#### **Program Z\_INDEP.EXE**

### 1. Introduction and notation.

The program performs the one (two)-tailed asymptotic test for testing the null hypothesis of independence (*H*) in a  $2\times 2$  table like Table I; in addition, the program determines the validity conditions for these tests. All the details of the following may be seen in [1].

		Characteristic A		TT ( 1	
		YES	NO	lotais	
Characteristic B	YES NO	$egin{array}{c} x_1 \ x_2 \end{array}$	<i>Y</i> 1 <i>Y</i> 2	n <sub>1</sub> n <sub>2</sub>	
Totals		$a_l$	$a_2$	п	

Table IPresentation of results in the form of a 2×2 table

The results in the above table can have been obtained using 3 types of sampling, which results in 3 types of statistical models and 3 types of test:

- i) *Model III* (the row marginal totals and the column marginal totals are fixed): The values of  $a_i$  and  $n_i$  (*i*=1, 2) are previously fixed, the sole random variable (r.v.) in the problem is  $x_1$  (for example) –a generalized hypergeometric r.v.– and its distribution under *H* is the hypergeometric one. The exact test for *H* is performed using a conditional test (the known Fisher's exact test) [2], which gives rise to a p-value of  $P_{III(E)}$ .
- ii) Model II (only the row marginal totals are fixed): The values of  $n_i$  (*i*=1, 2) are previously fixed, the r.v. for the problem are  $x_1$  and  $x_2$  (for example) –two independent binomial r.v. with parameters  $p_1$  and  $p_2$  and its joint distribution under H ( $p_1=p_2=p$ ) is a double-binomial based on the nuisance parameter p. The exact test for H is carried out using an unconditional test [3], which yields a p-value of  $P_{II(E)}$ .
- iii) Model I (no fixed marginal): Only the value of n is previously fixed, the r.v. for the problem are  $x_1$ ,  $y_1$  and  $x_2$  (for example) –a multinomial distribution with parameters  $p_{11}$ ,  $p_{12}$ ,  $p_{21}$  and  $p_{22}$  and its distribution under  $H(p_{ij}=p_{i\bullet}\times p_{\bullet j})$  is a multinomial based on the two nuisance parameters  $p_{\bullet l}$  and  $p_{1\bullet}$ . The exact test for H is carried out using an unconditional test [3], which yields a p-value of  $P_{I(E)}$ .

The exact p-values  $P_{III(E)}$ ,  $P_{II(E)}$  and  $P_{I(E)}$  are not unique (because they depend on which order statistic is used to obtain them), generally  $P_{III(E)} \ge P_{I(E)}$  (although not always) and they are

progressively more difficult to calculate (in that order). In particular, it is not possible at present to determine the last two (especially  $P_{I(E)}$ ) when the marginal are moderately large. The value of  $P_{III(E)}$  is given in many statistical packages. The value of  $P_{II(E)}$  is given by the StatXact package. Free programs for obtaining the values  $P_{I(E)}$  and  $P_{II(E)}$  may be copied at http://www.ugr.es/local/bioest/SMP.EXE and www.ugr.es/local/bioest/TMP.EXE respectively. If the p-value under a model for the generally most powerful statistic cannot be determined because of computational problems, the p-value under the same model, but for a different less powerful statistic may be determined. If it is still impossible, then the p-value under the higher model may be obtained. The details may be consulted in [4].

For teaching purposes, more ease or the impossibility of calculation, it is usual to resolve the above problem in an <u>approximate</u> manner using the <u>chi-square</u> test with the most appropriate <u>continuity correction</u> c (c.c.) [5]. But, given that the chi-square test is an asymptotic test, it will be subject to certain validity conditions (v.c.). It is usual to require that the minimum expected quantity

$$E = \frac{\min(n_1, n_2) \times \min(a_1, a_2)}{n}$$

be sufficiently large ( $E > E^*$ ), where  $E^*$  is a number which, as will be seen, does not have to be fixed nor have the classic value of 5.

