Kumamoto J. Sci., Ser. A, Vol. 8, No. 2, pp. 63–83 (1967)

OPTIMUM DESIGNS FOR SELECTING ONE OF THE TWO TREATMENTS, GENERAL CONSIDERATIONS

By

Masahiko SUGIMURA

Department of Mathematics and Physics, Kumamoto Women's University
(Received September 30, 1967)

Introduction

I. The problem to determine the optimum statistical procedure, in some specified sense, for choosing between two populations in the light of samples drawn from them, is very important in practical situations. In recent years, there have been a number of papers on this subject.

Let us enunciate this problem in the concrete form.

(1) We shall perform the two given treatments denoted by A and B on individuals drawn from a large number of individuals, treatment A on the first half individuals and treatment B on the rest, where the effects of treatments A and B are unknown to us.

Let us call the above trial *the preliminary trial.*

(2) We shall select one of the two treatments according to a certain statistical procedure in view of the observations supplied by the samples obtained in the preliminary trial, and then perform the selected treatment on all of the remaining individuals.

(3) In considering such a scheme mentioned at (1) and (2), we shall proceed to determine the optimum statistical procedure satisfying a certain criterion in some specified class of procedures.

Then our problem is what criterion we should specify in (3). We shall give the formulation of our criterion from the point of view of decision theory.

Let us now denote by δ an unknown parameter indicating a discrepancy between the effects of the two treatments A and B. Let us assume that there is an *a priori* defined interval, denoted by $\mathbf{I}=(\Delta_1, \Delta_2)$ of δ, where it is not necessary bounded. Let us consider two intervals $\Omega_0=(\Delta_1, \delta^*)$ and $\Omega_1=(\delta^*, \Delta_2)$ of δ for a specified real value δ^* of δ, where $\Delta_1<\delta^*<\Delta_2$.

We shall give a definition on the superiority or the inferiority between the two treatments A and B.

Definition 1: When it holds true that $\delta \in \Omega_0$, the treatment A is called to be *inferior* to the treatment B (, that is, the treatment B is called to be *superior* to the treatment A) and conversely when it holds true that $\delta \in \Omega_1$, the treatment A is called to be *superior* to the treatment B (, that is, the treatment B is called to be *inferior* to the treatment A).

Let us use the word "inferior" or "superior" throughout this paper on the basis of this definition.

We set up our statistical procedure in such a way that after the preliminary trial if the treatment B is decided to be superior to the treatment A then the treatment B must be selected from the two treatments and performed on all of the remaining individuals, and conversely that after the preliminary trial if the treatment A is decided to be superior to the treatment B then the treatment A must be selected from the two treatments and performed on all of the remaining individuals.

Let us now define *the net gain* associated with our statistical procedure as follows.

Definition 2: (1) *The definition of the gain in the preliminary trial.* When the true value of the parameter is δ the gain per one individual obtained from performing A is $G(\delta-\delta^*)$ and the gain per one individual obtained from performing B is $G(\delta^*-\delta)$, where G is a proportionality factor. (It should be noted that $G(\delta-\delta^*)$ is positive if $\delta \in \Omega_1$ and negative if $\delta \in \Omega_0$ and $G(\delta^*-\delta)$ is negative if $\delta \in \Omega_1$ and positive if $\delta \in \Omega_0$.

(2) *The definition of the gain associated with the terminal decision.* Let us assume that after the preliminary trial the treatment B has been decided to be superior to the treatment A, then the gain per any one individual of the remaining is $G(\delta^*-\delta)$, where it is noted that this proportionality factor G is the same with (1). While let us assume that after the preliminary trial the treatment A has been decided to be superior to the treatment B, then the gain per any one individual of the remaining is $G(\delta-\delta^*)$.

We assume that the net gain over the whole trials is expressed in terms of the gain (1) and (2).

Thus we can construct the expected net gain for all N individuals on the basis of this net gain.

We shall set up the following assumption concerning *a priori* distribution for the parameter δ throughout this paper.

Assumption: *An a priori distribution of the parameter δ is given to us and the distribution is of continuous type.*

In considering our statistical procedure, we are concerned with the scheme such that we consider the fixed number of individuals drawn from a group of a large number of individuals (say N), and also with another scheme where the number of individuals drawn is not fixed but a sequential procedure is followed.

We shall call the former *the fixed sample size plan* and the latter *the sequential plan.*

Thus our problem is to determine the sample size in the fixed sample size plan and to determine the stopping rule and the choice of terminal decision in the sequential plan which minimize the expected net gain over the *a priori* distribution of the parameter δ.

2. This problem has already been discussed concerning one parameter exponential, normal and binomial distributions, by Colton [1], [2] and the author [3], [4], [5], [6], [7], [8], [9], [10], and [11].

Our results can be applied to any area, where a choice between two candidates treatments can be performed in either of sequential or nonsequential statistical procedure, including medical areas. However, it is noted that some deeper considerations from ethical point of view should be added with reference to application to medical areas.

In this paper, we shall proceed to attempt these general considerations for our problem, that is, in chapter 1 we shall consider some criterions with regarding to the variance, and in chapter 2 we shall be in particular concerned with such a alternative procedure that the treatment selected as the superior at the terminal decision should be performed not only on all of the remaining individuals but also on the individuals who have, already in the preliminary trial, received the treatment decided as the inferior at the terminal decision, from our ethical point of view.

Chapter 1 Remarks for the Criterion

§1.1 The First Consideration.

We have merely discussed the maximization of the expected net gain denoted by *E Net Gain* in the previous papers [3] ~ [11].

For the sake of considering further strictly our problem from an ethical viewpoint, for instance, in the case of the fixed sample size plan, the optimum value p^* of the sampling proportion $p=n/N$ must be determined so that the expected net gain for any one individual has as large value as possible and simultaneously the variance of the net gain for any one individual has less value than a certain assigned value.

From this kind of stand point, we shall proceed to attempt some considerations of general principle in this chapter. In the case of the fixed sample size plan, we consider the expected net gain per any one individual drawn from all N individuals and denote it by $[E\ Net\ Gain]_u$.

Let us denote by A-group the group of n patients on which treatment A is performed in the preliminary trial, and by B-group the group of n patients on which treatment B is performed, and moreover by D-group the group of the remaining $N-2n$ patients on which the treatment selected as the better in the light of the observations supplied by the samples obtained in the preliminary trial is performed.

Thus, the probability that any one individual is selected as a member of A-group is

$$[{}_{N-1}C_{n-1}\cdot{}_{N-n}C_n]/[{}_NC_n\cdot{}_{N-n}C_n]=n/N=p,$$

and the probability that any one individual is selected as a member of B-group is

$$[{}_{N-1}C_n\cdot{}_{N-n-1}C_{n-1}]/[{}_NC_n\cdot{}_{N-n}C_n]=n/N=p,$$

and moreover the probability that any one individual is selected as a member of D-group and receives treatment A or treatment B as the result of the decision is

$$\{[{}_{N-1}C_n\cdot{}_{N-n-1}C_n]/[{}_NC_n\cdot{}_{N-n}C_n]\}\cdot P_A=(N-2n)\cdot P_A/N$$

or

$$(N-2n)\cdot P_B/N=(N-2n)(1-P_A)/N,$$

where P_j denotes the probability that the jth treatment is selected as the better at the conclusion of the decision, and each probability P_j may be determined on the basis of the procedure proposed in the plan considered $(j=A,B)$.

