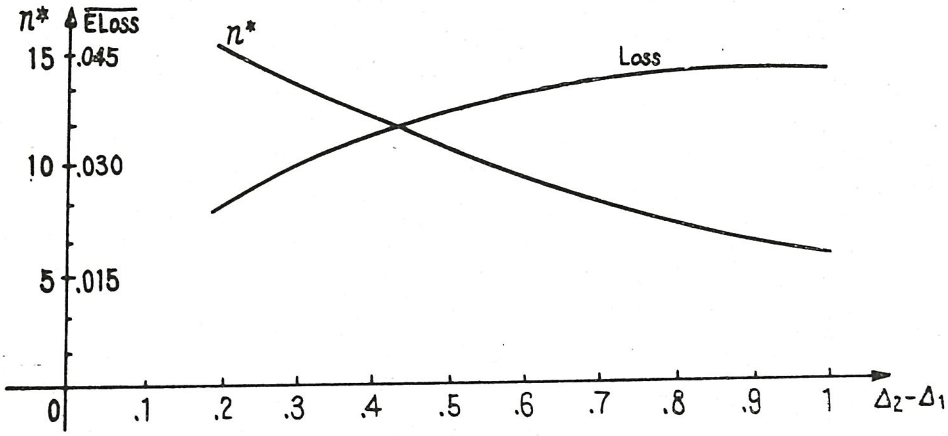


Fig. 1.1. Optimal n^* and Minimum $\overline{E\ Loss}/NC$ (Center 0.5).

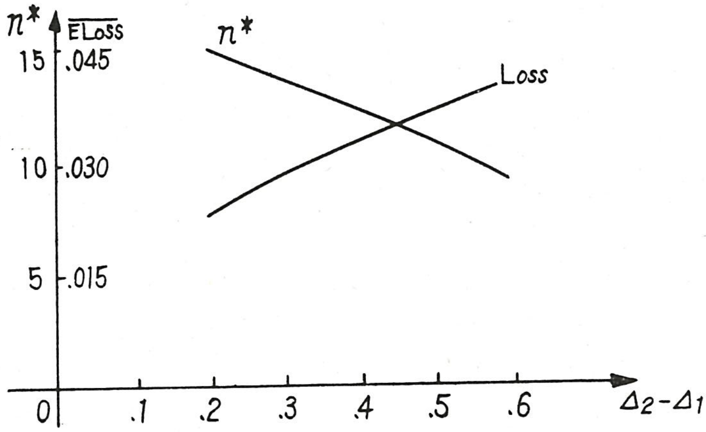


Fig. 1.2. Optimal n^* and Minimum $\overline{E\ Loss}/NC$ (Center 0.4).

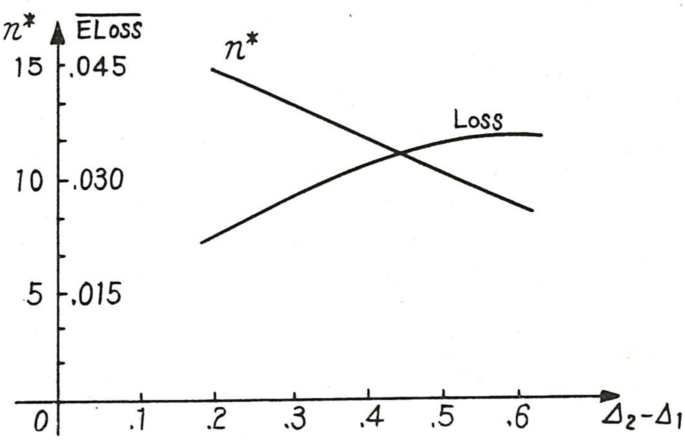


Fig. 1.3. Optimal n^* and Minimum $\overline{E\ Loss}/NC$ (Center 0.3 or 0.7).

Part II. Sequential Plan 3

2.1 Assumption

The assumptions are prepared throughout this Part as follows. These are

(1) These are N patients with a disease who are to be treated with one of the two treatments A and B. The effective proportions of both treatments, denoted by $\mathfrak{p}_A$ and $\mathfrak{p}_B$, are unknown $(j=A, B)$. N is fixed and large.

