Liet. mat. rink. LMD darbai, **48/49**, 2008, 294–298

On selecting the better of two binomial populations

Kęstutis MIKALAUSKAS (KU), Rimantas EIDUKEVIČIUS (VU)
e-mail: kestasmik@yahoo.com, rimantas.eidukevicius@mif.vu.lt

Abstract. A new procedure for selecting the better of two binomial populations by using sequential analysis proposed. It is based on well known Play-the-Winner (PW) and Vector-at-a Time (VT) procedures and constructed to avoid some disadvantages of PW and VT rules.

Keywords: clinical trials, play the winner rule.

1. Introduction

The paper is about selection the best of two treatments with a binomial response in view of a scientific rationale and human ethics. The goals are (i) to have a probability of at least P^* of selecting the better treatment when it is sufficiently better and (ii) to minimize the number of people put on the poorer treatment or equivalently minimizing the expected number of failures that could have been avoided by using the better treatment throughout.

In [6] Play-the-Winner Rule (PWR) proposed. This is sequential method: trials are made one at a time on either treatment, a success implies that the next observation shall be drawn from the same treatment, while a failure causes a switch to the other treatment. There are many modifications of this rule. In [5] randomized PWR proposed, some modifications of this method are described in [3] and [1].

Sobel and Weiss compare PW and Vector-at a time rules (VT) [4]. VT is a rule with an equal allocation, both populations are sampled for every trial, so it does not fulfil our conditions. PWR has disadvantage that it admits the situation when only one population is observed.

Considering this a new procedure is proposed. We call it Mixed Rule (MR). This procedure is based on Play-the-Winner and Vector-at a time rules. We start the experiment with VT procedure and continue it until we get result “success and failure” or “failure and success”. Further we apply only the treatment which gave result “success” until failure occurs. After that we return to applying VT rule. In this way at least one patient gets poorer treatment and more patients gets better treatment.

MR is compared with PW and VT procedures. Stopping rule is based on the difference of numbers of successes between two treatments [4] and the Sequential Probability Ratio Test [2] are used.

2. Analysis of the mixed rule

Following [4] let S(A) and S(B) be the numbers of A and B successes, $\Delta = p - p' \geqslant 0$, where p and p' are probabilities of treatments A and B respectively.

We terminate the treatment when $|S(A) - S(B)| = r$, where integer r is chosen to be the smallest such that

$$P(CS) \geqslant P^*, \quad \text{when } \Delta \geqslant \Delta^*, \tag{1}$$

where P^* and Δ^* are given by experimenter, CS denotes the event 'correct selection'.

We select treatment A when $S(A)-S(B) = r$ and treatment B when $S(A)-S(B) = -r$. Let N_b be the number of trials in which treatment B is used. We say that treatment A is better ($\Delta > 0$), so our purpose is to minimize E(N_b). CS is the choice A in our case, NT means 'next treatment'.

For the Mixed rule we denote $P(n) = P(CS|S(A) - S(B) = n, NT = A)$, $Q(n) = P(CS|S(A) - S(B) = n, NT = B)$, $B(n) = P(CS|S(A) - S(B) = n, NT = VT)$, $\lambda = p'/p < 1$.

We begin sampling from VT, hence $P(CS) = B(0)$. Further

$$\begin{aligned} &P(n) = pP(n+1) + qB(n), \quad Q(n) = p'Q(n-1) + q'B(n), \\ &B(n) = pq'P(n+1) + qp'Q(n-1) + (pp' + qq')B(n), \end{aligned} \tag{2}$$

where $q = 1 - p$ and $q' = 1 - p'$, with the boundary conditions

$$P(r) = B(r) = 1, \quad Q(-r) = 0. \tag{3}$$

From (2) and (3) we obtain

$$B(n) = \frac{q' - q\lambda^{r+n}}{q' - q\lambda^{2r}} \quad \text{and } P(CS) = B(0) = \frac{q' - q\lambda^{r}}{q' - q\lambda^{2r}}.$$