Whence, from **Def. 2** in **Introduction**, $[E\ Net\ Gain]_u$ may be obtained as follows, where $\delta^*=0$.

$$(1.1)\quad [E\ Net\ Gain]_u/G=\frac{n}{N}\delta-\frac{n}{N}\delta+\frac{N-2n}{N}\{\delta P_A-\delta(1-P_A)\}=(1-2p)(2P_A-1)\delta,$$

where G is a proportionality factor. This expression is the same as that of *E Net Gain* in the previous paper [3], except that N is not involved in the expression.

In the previous papers [3], [4], [6], and [7], we have exerted ourselves to determine the optimum value p^* of p so that $[E\ Net\ Gain]_u$ is merely maximized.

However, from our stand point mentioned in **Introduction**, we must simultaneously attend to the variation of the variance of the net gain for each individual.

The First Consideration (1): Explaining in detail, the optimum p^* must be determined so that $[E\ Net\ Gain]_u$ has as large value as possible under such a condition that $[Var.\ Net\ Gain]_u\leqq C$ for a certain preassigned positive number C, where the notation $[Var.\ Net\ Gain]_u$ denotes the variance of the net gain for each individual.

From (1.1) and **Def.2** of the net gain, $[Var.\ Net\ Gain]_u$ then results as follows.

$$(1.2)\quad [Var.\ Net\ Gain]_u/G^2=\{2p\delta^2+(1-2p)(2P_A-1)^2\delta^2\}-\{(1-2p)^2(2P_A-1)^2\delta^2\}$$
$$=2\{p+p(1-2p)(2P_A-1)^2\}\delta^2.$$

It seems that for arbitrary choice of δ both $[E\ Net\ Gain]_u$ and $[Var.\ Net\ Gain]_u$ decrease and approach zero as p approaches zero. While, it also seems that the former decreases and approaches zero, but the latter inversely increases and approaches the maximum δ^2, as p approaches maximum 1/2. Whence, the relation between $[Var.\ Net\ Gain]_u$ and $[E\ Net\ Gain]_u$ will be shown as **Fig. 1.1.** If the preassigned upper bound

C of [*Var. Net Gain*]$_u$ is equal to or larger than the value C_0 corresponding to Max. [*E Net Gain*]$_u$, then Max. [*E Net Gain*]$_u$ may be also desirable to us from the view-point of variance.

On the other hand, if the preassigned upper bound C is less than C_0, then the [*E Net Gain*]$_u$ corresponding to the C may be desirable to us, instead of Max. [*E Net Gain*]$_u$ (cf. **Fig. 1. 1**).

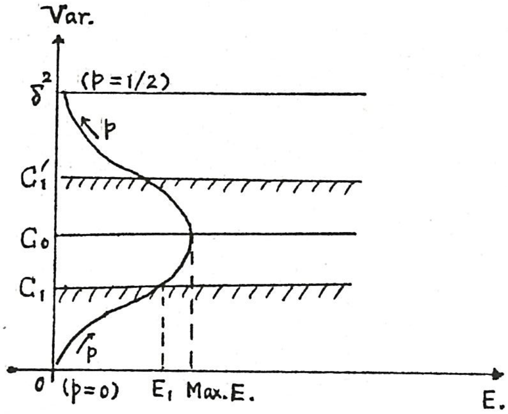

Fig. 1. 1 Relation between *Var. Net Gain* and *E Net Gain*.

The First Consideration (2) : On the other hand, the method also may be considered that the optimal value p^* must be determined under such a criterion that *Ratio*=[*E Net Gain*]^2_u/ [*Var. Net Gain*]$_u$ $\geqq k$ for a preassigned positive number k or the overall $[\overline{E\ Net\ Gain}]^2_u / [\overline{Var.\ Net\ Gain}]_u$ is maximized, where $\overline{E\ Net\ Gain}$ and $\overline{Var.\ Net\ Gain}$ denote the overall *E Net Gain* and *Var. Net Gain* obtained by integrating *E Net Gain* and *Var. Net Gain* respectively over the *a priori* distribution for the parameter δ.

The First Consideration (3) : In the first consideration (2), we have been concerned with the criterion on the *Ratio*=[*E Net Gain*]^2_u/ [*Var. Net Gain*]$_u$ that we must maximize the relative amount of the *Net Gain* corresponding to the amount of the variance.

But, in such a special case that for two values p_1 and p_2 of p [*E Net Gain*]$_{p_1}$<[*E Net Gain*]$_{p_2}$ and [*Ratio*]$_{p_1}$>[*Ratio*]$_{p_2}$, it seems that this criterion is not adequate to us, where [*E Net Gain*]$_{p_i}$ and [*Ratio*]$_{p_i}$ denote the values of them for a given value p_i of p respectively. (cf. **Fig. 1. 2**)

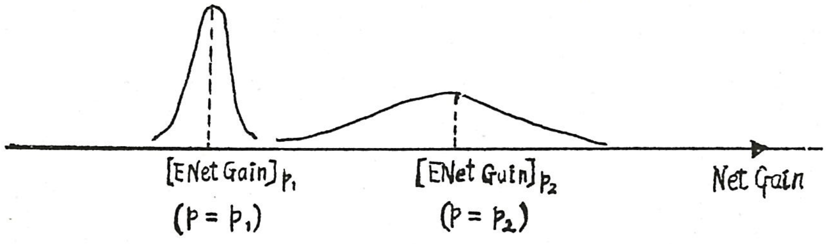

Fig. 1. 2 Frequency Curves of *Net Gain* in the Special Cases.

As alternative, we also may mutually compare the values of [*E Net Gain*]$_p-k(\alpha)\cdot\sqrt{[Var.\ Net\ Gain]_p}$ for various values of p, where $k(\alpha)$ indicates such a value that

$$Pr\{[Net\ Gain]_p-[E\ Net\ Gain]_p<-k(\alpha)\cdot\sqrt{[Var.\ Net\ Gain]_p}\}=\alpha$$

and α is a suitably preassigned value (for instance 0. 10, 0. 05 or 0. 01), and where [ ]$_p$ indicates the value of [ ] for a value of p. (cf. **Fig. 1. 3**)

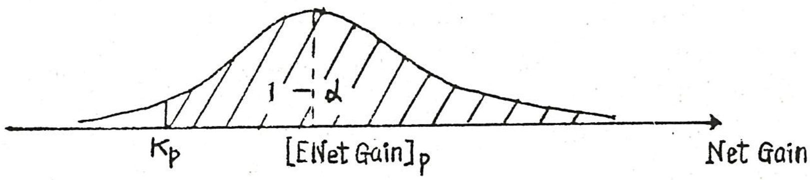

Fig. 1.3 K_p **indicating** $[E\ Net\ Gain]_p - k(\alpha)\cdot\sqrt{[Var.\ Net\ Gain]_p}$ **for a Value of** p.

In section 1.3, we shall determine numerically the optimum value of $p=n/N$ by comparing the values of K_p over given various values of p.

§1.2 The Second Consideration.

From the same stand point with the abovementioned, we shall proceed to determine the optimum value p^* of a sampling proportion p so that $[E\ Net\ Gain]_u$ is maximized under such a condition that $[Var.\ Net\ Gain]_u$ must be equal to or less than an assigned positive number.

In the first place, let us propose a procedure in two normal populations with unknown population means on the basis of the fixed sample size plan.

Perform the preliminary trial on $2n$ patients chosen at random from N patients, each treatment on n patients.