(2) We suppose that the clinical trial does not call for the fixed number of the participants, but the trial is perfomed sequentially on each pair of two patients chosen at random from all of the N patients by administrating treatment A on the one patient and B on the other. We shall use symbol 1 for the result of effectiveness and symbol 0 for the result of ineffectiveness. Let $a_1, a_2, \cdots, a_n$ be the results observed by performing treatment A from the first patient until the n-th patient, and $b_1, b_2, \cdots, b_n$ the results observed by performing treatment B from the first patient until the n-th patient. These results are arranged in the order observed.

$$(a_1, b_1), (a_2, b_2), \cdots, (a_n, b_n).$$

Let t_1 be the number of pairs (1, 0) and t_2 the number of pairs (0, 1) in this sequence. We want to consider only the pairs (0, 1) and (1, 0) throughout this Part.

Let a be the outcome of an observation obtained by performing treatment A (i.e., from the first population) and b the outcome of an observation obtained by performing B (i.e., from the second population). It is assumed that a is a binomial random variable with a population proportion $\mathfrak{p}_A$ and b is a binimial random variable with a population proportion $\mathfrak{p}_B$. Whence variable t_2 is distributed according to the binomial distribution so that the number of trials is $t=t_1+t_2$ and the parameter is a proportion

$$\mathfrak{p}=\frac{\mathfrak{p}_B(1-\mathfrak{p}_A)}{\mathfrak{p}_A(1-\mathfrak{p}_B)+\mathfrak{p}_B(1-\mathfrak{p}_A)}.$$

For each of the two treatments, odds $\mathfrak{p}_j/(1-\mathfrak{p}_j)$ indicates the number of the effective patients per ineffective patient, where $j=A, B$. We shall use the odds $\mathfrak{p}_j/(1-\mathfrak{p}_j)$ instead of the effective proportion $\mathfrak{p}_j$ as the parameter representing the effectiveness of the j-th treatment. Moreover, consider the odds ratio

$$\delta=\frac{\mathfrak{p}_B/(1-\mathfrak{p}_B)}{\mathfrak{p}_A/(1-\mathfrak{p}_A)}=\frac{\mathfrak{p}_B(1-\mathfrak{p}_A)}{\mathfrak{p}_A(1-\mathfrak{p}_B)},$$

the superiority or the inferiority of each treatment then may be measured by the outcome of the odds ratio δ, that is, treatment A is superior to treatment B if and only if $0 \leqq \delta < 1$ and treatment A is inferior to treatment B if and only if $\delta > 1$.

(3) The only cost involved is the consequence of treating a patient with the superior or the inferior of the two treatments and all other costs may be disregarded from the ethical point of view stated in our previous papers [6], [7], [8]. Moreover, it is assumed that the cost is directly proportional to the true value of the odds ratio δ, that is, in terms of the loss formulation, if a patient is treated with the inferior treatment a positive loss proportional to δ is scored for him.

(4) We shall assume that an *a priori* distribution for the odds ratio δ may be given by a probability density function $f(\delta)$, where $0 \leqq \Delta_1 \leqq \delta \leqq \Delta_2 < \infty$ for the preassigned values Δ_1 and Δ_2 ($0 \leqq \Delta_1 < 1$, $\Delta_2 > 1$).

2.2 Procedure

On the basis of the cumulative results t_2 that are observed by performing sequentially treatment A on one individual in each pair and treatment B on the other from the first pair until the n-th, a decision is made to select one of the two treatments as the better and use it on the remaining patients or to continue the trial by having an additional pair.

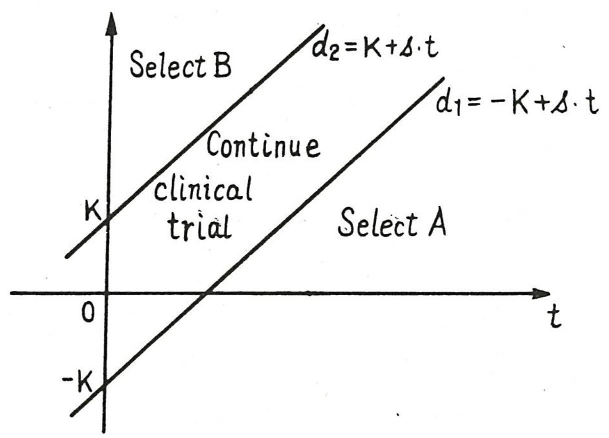
Then the next procedure is proposed.