By setting P(CS) equal to P* we get quadratic in λ^r equation. The solution of this gives

$$\lambda^r = (2qP^*)^{-1}\left(q - \sqrt{q^2 - 4qq'(1 - P^*)P^*}\right). \tag{4}$$

The purpose is to select such r that (1) is satisfied for all p and p'. Denote $p_0 = \frac{p+p'}{2}$. Then

$$q = 1 - p_0 - \frac{\Delta}{2} \quad \text{and } q' = 1 - p_0 + \frac{\Delta}{2}. \tag{5}$$

Using (4) and following [4] we get

$$p_0 \approx 1 - \frac{\Delta^*}{2} - 4\Delta^*(1 - P^*), \quad \text{when } P^* \to 1. \tag{6}$$

Now r is calculated from (6), (5) and (4).

Let $U(n) = E(N_b|S(A) - S(B) = n, NT = A)$, $V(n) = E(N_b|S(A) - S(B) = n, NT = B)$, $W(n) = E(N_b|S(A) - S(B) = n, NT = VT)$.

Then we have recurrence relations:

$$\begin{aligned} &U(n) = pU(n+1) + qW(n), \quad V(n) = p'V(n-1) + q'W(n) + 1, \\ &W(n) = pq'U(n+1) + qp'V(n-1) + (pp' + qq')W(n) + 1, \end{aligned}$$

Table 1. $E(N_b|\Delta = \Delta^*)$, $P^* = 0.95$ and $\Delta^* = 0.2$

p'	PW	VT	M
0	44.5	18.5	33
0.1	39.2	18.2	29.5
0.2	34	17.5	25.8
0.3	28.6	16.9	21.8
0.4	23.1	16.7	17.7
0.5	17.5	16.9	13.7
0.6	12.2	17.5	10.1
0.7	7.1	18.2	6.9
0.8	2.3	18.5	4.2

with boundary conditions $U(r) = V(r) = W(-r) = 0$.

We find that

$$E(N_b) = V(0) = \frac{p + qr}{p - p'} - \frac{(p + 2qr)\lambda^r(q\lambda^r - q')}{(p - p')(q\lambda^{2r} - q')}. \tag{7}$$

Comparison is based on the expecting number of patients, which receive poorer treatment. Let $P^* = 0.95$ and $\Delta^* = 0.2$ according to [4]. We analyze situation when there is no a priori information about parameters. Mixed Rule is preferred under condition $p' > 0.5$. This condition is satisfied in the most practical cases. In other cases Mixed Rule has not this advantage, but any of the procedures of this type can not give the best results for all cases. These results are shown in Table 1.

3. The sequential probability ratio test

This test is described in [2]. Let $X = (X_A, X_B)$ be the result of the trial. Suppose X has p.d.f. $f(X, \cdot)$. Denote N_v - the total number of vectors X. We wish to test H_0: $p = p' = \theta_0$ against H_1: $p = p' + \Delta = \theta_1$. Define $Z = \ln \frac{f(X,\theta_1)}{f(X,\theta_0)}$. Then following Eq.(2.4.3) from [2]

$$E_{\theta_1} N_v \approx \frac{(1 - \beta)\ln A_1 + \beta \ln A_2}{E_{\theta_1} Z}, \tag{8}$$

where $A_1 = \frac{1-\beta}{\alpha}$, $A_2 = \frac{\beta}{1-\alpha}$ and α is the size of the type I error, β is the size of the type II error.