Compute the difference $\bar{d}=\bar{x}_A-\bar{x}_B$ of two observed means $\bar{x}_A$ and $\bar{x}_B$.

If $\bar{d}>K$, then use treatment A on the remaining $N-2n$ patients;

If $\bar{d}<-K$, then use treatment B on the remaining $N-2n$ patients;

If $-K\leqq\bar{d}\leqq K$, then use half and half two treatments A and B on the remaining $N-2n$ patients,

where K is a positive number and n is a positive integer.

Our purpose here-upon is to determine the optimum values (K^*, n^*) of pair (K, n) so that $[E\ Net\ Gain]^2_u/[Var.\ Net\ Gain]_u$ is maximized, where the notations $[E\ Net\ Gain]_u$ and $[Var.\ Net\ Gain]_u$ denote the same with (1.1) and (1.2) respectively.

Our intention that from an ethical view-point we should like to confine ourselves to the gain based on the consequences of treating a patient with the superior or the inferior of the two treatments may be further strictly achieved by performing this kind of considerations.

§1.3 Applications of the First Consideration to the Fixed Sample Size Plan.

We here are concerned with the application of the first considerations in section 1.1 to the fixed sample size plan (in the case of two normal populations with unknown population means).

In this plan, the proposed procedure was as follows.

Procedure: In the first place, perform the preliminary trial $2n$ patients chosen at random from N patients, each treatment on n patients.

In the next place, compute the difference $\bar{d}=\bar{x}_A-\bar{x}_B$ between two observed means $\bar{x}_A$ and $\bar{x}_B$.

If $\bar{d}>0$, then use treatment A on the remaining $N-2n$ patients;

If $\bar{d}<0$, then use treatment B on the remaining $N-2n$ patients;

Tab.3.1 $\overline{E\ Net\ Gain}/G\sigma_0$ **for each** p **and each** R

R \ p	0.01	0.02	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.48	0.49
0.09	.02346	.03250	.04806	.06029	.06446	.06365	.05917	.05175	.04183	.02974	.01574	.00649	.00328
0.37	.04750	.06567	.09677	.12057	.12807	.12566	.11608	.10088	.08105	.05730	.03014	.01239	.00626
0.84	.07136	.09845	.14418	.17769	.18683	.18157	.16620	.14319	.11410	.08003	.04178	.01711	.00862
1.57	.09722	.13364	.19374	.23514	.24384	.23402	.21181	.18059	.14254	.09911	.05134	.02092	.01052
2.59	.12425	.16999	.24315	.28951	.29543	.27965	.25010	.21104	.16506	.11383	.05853	.02376	.01194
3.99	.15316	.20822	.29285	.34088	.34175	.31893	.28191	.23557	.18272	.12512	.06394	.02587	.01298
5.82	.18338	.24733	.34094	.38716	.38131	.35111	.30713	.25449	.19603	.13346	.06788	.02739	.01373
8.16	.21477	.28690	.38655	.42787	.41434	.37697	.32680	.26892	.20600	.13961	.07073	.02848	.01427
11.07	.24686	.32612	.42863	.46267	.44124	.39734	.34192	.27979	.21340	.14413	.07281	.02928	.01467
14.62	.27926	.36434	.46665	.49188	.46287	.41325	.35350	.28800	.21892	.14746	.07434	.02986	.01495

Tab.3.2 $\Phi(0,0;\rho)$, $\rho=Rp/(1+Rp)$ **and** $\Phi(0,0;\rho)=1/2-2T(0,\sqrt{(1-\rho)/(1+\rho)})$
(by D. B. Owen)

R \ p	0.01	0.02	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.48	0.49
0.09	.250160	.250320	.250640	.251440	.252082	.252892	.253536	.254192	.254848	.255512	.256168	.256666	.256666
0.37	.250640	.251120	.252892	.255676	.258330	.261030	.263428	.265858	.268330	.270652	.272822	.274096	.274464
0.84	.251280	.252568	.256496	.262396	.267802	.273004	.277794	.282332	.286390	.290538	.294158	.296398	.297010
1.57	.252406	.254848	.261540	.271732	.280430	.288352	.295582	.301794	.307766	.312986	.317886	.320598	.321500
2.59	.254028	.257828	.268330	.282908	.295168	.305388	.314306	.321960	.328914	.334854	.340426	.343380	.344372
3.99	.256168	.261708	.272092	.295990	.311010	.323110	.333176	.341656	.349124	.355486	.360930	.364082	.365138
5.82	.258834	.266562	.286194	.309912	.327278	.340426	.350892	.359628	.368994	.373432	.378882	.381634	.382738
8.16	.262052	.272458	.296806	.324268	.342636	.356518	.366994	.375602	.382738	.388886	.393976	.396824	.397682
11.07	.265858	.278922	.307968	.337988	.357292	.371002	.381358	.389446	.396252	.401704	.406646	.409278	.409862
14.62	.270290	.286390	.319468	.351146	.370466	.383850	.393690	.401418	.407818	.408600	.417244	.419636	.420530

Tab. 3.3 $[\overline{Var.\ Net\ Gain}]\ /\ C^2\sigma_0^2$ **for each** p **and each** R

R \ p	0.01	0.02	0.05	0.10	0.15	0.20
0.09	0.010017	0.020068	0.050371	0.101365	0.152643	0.204065
0.37	0.010070	0.020264	0.051551	0.105385	0.160341	0.215452
0.84	0.010153	0.020597	0.053431	0.111547	0.171575	0.231376
1.57	0.010285	0.021105	0.056092	0.119804	0.185706	0.250260
2.59	0.010468	0.021775	0.059480	0.129205	0.200715	0.268903
3.99	0.010711	0.022637	0.062677	0.139277	0.215215	0.285664
5.82	0.011013	0.023684	0.067881	0.148964	0.227987	0.299271
8.16	0.011377	0.024904	0.072417	0.157729	0.238244	0.309524
11.07	0.011801	0.026230	0.076812	0.165024	0.246218	0.316789
14.62	0.012281	0.027659	0.080894	0.170915	0.251981	0.321722

Tab. 3.4 [Ratio] $= [\overline{ENet\ Gain}]^2\ /\ [\overline{Var.\ Net\ Gain}]$

R \ p	0.01	0.02	0.05	0.10	0.15	0.20
0.09	0.056570	0.055846	0.053713	0.050107	0.046483	0.042732
0.37	0.230686	0.226107	0.212836	0.192896	0.174859	0.157944
0.84	0.517052	0.500424	0.455978	0.396549	0.348862	0.308312
1.57	0.947230	0.900232	0.785629	0.649233	0.552398	0.477035
2.59	1.520359	1.412565	1.170580	0.918459	0.756378	0.639515
3.99	2.259377	2.041791	1.619272	1.190760	0.952391	0.789599
5.82	3.152258	2.759525	2.038464	1.448231	1.128143	0.919547
8.16	4.190846	3.542700	2.473779	1.683527	1.282713	1.029489
11.07	5.347132	4.363775	2.888446	1.893352	1.413387	1.120152
14.62	6.591526	5.190585	3.273002	2.075675	1.523237	1.193984