Procedure: After the t-th pair,

if $t_2 \leqq -K + s \cdot t$, use treatment A on the remaining patients;

if $t_2 \geqq K + s \cdot t$, use treatment B on the remaining patients;

if $-K + s \cdot t < t_2 < K + s \cdot t$, continue the trial with another pair, where K is



a parameter that indicates the location of the boundaries and s is a parameter that indicates the common slope of the two parallel decision lines.

The problem is to determine the parameters K and s such that the expected loss is minimized.

Let $d_1=-K+s\cdot t$ and $d_2=K+s\cdot t$ briefly.

2.3 Construction of Overall Expected Loss Function

We assume now that a decision for selecting one of the two treatments has been already made in the t-th stage.

For any value δ, we shall denote by $L(\delta)$ the probability of selecting treatment A as the result of the decision made in the beforementioned procedure. The approximation formula gives

$$L(\delta)=\frac{e^{Kv}}{1+e^{Kv}} \text{ and } 1-L(\delta)=\frac{1}{1+e^{Kv}}, \tag{2. 1}$$

where v is any one non-zero real number that satisfies the following relation:

$$\mathfrak{p}=\frac{e^{sv}-1}{e^{v}-1} \quad \left(\mathfrak{p}=\frac{\mathfrak{p}_B(1-\mathfrak{p}_A)}{\mathfrak{p}_A(1-\mathfrak{p}_B)+\mathfrak{p}_B(1-\mathfrak{p}_A)}=\frac{\delta}{1+\delta}\right).$$

Therefore,

$$E(t)=\frac{K(2L(\delta)-1)}{s-\mathfrak{p}}=\frac{K(e^{Kv}-1)}{(s-\mathfrak{p})(1+e^{Kv})}, \tag{2. 2}$$

where $E(t)$ denotes the A.S.N. (the average number of the patients necessary for making a decision).

Note that we are merely concerned with the number t of the favorable pairs (0, 1) and (1, 0). (For the sake of computing the expected value of the total number of the pairs including also the pairs (0, 0) and (1, 1), we have merely to multiple the righthand side of the equation (2.2) by

$$\frac{1}{\mathfrak{p}_A(1-\mathfrak{p}_B)+\mathfrak{p}_B(1-\mathfrak{p}_A)}=\frac{1}{\mathfrak{p}_A+\mathfrak{p}_B-2\mathfrak{p}_A\mathfrak{p}_B}$$

where the multiplier means the expected number of trials required for each time of appearance of either the favorable pair (0, 1) or (1, 0). But, we have only to consider the matter connected with variable t, since we concentrate our considerations on the loss.)

If treatment B is inferior to A (i.e., $\delta<1$), then the expected loss $[E\ Loss]_B$ due to performing B is obtained by assumption (3) and the abovementioned procedure as follows.

$$(2.\ 3)\qquad \begin{aligned}[E\ Loss]_B &= C\delta[E(t)+(N-2E(t))\cdot Pr(\text{Select inferior})]\\ &= C\delta[E(t)+(N-2E(t))\cdot Pr(\text{Select } B)]\\ &= C\delta[E(t)+(N-2E(t))\cdot\{1-Pr(\text{Select } A)\}]\\ &= C\delta[E(t)+(N-2E(t))\cdot(1-L(\delta))],\end{aligned}$$

where C denotes a proportionality factor.

In the same manner, if treatment A is inferior to B (i.e., $\delta>1$), then the expected loss $[E\ Loss]_A$ due to performing A is obtained as follows.

$$(2.\ 4)\qquad \begin{aligned}[E\ Loss]_A &= C\delta[E(t)+(N-2E(t))\cdot Pr(\text{Select inferior})]\\ &= C\delta[E(t)+(N-2E(t))\cdot Pr(\text{Select } A)]\\ &= C\delta[E(t)+(N-2E(t))\cdot L(\delta)].\end{aligned}$$

By integrating over an *a priori* distribution of δ, the overall expected loss $\overline{E\ Loss}$ is obtained.

