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Abstract

This paper proposes and presents a chi-square statistical method for the analysis of response from one period cross over design for two sample data in which the sampled populations may be measurements that are numeric (assuming real values) and non-numeric assuming only values on the nominal scale. Test statistics are developed for testing the null hypothesis that subjects who receive each of the treatments ýrst do not differ in their response as well as the null hypothesis that subjects exposed to one of the treatment or experimental conditions ýrst do not on the average differ in their responses with those exposed to the other treatment or experimental condition ýrst. Estimates of the proportions responding positive; experiencing no change in response or responding negative are provided for

Keywords: Cross over; Treatment; Chi-square; Design; Patients

Introduction

Suppose subjects for a clinical trial are rst matched on characteristics associated with the outcome understudy such as a disease and randomly assigned the treatments T_1 and T_2. In particular, suppose as in a cross over design, each subject serves as his own control, that is, each patient receives each treatment. One half of the sample of 2n patients or subjects is randomly selected to be given the two treatments in one order and the other half to be given the treatments in the reversed order. at is n of the random sample of the 2n patients or subjects is given treatment, T_1 rst and treatment T_2 later and the remaining n subjects is given treatment T_2 rst and treatment T_1 later. A number of factors must be guarded against in analyzing the data from such studies. However, the order in which the treatments are given may a ect the response [1]. A test that is valid when order e ects are present has been described [2]. Another factor to be guarded against is the possibility that a treatment's e ectiveness may be long lasting and hence may a ect the response to the treatment given a er it. When this so-called carry over e ect operates and when it is unequal for the two treatments, then for comparing their e ectiveness, only the data from the rst period may be used [3]. Speci cally, the responses by the subjects given one of the treatments rst must be compared with the responses by the subjects given the other treatment rst. In this paper we present a method for analyzing data from a crossover design in which each subjects serves as his own control and analysis is based on responses by patients given one of the treatments rst and responses by patients given the other treatment rst. Here allowance is made for the possibility that patients or subjects may die or drop out of the study.

e Proposed Method

In general, let n_j subjects or patients be randomly assigned for treatment with T_j rst: for j=1,2 when n_1 and n_2 are not necessarily equal. Let y_{ij} be the response by the i^{th} subject administered treatment T_j rst for $i=1,2,\ldots,n_j$, j=1,2.

Two possibilities present themselves here namely: y_{ij} may be numeric assuming real values or it may be non-numeric assuming only values on the nominal scale of measurement. If the test score y_{ij} is the numeric, assuming responses or values in the range (c_1,c_2) where c_1 and

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α level of significance $\chi_j^2 \geq \chi_{1-\alpha;1}^2$ otherwise H_0 is accepted where $\chi_{1-\alpha;1}^2$ is obtained from an appropriate chi-square table with 1 degree of freedom at α level of signi cance.

Of greater interest however is testing the null hypothesis H_0 that patients or subjects who take treatment T_1 rst have the same positive response rate as patients who take treatment T_2 rst. is is equivalent to testing the null hypothesis

$$H_0 : \pi_1^+ - \pi_1^- = \pi_2^+ - \pi_2^- \; or \; (\pi_1^+ - \pi_1^-) - (\pi_2^+ - \pi_2^-) = 0$$

vs

$$H_1 : (\pi_1^+ - \pi_1^-) - (\pi_2^+ - \pi_2^-) \neq 0 \tag{17}$$

e null hypothesis may be tested using the test statistics

$$\chi^2 = \frac{(W_1 - W_2)^2}{Var\,(W_1 - W_2)} = \frac{\left(n_1(\hat{\pi}_1^+ - \hat{\pi}_2^-) + n_2(\hat{\pi}_2^+ - \hat{\pi}_2^-)\right)^2}{Var\,(W_1 - W_2)} \tag{18}$$

Which under H_0 has a chi-square distribution with 1 degree of freedom for su ciently large values of n_1 and n_2 where

$$Var\,(W_1 - W_2) = VarW_1 + VarW_2 - 2\,\text{cov}(W_1, W_2) \tag{19}$$

Now

$$\text{cov}\,(W_1, W_2) = E(W_1W_2) = E(W_1)E(W_2)$$
$$= E\sum_{r=1}^{n_1}\sum_{s=1}^{n_2} U_{r1}U_{s2} - E\sum_{r=1}^{n_1} U_{r1} E\sum_{s=1}^{n_2} U_{s2}$$
$$= \sum_{r=1}^{n_1}\sum_{s=1}^{n_2} E(U_{r1}U_{s2}) - \sum_{r=1}^{n_1} E(U_{r1}) \sum_{s=1}^{n_2} E(U_{s2})$$

Now $U_{r1}U_{s2}$ can only assume the values 1,0 and -1. It assumes the value 1 if U_{r1} and U_{s2}

su ciently large n_1 and n_2. e null hypothesis of equation 17 is rejected at the α level of signi cance if $\chi^2 \geq \chi^2_{1-\alpha;1}$.

Otherwise the null hypothesis is accepted. Also the test statistic of equation 22 may equivalently be expressed in terms of sample proportions as:

$$\chi^2 = \frac{n_1 n_2 \left((\hat{\pi}_1^+ - \hat{\pi}_1^-) - (\hat{\pi}_2^+ - \hat{\pi}_2^-)\right)^2}{n_2\left(\hat{\pi}_1^+ + \hat{\pi}_1^- - (\hat{\pi}_1^+ - \hat{\pi}_1^-)^2\right) + n_1\left(\hat{\pi}_2^+ + \hat{\pi}_2^- - (\hat{\pi}_2^+ - \hat{\pi}_2^-)^2\right)}$$

change in response or responding negative are provided for subjects exposed to each treatment rst as well as for the two treatments together.

e proposed method which is illustrated with some sample data can be used with either numeric or non-numeric data and is shown to be at least as powerful as the traditional two sample small t-test.

Reference

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