Tab. 3.6 $D=\sqrt{[\overline{Var.\ Net\ Gain}]}$ **for each** p, R

R \ p	0.01	0.02	0.05	0.10	0.15	0.20
0.09	0.100087	0.141663	0.224435	0.318379	0.390696	0.451736
0.37	0.100354	0.142354	0.227050	0.324630	0.400426	0.464168
0.84	0.100765	0.143519	0.231152	0.333987	0.414216	0.481016
1.57	0.101418	0.145276	0.236839	0.346127	0.430937	0.500260
2.59	0.102317	0.147564	0.243886	0.359452	0.448012	0.518558
3.99	0.103495	0.150458	0.250354	0.373199	0.463912	0.534476
5.82	0.104944	0.153897	0.260540	0.385959	0.477480	0.547057
8.16	0.106665	0.157813	0.269104	0.397151	0.488103	0.556349
11.07	0.108635	0.161959	0.277151	0.406232	0.496204	0.562840
14.62	0.110824	0.166312	0.284420	0.413419	0.501976	0.567205

0.25	0.30	0.35	0.40	0.45	0.48	0.49
0.255231	0.305975	0.356055	0.405241	0.453296	0.481503	0.490777
0.269606	0.322094	0.372121	0.418864	0.461680	0.485248	0.492721
0.289007	0.343003	0.391985	0.435135	0.471337	0.489493	0.494905
0.310807	0.365197	0.412348	0.450950	0.480378	0.493355	0.496881
0.330885	0.384657	0.429181	0.463477	0.487232	0.496218	0.498332
0.347822	0.400156	0.441955	0.472622	0.491977	0.498168	0.499315
0.360647	0.411246	0.451432	0.478556	0.494994	0.499352	0.499910
0.369751	0.418707	0.456175	0.482203	0.496749	0.500059	0.500253
0.375911	0.423425	0.459556	0.484211	0.497707	0.500421	0.500423
0.379764	0.426292	0.461501	0.483992	0.498170	0.500585	0.500517

for each *p* and each *R*

0.25	0.30	0.35	0.40	0.45	0.48	0.49
0.038816	0.034601	0.029911	0.024416	0.017288	0.010950	0.007748
0.141639	0.125154	0.107654	0.087778	0.062306	0.039591	0.028050
0.272145	0.237940	0.203456	0.165446	0.117544	0.074850	0.053084
0.414157	0.358143	0.303835	0.246070	0.174551	0.111201	0.078891
0.546993	0.467798	0.393771	0.317192	0.224250	0.142719	0.101234
0.666041	0.563668	0.470749	0.376952	0.265430	0.168623	0.119552
0.766323	0.642497	0.531798	0.424226	0.297446	0.188609	0.133645
0.848819	0.705893	0.581712	0.460887	0.321923	0.203743	0.144295
0.914948	0.755846	0.619552	0.488942	0.340353	0.215062	0.152241
0.967850	0.794890	0.648699	0.511676	0.354240	0.223538	0.158172

0.25	0.30	0.35	0.40	0.45	0.48	0.49
0.505204	0.553151	0.596704	0.636585	0.673273	0.693904	0.700554
0.519236	0.567533	0.610017	0.647197	0.679470	0.696597	0.701941
0.537594	0.585665	0.626087	0.659647	0.686540	0.699638	0.703495
0.557500	0.604315	0.642144	0.671528	0.693093	0.702393	0.704898
0.575226	0.620207	0.655119	0.680792	0.698020	0.704427	0.705926
0.589765	0.632579	0.664797	0.687475	0.701411	0.705810	0.706623
0.600539	0.641284	0.671886	0.691777	0.703558	0.706648	0.707043
0.608072	0.647076	0.675407	0.694408	0.704804	0.707148	0.707285
0.613115	0.650712	0.677906	0.695852	0.705483	0.707404	0.707406
0.616250	0.652910	0.679338	0.695695	0.705811	0.707520	0.707472

Tab. 3.7 [*E Net Gain*] −*D* for each *p*, *R*

R \ p	0.01	0.02	0.05	0.10	0.15	0.20
0.09	−0.076282	−0.108185	−0.172419	−0.247110	−0.306462	−0.358353
0.37	−0.052154	−0.074663	−0.122302	−0.182053	−0.232983	−0.279697
0.84	−0.028308	−0.041992	−0.075064	−0.123668	−0.169560	−0.213927
1.57	−0.002712	−0.007437	−0.026914	−0.067234	−0.110649	−0.154741
2.59	0.023843	0.027817	0.019982	−0.014966	−0.058375	−0.103868
3.99	0.052070	0.064533	0.068223	0.034043	−0.011177	−0.059543
5.82	0.081380	0.101753	0.111446	0.078514	0.029671	−0.022467
8.16	0.111696	0.139223	0.154149	0.118155	0.064707	0.008143
11.07	0.142572	0.176367	0.193879	0.152739	0.093713	0.032854
14.62	0.173705	0.212595	0.230137	0.182202	0.117560	0.052577

The optimum value p^* of a sampling proportion p must be determined so that the expected net gain $[E\ Net\ Gain]_u$ of (1.1) is relatively maximized to the value of the variance of the net gain denoted by $[Var.\ Net\ Gain]_u$ in (1.2).

From (1.1) and (1.2), we have

$$[E\ Net\ Gain]_u/G=(1-2p)(2p_A-1)\delta$$

and

$$[Var.\ Net\ Gain]_u/G=2\{p+p(1-2p)(2p_A-1)^2\}\delta^2$$

respectively, and, from the abovementioned procedure and the normality of $\bar{x}_j$ ($j=A$, B), we have

$$P_A=Pr\{\text{Selecting } A\}=Pr\{\bar{d}\geqq 0\}=1-\Phi(-(\sqrt{Np}\,\delta)/(\sqrt{2}\,\sigma)),$$

where $\delta=\mu_A-\mu_B$, $p=n/N$, σ^2 is a common known variance of X_j's ($j=A, B$), and $\Phi(t) = (2\pi)^{-\frac{1}{2}}\int_{-\infty}^{t} exp\{-u^2/2\}du$.

In this plan, we therefore have

$$(3.1)\quad [E\ Net\ Gain]_u/G= (1-2p)(1-2\Phi(-(\sqrt{Np}\,\delta)/(\sqrt{2}\,\sigma))\delta$$

and

$$(3.2)\quad [Var.\ Net\ Gain]_u/G^2=2\{p+p(1-2p)(1-2\Phi(-(\sqrt{Np}\,\delta)/(\sqrt{2}\,\sigma)))\}\delta^2,$$

where δ is an unknown fixed value.

Whence, our problem now is to determine the optimum value p^* of p so that

$$[\overline{E\ Net\ Gain}]_u/G=\int_{-\infty}^{\infty}(1-2p)(1-2\Phi(-(\sqrt{Np}\,\delta)/(\sqrt{2}\,\sigma)))\delta f(\delta)\,d\delta$$

is maximized under the next condition,

$$[\overline{Var.\ Net\ Gain}]_u/G^2=\int_{-\infty}^{\infty}\{p+p(1-2p)(1-2\Phi(-(\sqrt{Np}\,\delta)/(\sqrt{2}\,\sigma)))^2\}\delta^2 f(\delta)\,d\delta,$$

where $[\overline{E\ Net\ Gain}]_u$ and $[\overline{Var.\ Net\ Gain}]_u$ are obtained by integrating $[E\ Net\ Gain]_u$ and $[Var.\ Net\ Gain]_u$ respectively over the *a priori* normal distribution for the parameter δ, and where $f(u)=(2\pi)^{-\frac{1}{2}}\sigma_0^{-1}exp(-u^2/(2\sigma_0^2))$.