$$(2.\ 5)\qquad \begin{aligned}\overline{E\ Loss}/NC &= \frac{1}{NC}\left\{\int_{\Delta_1}^{1}[E\ Loss]_B f(\delta)d\delta+\int_1^{\Delta_2}[E\ Loss]_A f(\delta)d\delta\right\}\\ &= \int_{\Delta_1}^{1}\delta\left\{\frac{E(t)}{N}+\left(1-\frac{2E(t)}{N}\right)(1-L(\delta))\right\}f(\delta)d\delta\\ &\quad+\int_1^{\Delta_2}\delta\left\{\frac{E(t)}{N}+\left(1-\frac{2E(t)}{N}\right)L(\delta)\right\}f(\delta)d\delta.\end{aligned}$$

Assumption (4′): We should like to suppose here upon a uniform probability distribution $f(\delta)=\dfrac{1}{\Delta_2-\Delta_1}$ about an *a priori* distribution for δ.

Moreover, it may be and will be assumed that $\mathfrak{p}=\delta_1/(\delta_1+1)$ approximately for $\delta<1$ where $\delta_1=(\Delta_1+1)/2$, and similarly $\mathfrak{p}=\delta_2/(\delta_2+1)$ approximately for $\delta>1$ where $\delta_2=(\Delta_2+1)/2$. Therefore,

$$L(\delta)=\frac{e^{vK}}{1+e^{vK}},$$

where v is any one non-zero real number that satisfies the relation for $\delta<1$:

$$(2.\ 6.\ 1)\qquad \frac{\delta_1}{\delta_1+1}=\frac{e^{vs}-1}{e^{v}-1}$$

and the relation for $\delta>1$:

$$(2.\ 6.\ 2)\qquad \frac{\delta_2}{\delta_2+1}=\frac{e^{vs}-1}{e^{v}-1}$$

and so $L(\delta)$ are independent of the parameters $\mathfrak{p}$ and δ in both cases. Let us denote the v satisfying (2.6.1) by v_1 and the v satisfying (2.6.2) by v_2.

Thus, if we take into consideration the assumption (4′) and the abovementioned approximate condition, then the overall expected loss $\overline{E\ Loss}/NC$ results in the next formula (2.7).

$$\text{(2.7)}\quad \overline{E\ Loss}/NC=\frac{1}{\Delta_2-\Delta_1}\left[\int_{\Delta_1}^{1}\delta\left(1-\frac{E_1(t)}{N}\right)d\delta-\int_{\Delta_1}^{1}\delta\left(1-\frac{2E_1(t)}{N}\right)L_1 d\delta\right.$$
$$\left.+\int_1^{\Delta_2}\delta\cdot\frac{E_2(t)}{N}d\delta+\int_1^{\Delta_2}\delta\left(1-\frac{2E_2(t)}{N}\right)L_2 d\delta\right]$$
$$=\frac{1}{\Delta_2-\Delta_1}\left[(1-L_1)\int_{\Delta_1}^{1}\delta\, d\delta-\frac{(1-2L_1)}{N}\int_{\Delta_1}^{1}\delta E_1(t)d\delta\right.$$
$$\left.+L_2\int_1^{\Delta_2}\delta\, d\delta+\frac{(1-2L_2)}{N}\int_1^{\Delta_2}\delta E_2(t)d\delta\right],$$

where

$$\text{(2.8)}\quad L_i=\frac{e^{Kv_i}}{1+e^{Kv_i}}$$ and v_i is any one non-zero real number that satisfies the relation:

$$\text{(2.9)}\quad \mathfrak{p}_i=\frac{e^{sv_i}-1}{e^{v_i}-1}\ \text{ and }\ \mathfrak{p}_i=\frac{\delta_i}{\delta_i+1}=\frac{\Delta_i+1}{\Delta_i+3}\qquad (i=1,\ 2),\ \text{and also}$$

$$\text{(2.10)}\quad E_i(t)=\frac{K(2L_i-1)}{s-\mathfrak{p}}=\frac{K(2L_i-1)(\delta+1)}{s+(s-1)\delta}\qquad (i=1,\ 2).$$