For the VT procedure X_A (X_B) is 1 if the result is success and 0 otherwise and

$$f(X, \theta_0) = \begin{cases} p'^2, & X = (1, 1), \\ p'(1 - p'), & X = (1, 0), \\ (1 - p')p', & X = (0, 1), \\ (1 - p')^2, & X = (0, 0). \end{cases} \tag{9}$$

Table 2. $E_{H_1}(N_b)$, $P^* = 0.95$, $\Delta = 0.2$

p'	VT	M
0.1	17.2	13.4
0.2	25.3	19
0.3	30.4	21.7
0.4	32.7	21.8
0.5	32.2	19.3
0.6	29.0	14.5
0.7	22.8	7.6

Table 3. $E_{H_1}(N_b)$ and $E_{H_0}(N_b)$, $P^* = 0.95$, $\Delta = 0.2$, entries were determined from simulations

p'	PW	VT	M
0.1	16.2	20.1	16.7
0.2	21.7	28.1	22.1
0.3	24.3	33.3	25.1
0.4	25.4	37.1	26.2
0.5	21.6	34.6	22.5
0.6	16.8	31.1	17.9
0.7	9.7	24.5	11.2
0.8	2.5	14.0	4.8

p'	PW	VT	M
0.1	24.0	24.5	24.5
0.2	30.6	31.1	30.9
0.3	33.8	34.5	34.1
0.4	36.1	37.1	36.4
0.5	32.4	33.3	32.7
0.6	27.0	28.3	27.3
0.7	18.6	20.2	18.9
0.8	2.5	4.8	3.2

We get $f(X, \theta_1)$ from (9) with $\Delta = 0$. So

$$E_{\theta_1} Z = (p' + \Delta) \ln \frac{p' + \Delta}{p'} + (1 - p' - \Delta) \ln \frac{1 - p' - \Delta}{1 - p'}.$$

Further the expected number of N_v under H_1 is found from (8) and $E_{\theta_1} N_b = E_{\theta_1} N_v$, $E_{\theta_1} N_b$ – the expected number of trials in which treatment B is used under H_1: $p = p' + \Delta$.

For the Mixed Rule X_A (X_B) is of form (S...SF), suppose X_A has i successes and X_B has j successes, $i, j = 0.1, 2, \ldots$, $X = (X_A, X_B)$. The distribution of independent random variables X_A and X_B is geometric, so $f(X, \theta_0) = (p')^{i+j}(1 - p')^2$, $f(X, \theta_1) = (p' + \Delta)^i (1 - p' - \Delta)(p')^j (1 - p')$. Hence $E_{\theta_1} Z = \frac{p'+\Delta}{1-p'-\Delta} \ln \frac{p'+\Delta}{p'} + \ln \frac{1-p'-\Delta}{1-p'}$.

Now the expected number of N_b under H_1 $E_{\theta_1} N_b = \frac{E_{\theta_1} N_v}{1-p'}$, because X_B has a geometric distribution.

These results are shown in Table 2, the entries in Table 3 were determined from simulations. In this case Mixed rule performs better than VT and similar to PWR with all p'.

References

1. M. Fushimi, An improved version of a Sobel-Weiss Play the winner procedure for selecting the better of two binomial populations, *Biometrika*, **60**, 517–523 (1973).

2. Z. Govindarajulu, *Sequential Statistics*, World Scientific Publishing Co. Pte. Ltd., Singapore (2004).
3. D.G. Hoel, An inverse stopping rule for Play the winner sampling, *J. Am. Statist. Ass.*, **67**, 148–151 (1972).
4. M. Sobel, G.H. Weiss, Play the winner sampling for selecting the better of two binominal populations, *Biometrika*, **57**, 357–365 (1970).
5. L.J. Wei, S. Durham, The randomized Play the winner rule in medical trials, *J. Am. Statist. Ass.*, **73**, 840–843 (1978).
6. M. Zelen, Play the winner rule and the controlled clinical trial, *J. Am. Statist. Ass.*, **64**, 131–146 (1969).

REZIUMĖ

K. Mikalauskas, R. Eidukevičius. Apie geresnio gydymo būdo parinkimą

Šiame straipsnyje nagrinėjamas geresnio gydymo būdo parinkimo nuosekliosios analizės metodais uždavinys. Pasiūlyta ir išnagrinėta nauja procedūra. Gauti rezultatai rodo, kad pasiūlytoji procedūra kai kuriais atvejais duoda geresnius rezultatus.

Raktiniai žodžiai: klinikiniai tyrimai, taisyklė „žaidžia nugalėtojas“.