0.25	0.30	0.35	0.40	0.45	0.48	0.49
−0.405669	−0.450257	−0.493504	−0.537113	−0.584747	−0.621289	−0.638887
−0.323821	−0.366756	−0.409866	−0.455449	−0.509866	−0.557991	−0.584377
−0.257144	−0.299983	−0.343683	−0.391335	−0.451161	−0.508225	−0.541409
−0.198720	−0.242662	−0,288186	−0.338413	−0.403523	−0.468166	−0.506909
−0.149794	−0.196011	−0.244024	−0.297370	−0.367472	−0.438306	−0.481319
−0.108449	−0.157652	−0.208672	−0.265389	−0.340044	−0.415977	−0.462298
−0.074827	−0.127257	−0.181916	−0.241204	−0.319847	−0.399757	−0.448565
−0.047846	−0.103419	−0.160273	−0.222983	−0.304910	−0.387956	−0.438614
−0.026652	−0.084986	−0.144314	−0.209281	−0.293905	−0.379346	−0.431389
−0.009987	−0.070797	−0.132185	−0.198054	−0.285725	−0.373005	−0.426103

Whence,

(3.3) $[\overline{E\ Net\ Gain}]_u/G=2\,(2\pi)^{-\frac{1}{2}}\sigma_0\,(1-2p)\sqrt{Rp/(1+Rp)}$,

where $R=(N\sigma_0^2)/(2\sigma^2)$. Therefore,

$$[\overline{E\ Net\ Gain}]_u^2/G^2=2\pi^{-1}\sigma_0^2\,(1-2p)^2\cdot(Rp)/(1+Rp).$$

On the other hand,

(3.4) $[\overline{Var.\ Net\ Gain}]_u/G^2$

$$=2p(1-p)\,\sigma_0^2-4p(1-2p)\,\sigma_0^2\int_{-\infty}^{\infty}z^2\,\Phi(-\sqrt{Rp}\,z)\,\varphi(z)\,dz$$

$$+4p(1-2p)\,\sigma_0^2\int_{-\infty}^{\infty}z^2\{\Phi(-\sqrt{Rp}\,z)\}^2\,\varphi(z)\,dz$$

$$=2p\,\sigma_0^2\left[p+2(1-2p)\left\{\frac{Rp}{\pi(1+Rp)\sqrt{1+2Rp}}+\Phi(0,0;\rho)\right\}\right],$$

where $\Phi(x,y;\rho)$ is a bi-variate standard normal distribution function with $\rho_{xy}=(Rp)/(1+Rp)$.

Consequently, we should like to determine the optimum value p^* of p so that the next ratio $[\overline{E\ Net\ Gain}]_u^2/[\overline{Var.\ Net\ Gain}]_u$ is maximized.

(3.5) $Ratio=[\overline{E\ Net\ Gain}]_u^2/[\overline{Var.\ Net\ Gain}]_u$

$$=\frac{(1-2p)^2R}{\pi p(1+Rp)+2(1-2p)\left\{\frac{Rp}{\sqrt{1+2Rp}}+\pi(1+Rp)\,\Phi(0,0;\rho)\right\}}.$$

Numerical Example (1°): The First Consideration (1).

In each case of $R=(N\sigma_0^2)/(2\sigma^2)=0.09$, 0.37, 0.84, 1.57, 2.59, 3.99, 5.82, 8.16, 11.07 and 14.62, we shall compute the value of $[\overline{E\ Net\ Gain}]_u/(G\sigma_0)$ of (3.3) and the value of $[\overline{Var.\ Net\ Gain}]_u/(G^2\sigma_0^2)$ of (3.4) for each of the given values of p (i.e., $p=0.01$, 0.02, 0.05, 0.10, 0.15, 0.20, 0.25, 0.30, 0.35, 0.40, 0.45, 0.48, and 0.49).

The curve of **Fig. 3.1** can be drawn by plotting each point ($[\overline{E\ Net\ Gain}]_u/(G\sigma_0)$, $[\overline{Var.\ Net\ Gain}]_u/(G^2\sigma_0^2)$) for each value of p, in each of the given values of R.

Numerical Example (2°): The First Consideration (2).

In each case of $R=0.09$, 0.37, 0.84, 1.57, 3.99, 5.82, 8.16, 11.07, and 14.62, the value in the neighborhood of the maximum value of [*Ratio*] of (3.5) is given in the following **Tab. 3.4** by inspection.

The maximum value of [*Ratio*] is indicated by inspection in **Tab. 3.5**, for each R.

Tab. 3.5 The Optimum Values of p.

R	0.09	0.37	0.84	1.57	2.59
Max. [*Ratio*]	0.056570	0.230686	0.517052	0.947230	1.520359
p^*	0.01	0.01	0.01	0.01	0.01
R	3.99	5.82	8.16	11.07	14.62
Max. [*Ratio*]	2.259377	3.152258	4.190846	5.347132	6.591526
p^*	0.01	0.01	0.01	0.01	0.01

(p^* denotes the optimum value of p corresponding to maximum [*Ratio*] for each R.)

It is shown that the optimum value p^* of p is always equal to 0.01 for each of the given values of R. It seems that the p^* attain always the $[\overline{Var.\ Net\ Gain}]_u$ increases monotoneously as p increases.

Numerical Example (3°): The First Consideration (3).

The standard deviation $D=\sqrt{[\overline{Var.\ Net\ Gain}]_u}$ for each p, R is shown in **Tab. 2.6**.

Letting $k(\alpha)=1$ in the first consideration (3) of section 1.1, we obtain **Tab. 3.8** indicating the optimum value p^* of p.

Tab. 3.8 Max. $\{[\overline{E\ Net\ Gain}]_u-D\}$ and p^*.

R	0.09	0.37	0.84	1.57
Max. $\{[\overline{E\ Net\ Gain}]_u-D\}$	−0.076282	−0.052154	−0.028308	−0.002712
p^*	0.01	0.01	0.01	0.01
R	2.59	3.99	5.82	8.16
Max. $\{[\overline{E\ Net\ Gain}]_u-D\}$	0.027817	0.068223	0.111446	0.154149
p^*	0.02	0.05	0.05	0.05
R	11.07	14.62		
Max. $\{[\overline{E\ Net\ Gain}]_u-D\}$	0.193879	0.230137		
p^*	0.05	0.05		

If we consider only the maximization of $[\overline{E\ Net\ Gain}]_u$ regardless of the variance of the *Net Gain* as in the previous paper [3], then we obtain the optimum value p^* of p shown in **Tab. 3.9**. (i.e., $k(\alpha)=0$)

Tab. 3.9 Max. {$\overline{[E\ Net\ Gain]_n}$} and p^*.