Whence,

$$\text{(2.11)}\quad \overline{E\ Loss}/NC=\frac{1}{\Delta_2-\Delta_1}\left[\frac{1-\Delta_1^2}{2(1+e^{Kv_1})}+\frac{K(1-e^{Kv_1})^2}{N(1+e^{Kv_1})^2}\int_{\Delta_1}^{1}\frac{\delta(1+\delta)}{s+(s-1)\delta}d\delta\right.$$
$$\left.+\frac{(\Delta_2^2-1)e^{Kv_2}}{2(1+e^{Kv_2})}-\frac{K(1-e^{Kv_2})^2}{N(1+e^{Kv_2})^2}\int_1^{\Delta_2}\frac{\delta(1+\delta)}{s+(s-1)\delta}d\delta\right]$$
$$=\frac{1}{\Delta_2-\Delta_1}\left[\frac{1-\Delta_1^2}{2(1+e^{Kv_1})}-\frac{K(1-e^{Kv_1})^2}{N(1+e^{Kv_1})^2}\cdot\right.$$
$$\frac{1}{2(s-1)^3}\left\{((s-1)\Delta_1-1)^2-(s-2)^2-2s\log\left|\frac{2s-1}{s+(s-1)\Delta_1}\right|\right\}$$
$$+\frac{(\Delta_2^2-1)e^{Kv_2}}{2(1+e^{Kv_2})}-\frac{K(1-e^{Kv_2})^2}{N(1+e^{Kv_2})^2}\cdot$$
$$\left.\frac{1}{2(s-1)^3}\left\{((s-1)\Delta_2-1)^2-(s-2)^2+2s\log\left|\frac{s+(s-1)\Delta_2}{2s-1}\right|\right\}\right].$$

For the purpose of determinating the optimum values K^*, s^* of the parameters K, s so that $\overline{E\ Loss}/NC$ of (2.11) is minimized, we should like to partially differentiate (2.11) by K and s, and set these derivatives equal to zero. Whence the next relations are obtained.

The first relation is

$$\frac{(1-\Delta_1^2)v_1e^{Kv_1}}{(1+e^{Kv_1})^2}+\frac{(1-e^{Kv_1})(1-4v_1Ke^{Kv_1}-e^{2Kv_1})}{N(s-1)^3(1+e^{Kv_1})^3}\cdot \left\{((s-1)\Delta_1-1)^2-(s-2)^2-2s\log\left|\frac{2s-1}{s+(s-1)\Delta_1}\right|\right\}$$
$$=\frac{(\Delta_2^2-1)v_2e^{Kv_2}}{(1+e^{Kv_2})^2}-\frac{(1-e^{Kv_2})(1-4v_2Ke^{Kv_2}-e^{2Kv_2})}{N(s-1)^3(1+e^{Kv_2})^3}\cdot \left\{((s-1)\Delta_2-1)^2-(s-2)^2+2s\log\left|\frac{s+(s-1)\Delta_2}{2s-1}\right|\right\}. \tag{2.12}$$

The second relation is

$$\left\{\frac{(1-\Delta_1^2)Ke^{Kv_1}v_1}{(1+e^{Kv_1})^2\left\{\left(\frac{1+\Delta_1}{3+\Delta_1}\right)e^{(1-s)v_1}-s\right\}}\right\}$$
$$+\frac{K}{N}\left\{\frac{-4Kv_1e^{Kv_1}(1-e^{Kv_1})\left(((s-1)\Delta_1-1)^2-(s-2)^2-2s\log\left|\frac{2s-1}{s+(s-1)\Delta_1}\right|\right)}{(1+e^{Kv_1})^3(s-1)^3\left\{\left(\frac{1+\Delta_1}{3+\Delta_1}\right)e^{(1-s)v_1}-s\right\}}\right.$$
$$\left.+\frac{(1-e^{Kv_1})^2\left[(1-\Delta_1)\{(1+\Delta_1)s^2-2(3+\Delta_1)s+5+\Delta_1\}-\frac{2(1-\Delta_1)s(s-1)}{(2s-1)(s+(s-1)\Delta_1)}+2(2s+1)\log\left|\frac{2s-1}{s+(s-1)\Delta_1}\right|\right]}{(1+e^{Kv_1})^2(s-1)^4}\right\} \tag{2.13}$$