R	0.09	0.37	0.84	1.57	2.59
Max. $\overline{[E\ Net\ Gain]_n}$	0.06446	0.12807	0.18683	0.24384	0.29543
p^*	0.15	0.15	0.15	0.15	0.15
R	3.99	5.82	8.16	11.07	14.62
Max. $\overline{[E\ Net\ Gain]_n}$	0.34175	0.38716	0.42787	0.46267	0.49188
p^*	0.15	0.10	0.10	0.10	0.10

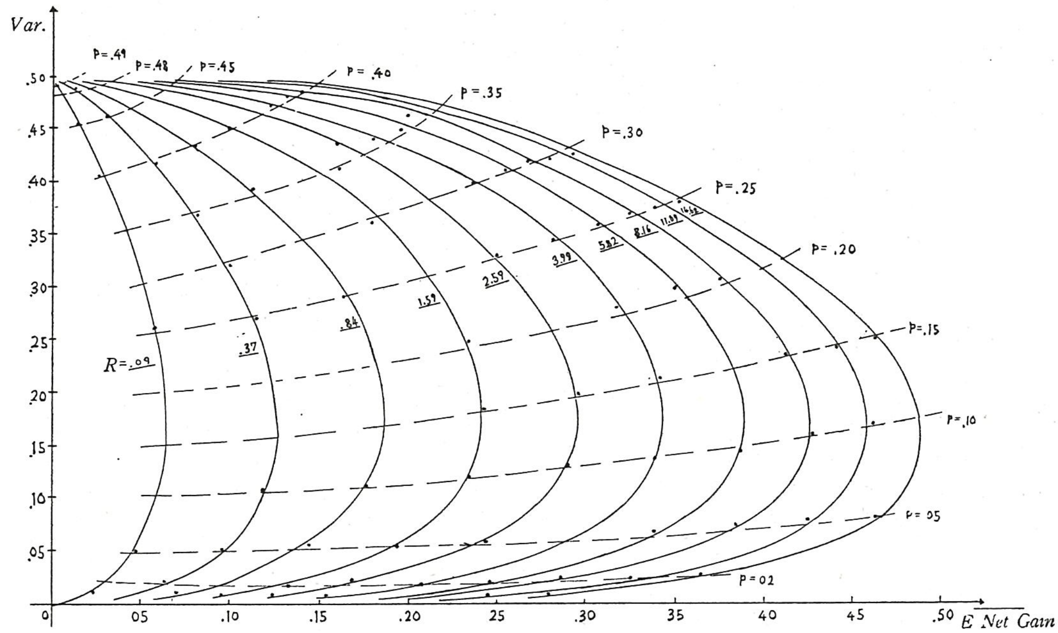

Fig. 3.1. The Relation between $\overline{E\ Net\ Gain}$ and $\overline{Var.\ Net\ Gain}$ for each p and each R.

Chapter 2 Alternative Procedure for Medical Application

§2.1 Iutroduction.

We have, so far, been concerned with such a procedure that

(1) the preliminary trial will be performed on $2n$ drawn from the N individuals, n on each treatment, and then

(2) the treatment selected as the better at the terminal decision will be performed on the remaining $N-2n$, where we have considered $2n$ fixed in the fixed sample size

plan and we have considered, in the sequential plan, the situation such that it is not fixed but a sequential procedure is followed.

Our results can be applied to any area, where a choice between two candidates treatments can be performed in either of sequential or non-sequential statistical procedure, including medical areas. However it is noted that particular considerations should be added with reference to application to medical areas.

Indeed, so far as medical applications are concerned, a deeper consideration from ethical point of view should be required particularly with respect to giving some securities from receiving the inferior treatment for every individuals.

Therefore, we shall now propose an alternative procedure in which the treatment selected as the superior in the terminal decision should be performed not only on all of the remaining individuals but also on the individuals who have, already in the preliminary trial, received the treatment decided as the inferior in the terminal decision.

In the following sections, we want to perform our problem on the basis of this new procedure, concerning the case of the fixed sample size plan in section 2.2 and concerning the case of the sequential plan in section 2.3.

§2.2 Application of Alternative Procedure to the Fixed Sample Size Plan.

We shall be firstly concerned with the fixed sample size plan in the distributions of Type I. (*cf.* [11])

The individuals responses due to each treatment are assumed to be normally distributed with unknown mean (μ_A for treatment A and μ_B for treatment B) and known variance σ^2 (the same for the two treatments). Moreover, we assume that parameter δ has an *a priori* distribution with the probability density function

$$g(\delta)=(2\pi)^{-\frac{1}{2}}\sigma_0^{-1}\exp(-\delta^2/(2\sigma_0^2)),$$

where σ_0^2 is known to us.

Let us denote by $\bar{d}$ the observed difference between $\bar{x}_A$ and $\bar{x}_B$, where $\bar{x}_j$ denotes the observation mean from performing the j th treatment on n individuals ($j=A, B$).

We shall set up an action of the terminal decision as follows.

Perform a preliminary trial on $2n$ individuals drawn from all N individuals, treatment A on n and treatment B on another n.

If $\bar{d}>0$, then perform treatment A on all of the remaining $N-2n$ and also on n individuals who have already received treatment B in the preliminary trial, and

if $\bar{d}<0$, then perform treatment B on all of the remaining $N-2n$ and also on n individuals who have already received treatment A in the preliminary trial, where $\bar{d}$ is distributed according to the normal distribution with unknown mean δ and known variance $2\sigma^2/n$.

Tab. 2.1 The Number of Individuals that the Loss will be scored.

		The Case that $\delta \in \Omega_0$	The Case that $\delta \in \Omega_1$
Preliminary Trial	The Number of Individuals receiving A	$\underline{n_A}$ (Probability 1)	n_A (Probability 1)
	The Number of Individuals receiving B	n_B (Probability 1)	$\underline{n_B}$ (Probability 1)
Action of Terminal Decision	Perform A on the remainder	$\underline{(N-2n)+n_B}$ (Probability$=P_r\{\bar{d}>0\}$)	$(N-2n)+n_B$ (Probability$=P_r\{\bar{d}>0\}$)
	Perform B on the remainder	$(N-2n)+n_A$ (Probability$=P_r\{\bar{d}<0\}$)	$\underline{(N-2n)+n_A}$ (Probability$=P_r\{\bar{d}<0\}$)

($n_A=n_B=n$ and the numbers underlined indicate the number of individuals that the loss will be scored by some probability shown within the bracket, and $\Omega_0=(-\infty,0)$, $\Omega_1=(0,+\infty)$.)

We then obtain the expected net gain for all N individuals, where we can take δ as positive without loss of generality and $\delta^*=0$.

(2.1) $$E\ Net\ Gain = G\delta(N-n)\{Pr(\text{Select } A) - Pr(\text{Select } B)\}.$$

Letting $\overline{E\ Net\ Gain}$ denote the result of integrating $E\ Net\ Gain$ over the probability distribution for δ, we obtain

(2.2) $$\overline{E\ Net\ Gain}/NG\sigma_0 = 2(2\pi)^{-\frac{1}{2}}(1-p)\left(\frac{Rp}{1+Rp}\right)^{\frac{1}{2}},$$

where $p=n/N$ and G is a proportionality factor.

To determine the optimum value p^* of p that maximize (2.2), we differentiate (2.2) with respect to p and set the derivative equal to zero. This gives the quadratic

(2.3) $$2Rp^2+3p-1=0.$$

Solving for p gives

(2.4) $$p^* = \frac{\sqrt{9+8R}-3}{4R} = \frac{2}{\sqrt{9+8R}+3}.$$

(The sign of the second derivative with respect to p at $p=p^*$ is negative, verifying location of a maximum.)

Substituting the p^* of (2.4) into the expression for $\overline{E\ Net\ Gain}/NG\sigma_0$ in (2.2) gives

(2.5) $$[\overline{E\ Net\ Gain}/NG\sigma_0]_{p*} = 2(2\pi)^{-\frac{1}{2}}\left(\frac{3+4R-\sqrt{9+8R}}{9+4R+3\sqrt{9+8R}}\right)^{\frac{1}{2}}.$$

We shall compare numerically the optimum value p^* of the new procedure with that of the previous procedure (cf. the previous paper [3] and compare the maximum value of $(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0)$ of the new procedure with that of the previous, for various values of $R=(N\sigma_0^2)/(2\sigma^2)$.

Tab.2.2 Comparison of the New Procedure to the Previous.

R	Previous Procedure		New Procedure		Per Cent Additional Gain of New Over Previous
	p^*	$(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0)$	p^*	$(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0)$	
0	0.167	0	0.333	0	—
0.5	0.158	0.185	0.303	0.253	36.8
1	0.152	0.253	0.281	0.337	33.2
2	0.140	0.337	0.250	0.433	28.5
4	0.125	0.433	0.213	0.534	23.3
6	0.119	0.492	0.190	0.591	20.1
10	0.100	0.566	0.161	0.659	16.4
20	0.080	0.659	0.125	0.740	12.3
50	0.057	0.762	0.086	0.823	8.0
100	0.043	0.823	0.070	0.870	5.7
∞	0	1.000	0	1.000	0

The results show

(1) the p required in the new procedure is larger than that of the previous procedure for each R, but

(2) the maximum value of the over-all expected net gain of the new procedure is larger than that of the previous procedure for each R, and

(3) the relative advantage of the new over the previous procedure can be observed for each R and it decreases as R increases.

§2.3 Application of Alternative Procedure to the Sequential Plan.

In this section, we shall be concerned with our problem in the distributions of Type I (cf. [11]) on the basis of the sequential plan (in the previous papers [8]~[11]).

The individuals responses due to each treatment are assumed to be normally distributed with unknown mean (μ_A for treatment A and μ_B for treatment B) and known variance σ^2 (the same for the two treatments). Moreover, we assume that parameter δ has an *a priori* distribution with the probability density function

$$g(\delta)=(2\pi)^{-\frac{1}{2}}\sigma_0^{-1}exp(-\delta^2/(2\sigma_0^2)).$$

The trial then is performed sequentially on a pair of individuals at a time, one member of the pair on treatment A and the other on treatment B.

Let us denote by $d_m=\sum_1^m(x_A-x_B)$ the cumulative sum of the observed difference within each pair in the preliminary trial.

We shall set up an action of the terminal decision as follows.

After the mth pair, if $d_m \geqq k\sigma^2$, then perform treatment A on all of the remaining and also on the individuals who have already received treatment B in the preliminary trial, and if $d_m \leqq -k\sigma^2$, then perform treatment B on all of the remaining and also on the individuals who have already received treatment A in the preliminary trial, and

If $-k\sigma^2 < d_m < k\sigma^2$, then continue with another pair, where k is a positive number.

We then obtain the expected net gain for all N individuals, where we can take δ as positive without loss of generality and $\delta^*=0$.

(3.1) E *Net Gain* $= G\delta(N-E(n))\{Pr(\text{Select } A) - Pr(\text{Select } B)\}$,

where $E(n)$ denotes the A. S. N. of the sequential trial.

It can be shown that application of the approximate formulae for unrestricted sequential sampling gives

$$Pr(\text{Select } B) = \frac{1}{(e^{k\delta}+1)}, \quad E(n) = k\sigma^2 \cdot \frac{(e^{k\delta}-1)}{\delta(e^{k\delta}+1)}$$

Letting $\delta/\sigma_0 = z$, $k\sigma_0 = a$, and letting $\overline{E \text{ Net Gain}}$ denote the result of integrating E *Net Gain* over the probability distribution for δ, we obtain

$$(3.2) \quad \overline{E \text{ Net Gain}}/NG\sigma_0 = 4\left(1+\frac{1}{R}\right)\int_0^\infty \frac{ae^{az}}{(e^{az}+1)^2}\varphi(z)\,dz - \frac{a}{2R},$$

where $R = (N\sigma_0^2)/(2\sigma^2)$.

To determine the optimum value a^* of a maximizing (3.2), we differentiate (3.2) with respect to a and set the derivative equal to zero. This gives the equation involving a and R. But it is not feasible that we work out analytically this equation for a in terms of R.

Therefore, solving for R in terms of a gives

$$(3.3) \qquad R = \frac{1}{8\dfrac{d}{da}\displaystyle\int_0^\infty \frac{ae^{az}}{(e^{az}+1)^2}\varphi(z)\,dz} - 1.$$

Thus for arbitrary choice of a, (3.3) gives the R such that the chosen a is optimal.

Using (3.3) we express (3.2) in terms of a only.

$$(3.4) \quad \overline{E \text{ Net Gain}}/NG\sigma_0 = 4 \cdot \frac{\displaystyle\int_0^\infty \frac{ae^{az}}{(e^{az}+1)^2}\varphi(z)\,dz - a\frac{d}{da}\int_0^\infty \frac{ae^{az}}{(e^{az}+1)^2}\varphi(z)\,dz}{1-8\dfrac{d}{da}\displaystyle\int_0^\infty \frac{ae^{az}}{(e^{az}+1)^2}\varphi(z)\,dz}.$$

Expressing $e^{-az}/(1+e^{-az})$ in an infinite series involing terms e^{-jaz} and integrating term by term, we obtain

$$(3.5) \qquad R = \frac{(2\pi)^{\frac{1}{2}}}{8} \cdot \frac{a}{\displaystyle\sum_{j=1}^{\infty}(-1)^{j+1}(ja)\{G(ja)+(ja)\,G'(ja)\}} - 1$$

and

(3.6) $$\overline{E\ Net\ Gain}/NG\sigma_0=4(2\pi)^{-\frac{1}{2}}a\cdot\frac{\sum_{j=1}^{\infty}(-1)^j(ja)^2G'(ja)}{a-8(2\pi)^{-\frac{1}{2}}\sum_{j=1}^{\infty}(-1)^{j+1}(ja)\{G(ja)+(ja)G'(ja)\}},$$

where $G(u)=\Phi(-u)/\varphi(u)$ (Mill's Ratio).

We can now consider the numerical evaluation of $\overline{E\ Net\ Gain}/(NG\sigma_0)$ for variou R. Arbitrarily, values of a of .5 (.5) 5.0 were selected. Using (3.5), R can b determined such that the chosen a is optimal.

In **Tab. 3.1**, we shall compare the maximum value of $(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0$ based on the new procedure with that based on the previous procedure (*cf.* Colton [1] and the previous papers [8] ~ [11].

Tab. 3.1 Comparison of the Maximum $\overline{E\ Net\ Gain}$ based on the New Procedure with That based on the Previous Procedure.

R	$\mathfrak{G}$	$\mathfrak{G}_0$
0.37	0.201	$0.201 < \mathfrak{G}_0 < 0.370$
1.47	0.370	$0.370 < \mathfrak{G}_0 < 0.501$
3.37	0.501	$0.601 < \mathfrak{G}_0 < 0.678$
6.26	0.601	$0.678 < \mathfrak{G}_0 < 0.736$
10.37	0.678	$0.736 < \mathfrak{G}_0 < 0.781$
15.96	0.736	$0.781 < \mathfrak{G}_0 < 0.817$
23.29	0.781	$0.845 < \mathfrak{G}_0 < 0.867$
32.63	0.817	$0.867 < \mathfrak{G}_0$
44.28	0.845	$\wedge$ $\mathfrak{G}_0$
58.49	0.867	$\wedge$ $\mathfrak{G}_0$

($\mathfrak{G}_0$ denotes the maximum value of $(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2GN\sigma_0)$ based on the new procedure and $\mathfrak{G}$ denotes that based on the previous procedure.)