$$=\left\{\frac{(\Delta_2^2-1)Kv_2e^{Kv_2}}{(1+e^{Kv_2})^2\left\{\left(\frac{1+\Delta_2}{3+\Delta_2}\right)e^{(1-s)v_2}-s\right\}}\right\}$$
$$-\frac{K}{N}\left\{\frac{-4Kv_2e^{Kv_2}(1-e^{Kv_2})\left(((s-1)\Delta_2-1)^2-(s-2)^2+2s\log\left|\frac{s+(s-1)\Delta_2}{2s-1}\right|\right)}{(1+e^{Kv_2})^3(s-1)^3\left\{\left(\frac{1+\Delta_2}{3+\Delta_2}\right)e^{(1-s)v_2}-s\right\}}\right.$$

$$+\frac{(1-e^{Kv_2})^2\Big[(1-\Delta_2)\{(1+\Delta_2)s^2-2(3+\Delta_2)s+5+\Delta_2\}}{}\cdots\cdots$$

$$\cdots\cdots\frac{+\dfrac{2(\Delta_2-1)s(s-1)}{(2s-1)(s+(s-1)\Delta_2)}-2(2s+1)\log\left|\dfrac{s+(s-1)\Delta_2}{2s-1}\right|\Big]}{(1+e^{Kv_2})^2(s-1)^4}\Bigg\}.$$

Thus, compute respectively the values v_1, v_2 from (2.6.1) and (2.6.2) for the preassigned Δ_1 and Δ_2, where v_1, v_2 are obtained in the forms of functions of parameter s. Secondly, substitute these values of v_1, v_2 for (2.12) and (2.13) and numerically work at the two equations (2.12) and (2.13) with regard to K and s. Finally, the optimum values K^*, s^* of the two parameters K, s so that $\overline{E\ Loss}/NC$ of (2.11) is minimized will be determined. Moreover, substituting these optimum values K^*, s^* for $\overline{E\ Loss}/NC$ of (2.11), the minimized value $[\overline{E\ Loss}/NC]_{K^*,s^*}$ of $\overline{E\ Loss}/NC$ will be obained.

We should be concerned with some numerical examples in the next section.

2.4 Numerical Examples

In our numerical examples, we shall fix the value of the slope s, that is, $s=0.75$, 0.85 for simplification, and consider various cases of *a priori* distributions for δ on the basis of the assumption (4′), where let $N=100$ in all cases.

The given types of *a priori* distribution: $0\leqq\Delta_1<1<\Delta_2$, where $<\Delta_1, \Delta_2>=$ $<0.667, 1.5>$, $<0.5, 2>$, $<0.333, 3>$, $<0.25, 4>$, $<0.2, 5>$, $<0.167, 6>$, and $<0.1, 10>$.

In the first place, compute numerically v_i from (2.6.1) and (2.6.2) for $i=1, 2$. Since the value of the slope now has been fixed, we may next compute only the value of the optimum K^*. Whence the value of the optimum K^* is merely numerically computed from (2.12) for each given $<\Delta_1, \Delta_2>$ and each fixed s, and the value of $[\overline{E\ Loss}/NC]_{K^*,s}$ for each K^* and each given s is obtained from (2.11). The computed values of K^* and the values of $[\overline{E\ Loss}/NC]_{K^*,s}$ for K^* and s are given in Table 2.1, and the two curves of points $(\log_{10}\Delta_2-\log_{10}\Delta_1, [\overline{E\ Loss}/NC]_{K^*,s})$ are given in Figure 2.1.

From Table 2.1 and Figure 2.1, the next conclusions may be introduced.

Conclusions: (1) In both cases of $s=0.75$ and 0.85, $[\overline{E\ Loss}/NC]_{K^*,s}$ increases as the width of the interval of given *a priori* distribution increases, but the degree of the increase grows rather flat for larger values of the width. (2) It seems that $[\overline{E\ Loss}/NC]_{K^*,.75}$ have less values than that of $[\overline{E\ Loss}/NC]_{K^*,.85}$.

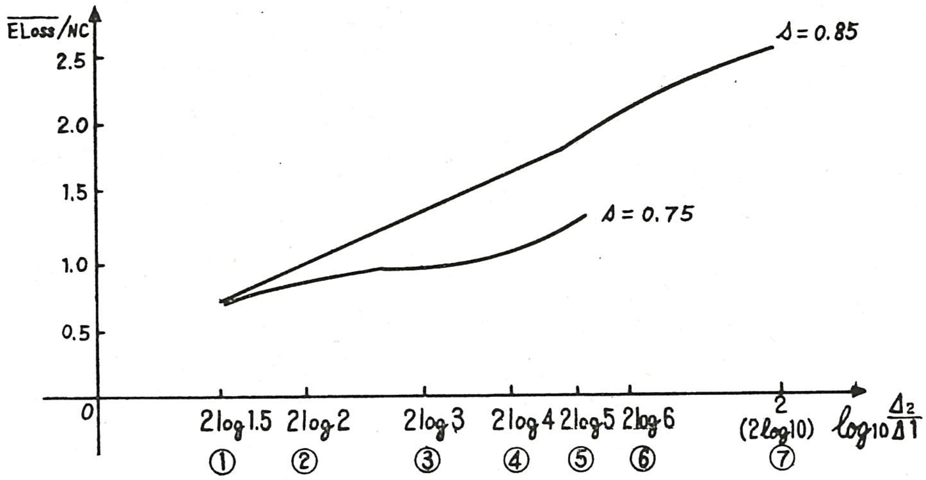


Fig. 2.1. Gurves ($\log_{10}\frac{\Delta_2}{\Delta_1}$, $[\overline{E\ Loss}/NC]_{K^*,s}$).

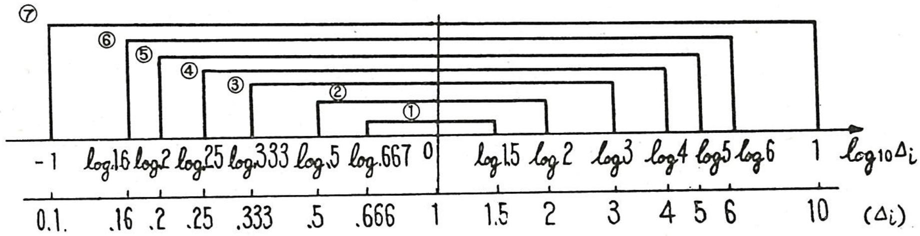


Fig. 2.2. The given *a priori* distributions.

Table 2.1. K^* and $[\overline{E\ Loss}/NC]_{K^*,s}$ ($N=100$).

$\log_{10}\frac{\Delta_2}{\Delta_1}$	s / $<\Delta_1, \Delta_2>$	0.85 K^*	0.85 $[\overline{E\ Loss}/NC]_{K^*,.85}$	0.75 K^*	0.75 $[\overline{E\ Loss}/NC]_{K^*,.75}$
① $2\log_{10} 1.5$	$<.667, 1.5>$	1.27060	0.72374	1.81120	0.68574
② $2\log_{10} 2$	$<.5, 2>$	1.32230	0.94197	1.76030	0.84873
③ $2\log_{10} 3$	$<.333, 3>$	1.39170	1.33946	0.36340	0.87475
④ $2\log_{10} 4$	$<.25, 4>$	1.35100	1.65285	—	—
⑤ $2\log_{10} 5$	$<.2, 5>$	1.13890	1.83584	1.23870	1.25459
⑥ $2\log_{10} 6$	$<.167, 6>$	1.34660	2.13067	—	—
⑦ $2\log_{10} 10$	$<.1, 10>$	0.10780	2.52420	—	—

Table 2.1 FACOM 270-20/30 FORTRAN LIST

Program for computation of v_i based on (2.9)

```
      DIMENSION D (20), S (9)
      READ (40, 100), (S (I), I=1, 9)
      READ (40, 101), (D (I), I=1, 20)
  100 FORMAT (9F 4.2)
```

```
101 FORMAT (10F 7.3)
    DO 1 I=1, 9
    SS=S (I)
    DO 1 J=1, 20
    W=15.0
    K=0
***
    C1=2.0/(D(J)+3.0)
    C2=(D(J)+1.0)/(D(J)+3.0)
  9 A=EXP (W)
    K=K+1
    AS=A**SS
    V=W-(C1+C2*A-AS)/(C2*A-SS*AS)
    IF (ABS(V-W)-1.E-8) 3, 3, 10
 10 W=V
    IF (K-40) 9, 3, 3
  3 WRITE (50, 200), S (I), D (J), V, V, K
***
  1 WRITE (30, 300), S (I), D (J), V
    STOP
200 FORMAT (F 7.4, F 12.5, F 16.10, E 17.5, I7)
300 FORMAT (2E 12.5, E 18.9)
    END
```