The results show

(1) the maximum value of $(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0)$ based on new procedure i larger than that based on the previous procedure for each R, and,

(2) let us denote by k^* the optimum value of k indicating the location of bounda ries at the termination of sequential process, then k^* based on the new procedure i larger than that based on the previous procedure.

In **Tab. 3.2**, a comparison is made of the maximum value of $(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})/(2NG\sigma_0)$ based on the fixed sample size plan (in section 2.2) to that based on th sequential plan (in this section), concerning the new procedure.

Tab.3.2 Comparison of the Optimum Sequential Plan to the Optimum Fixed Sample Size Plan.

R	Fixed Optimum Plan	Sequential Optimum Plan	Per Cent Additional Gain of Seq. Over Fixed
	$(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})\ /\ (2NG\sigma_0)$	$(2\pi)^{\frac{1}{2}}(\overline{E\ Net\ Gain})\ /\ (2NG\sigma_0)$	
0.185	0.161	0.201	24.8
0.735	0.298	0.370	24.2
1.685	0.408	0.501	22.8
3.130	0.498	0.601	20.7
5.185	0.571	0.678	18.7
7.980	0.630	0.736	16.8
11.645	0.678	0.781	15.2
16.315	0.717	0.817	13.9
22.140	0.750	0.845	12.7
29.245	0.777	0.867	11.6

The results show

(1) the maximum value of the over-all expected net gain based on the sequential plan is larger than that based on the fixed sample size plan for each R, and

(2) the relative advantage of the sequential over the fixed sample size plan can be numerically proved for each R and it decreases as R increases.

Appendix

We shall correct several errors and misprints in the previous papers [**4**] and [**9**].

(I) Correction to "Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 2" (Kumamoto J. Sci. Ser. A, **7**, No. 4, 87~94 (1967))

(1) In assumptions (4) of §2, eliminate the part ", that is, $\mu_B=\mu_A-\delta$ has an *a priori* normal distribution with mean μ_A and known variance σ_0^2."

(2) (2.3): The expected loss due to performing A should be denoted by L_A.

(3) (2.5): $f_{n-1}(t;\ \delta_0)\,dt=\left\{e^{-\frac{\delta_0^2}{2}}\Big/\left(\sqrt{\pi}\,\Gamma\left(\frac{n-1}{2}\right)\right)\right\}\cdot\sum_{k=0}^{\infty}\cdots\cdots.$

(4) (2.6): $F_{n-1}(0)\fallingdotseq\Phi(-\delta_0)$.

(5) (2.7): $\overline{E\ Loss}/NC=\sigma_0\left\{(2\pi)^{-\frac{1}{2}}-(1-p)\int_{-\infty}^{\infty}z\,\varphi(z)\,\Phi(-\delta_0)\,dz\right\}$

$$=(2\pi)^{-\frac{1}{2}}\sigma_0\left\{1-(1-p)\sqrt{2Rp/(1+2Rp)}\right\},$$

(6) (2.10): $[\overline{E\ Loss}/NC]_{p*}=(2\pi)^{-\frac{1}{2}}\sigma_0\left\{1-\frac{1}{4}(\cdots\cdots\cdots)^{\frac{1}{2}}\right\}.$

(7) Correct the first part in **2.3** as follows; "If $\delta<0$, then the expected loss due to performing the treatment A is as follows. $[E\ Loss]_A=C\delta\{-(N-n)+(N-2n)\cdot Pr(\bar{D}<0)\}$. While if $\delta>0$, then the expected loss due to performing the treatment B is

as follows. $[E\ Loss]_B = C\delta\{n + (N-2n)\cdot Pr(\bar{D}<0)\}$".

(8) (3.3): $\overline{E\ Loss}/NC = \sigma_0\{(2\pi)^{-\frac{1}{2}} + (1-2p)\int_{-\infty}^{\infty} F_{2n-2}(0)\, z\varphi(z)\, dz,$

(9) (3.5): $\begin{cases} F_{2n-2}(0) \fallingdotseq \Phi(-\delta_0) = \Phi(-\sqrt{Rp}\, z), \text{ where } \cdots\cdots\cdots. \\ \overline{E\ Loss}/NC = (2\pi)^{-\frac{1}{2}}\sigma_0\{1-(1-2p)\sqrt{Rp/(1+Rp)}\}, \cdots\cdots\cdots. \end{cases}$

(II) Correction to "Optimum Designs for Selecting One of Two Treatments, Sequential Plan 2" (Kumamoto J. Sci. Ser. A, 8, No. 1, 11~19 (1967)).

(1) Correct assumption (4) in **2. Assumptions** as follows.

"Moreover, we shall assume that the true mean difference $\delta = \mu_A - \mu_B$ is distributed in accordance with an *a priori* normal distribution with zero mean and known variance σ_0^2.

(2) Correct the second instruction in **Procedure** as follows. "If $d \leqq -K\sigma + n\mu_A$, use treatment A on the remaining $N-n$ patients;".

Acknowledgement

The author wishes to express his heartiest thanks to Professor Dr. T. Kitagawa of Kyushu University, for his kind advice and valuable suggestions in connection with this work.

The author is also deeply indebted to Dr. C. Asano of Shionogi Research Laboratory and Dr. N. Furukawa of Kyushu Univ., for their valuable suggestions in the course of this work.

References

[1] Colton, T., "*A Models for Selecting One of Two Medical Treatments*", J. Am. Stat. Assoc., **58**, 388~400 (1963).

[2] Colton, T., "*A Two-Stage Model for Selecting One of Two Treatments*", Biometrics, **21**, 169~180 (1965).

[3] Sugimura, M., "*Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 1*", Mem. Fac. Gen. Educ. Kumamoto Univ., Ser. Nat. Sci., **2**, 1~7 (1967).

[4] Sugimura, M., "*Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 2*", Kumamoto J. Sci. Ser. A, **7**, No.4, 87~94 (1967).

[5] Sugimura, M., and Asano, C., "*Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 3*", Kumamoto J. Sci. Ser. A, **7**, No.4, 95~102 (1967).

[6] Sugimura, M., "*Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 4.1*", J. Kumamoto Women's Univ., **19**, 65~71 (1967).

[7] Sugimura, M., "*Optimum Designs for Selecting One of Two Medical Treatments, Fixed Sample Size Plan 5*", J. Kumamoto Women's Univ., **20** (Received Feb. 2, 1967).

[8] Sugimura, M., and Asano, C., "*Optimum Designs for Selecting One of Two Medical Treatments, Sequential Plan 1*", Bull. Math. Stat., **12**, No.3~4, 1~9 (1967).

[9] Sugimura, M., "*Optimum Designs for Selecting One of Two Treatments, Sequential Plan 2*", Kumamoto J. Sci. Ser. A, 8, No.1, 11~19 (1967).

[10] Sugimura, M., and Asano, C., "*Optimum Designs for Selecting One of Two Treatments, Fixed Sample Size Plan 6 and Sequential Plan 3*", Kumamoto J. Sci. Ser. A, 8, No.1, 21～57 (in press, Received April 1, 1967).

[11] Sugimura, M., "*Optimum Designs for Selecting One of Two Treatments in a Population with One Parameter Exponential Distribution*", Bull. Math. Stat., **13**, No.1～2 (Received September 30, 1967).

[12] Wald, A., "*Sequential Analysis*", John Wiley and Sons: New York (1947).