Program for computation of K^* based on (2.12)

```
  1 READ (40, 100) S, D1, D2, V1, V2
    FK=-0.09999999
    DISS=0.0
    DF=0.1
  2 C1=V1*(1.0-D1**2)
    C2=100.0*(S-1.0)*(S-1.0)*(S-1.0)
    C20=(2.0*S-1.0)/(S+(S-1.0)*D1)
    C3=((S-1.0)*D1-1.0)*((S-1.0)*D1-1.0)-(S-2.0)*(S-2.0)-2.0*S*ALOG(ABS(C20))
    C4=V2*(D2**2-1.0)
***
    C21=(S+(S-1.0)*D2)/(2.0*S-1.0)
    C5=((S-1.0)*D2-1.0)*((S-1.0)*D2-1.0)-(S-2.0)*(S-2.0)+2.0*S*ALOG(ABS(C21))
  3 FK=FK+DF
    EA=FK*V1
    A=EXP (EA)
    TL=C1*A/((1.0+A)*(1.0+A))+C3*(1.0-A)*(1.0-4.0*EA*A-A*A)/(C2*(C2*(1.0+A)**3)
    EB=FK*V2
    B=EXP (EB)
***
    TR=C4*B/((1.0+B)*(1.0+B))-C5*(1.0-B)*(1.0-4.0*EB*B-B*B)/(C2*(1.0+B)**3)
    DIS=TR-TL
    IF (DIS*DISS) 5, 4, 4
  4 DISS=DIS
    IF (FK-50.0) 3, 8, 8
  5 IF (DF-0.0001) 7, 7, 6
  6 FK=FK-DF
    DF=DF*0.1
    GO TO 3
***
  7 WRITE (50, 200) S, D1, D2, V1, V2, FK
```

```
      GO TO 1
    8 WRITE (50, 200) S, D1, D2, V1, V2
      GO TO 1
  100 FORMAT (F 3.2, 2F 6.3, 2F 8.7)
  200 FORMAT (3F 10.4, 3F 15.8)
      END
```

Program for computation of $\overline{E\ Loss}/NC$ based on (2.11)

```
      WRITE (50, 201)
  201 FORMAT (4H S, 8X, 2H D1, 7X, 2H D2, 2X, 2H V1, 7X, 2H V2, 12X, 1HK, 13X, 5HELOSS)
    1 READ (40, 100), S, D1, D2, V1, V2, FK
  100 FORMAT (F 3.2, F 4.3, F 6.3, 2F 8.7, F 5.4)
      EA=FK*V1
      EB=FK*V2
      A=EXP (EA)
      B=EXP (EB)
      T1=((1.0+D1)*(1.0-D1))/(2.0*(1.0+A))
      T3=(B*(D2-1.0)*(D2+1.))/(2.0*(1.0+B))
***
      U=(2.0*S-1.0)/(S+(S-1.0)*D1)
      C1=((S-1.0)*D1-1.0)*((S-1.0)*D1-1.0)-(S-2.0)*(S-2.0)-2.0*S*ALOG (U)
      C1=C1/(2.0*(S-1.0)*(S-1.0)*(S-1.0))
      T=((FK*(1.0-A)*(1.0-A))/(100.0*(1.0+A)*(1.0+A)))*C1
      R=(S+(S-1.0)*D2)/(2.0*S-1.0)
      C2=((S-1.0)*D2-1.0)*((S-1.0)*D2-1.0)-(S-2.0)*(S-2.0)+2.0*S*ALOG (R)
      C2=C2/(2.0*(S-1.0)*(S-1.0)*(S-1.0))
      T4=((C2*FK*(1.0-B)*(1.0-B))/(100.0*(1.0+B)*(1.0+B))
      T=(T1-T+T3-T4)/(D2-D1)
      WRITE (50, 200), S, D1, D2, V1, V2, FK, T
***
  200 FORMAT (F 7.3, F 9.3, F 9.3, F 10,6, F 10.6, F 16.10, F 16.10, /)
      GO TO 1
      STOP
      END
```

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