For the following, one must bear in mind that:

1) It is understood that if  $P_E$  is the p-value obtained by the exact test and  $P_A$  is the p-value obtained by the chi-square asymptotic test, then the condition  $E > E^*$  must guarantee that:

$$|P_A - P_E| \le \delta P_E \text{ where } \delta = \begin{cases} 1 & \text{if } P_E \le 1\% \\ 1.15 - 15 \times P_E & \text{if } 1\% < P_E \le 5\% \\ 0.5 - 2 \times P_E & \text{if } 5\% < P_E \le 10\% \\ 0.3 & \text{if } P_E > 10\% \end{cases}$$

In particular, this means that any value  $3\% \le P_A \le 7\%$  is an acceptable estimation of  $P_E = 5\%$ . The values of  $E^*$  and  $P_A$  are obtained as indicated below. The values of  $P_E$  are obtained for the models *I*, *II* and *III* using the unconditional, unconditional and conditional exact tests, respectively, based on the orders of Yates's chi-square, Barnard [3] and Yates's chi-square respectively. The reasons for this may be seen in [1].

2) In the <u>one-tailed test</u> there are two possible alternatives *K*:

*KR* (one right tail): "The association is positive";

*KL* (one left tail): "The association is negative".

Although the program determines the p-value in both cases, the description which follows only considers those results and hypotheses which yield a p-value <0.5 (in order to facilitate the explanation). This means that the one-tailed tests which follow refer to the alternative that is compatible with the results (*KR* if *N*>0 or *KL* if *N*<0, where  $N = x_1y_2 - x_2y_1$ ) and are valid only when

the results verify -c < N < +c: in the other cases the p-value is  $\ge 0.5$ .

- 3) In the <u>two-tailed test</u> (alternative K: "There is positive or negative association) the chi-square quantity depends on the term |N|-c. In every case it is understood that |N|-c=0 when -c ≤ N ≤ +c.
- 4) If F(•) refers to the distribution function of a typical normal r.v., then the p-value of the statistic χ≥0 for the one- or two-tailed test is 1-F(χ) or 2×{1-F(χ)}, respectively.

# 2. Calculating the asymptotic p-value under the Model III (both marginal totals are fixed).

### 2.1. One-tailed test.

The <u>classic statistic</u> is the chi-square statistic with <u>Yates</u>'s c.c. Thus the p-value is given by  $P_Y = 1-F(\chi_Y)$ , where:

$$\chi_Y^2 = \frac{\left\{ \left| x_1 y_2 - x_2 y_1 \right| - n/2 \right\}^2}{a_1 a_2 n_1 n_2} n \tag{1}$$

The <u>optimal statistic</u> [6] is the chi-square statistic with <u>Conover</u>'s c.c. [7]. Thus the p-value is given by  $P_{III} = 1 - F(\chi_{III})$ , where:

$$\chi_{III}^2 = \chi_Y^2 + \frac{n^3}{4a_1 a_2 n_1 n_2}$$
(2)

For the above tests to be valid, it is necessary that:

$$E > E^{*} = \frac{1}{K+1} \left[ \frac{n}{2} \left\{ 1 - \sqrt{\frac{C}{C+4y}} \right\} \right]^{-} \text{ where } \begin{cases} C = \frac{(n-2)^{2}}{n-1} \\ y = \begin{cases} 7.785 + 20.627x \text{ for Yates's case} \left(\chi_{Y}^{2}\right) \\ 6.486 + 19.111x \text{ for Conover's case} \left(\chi_{III}^{2}\right) \end{cases} \\ x = \frac{(K-1)^{2}}{K} \\ K = \begin{cases} \frac{\max(n_{1}, n_{2})}{\min(n_{1}, n_{2})} & \text{if } |n_{2} - n_{1}| \le |a_{2} - a_{1}| \\ \frac{\max(a_{1}, a_{2})}{\min(a_{1}, a_{2})} & \text{if } |n_{2} - n_{1}| > |a_{2} - a_{1}| \\ [z]^{-} & = \text{ the integral part of } z \end{cases}$$
(3)

<u>A universal</u> (and conservative) <u>condition</u> is  $E^*=19.2$  (20.7) for the case  $P_{III}$  ( $P_Y$ ). <u>The universal condition when  $n \le 500$  is reduced to  $E^*=8.1$  for the case  $P_{III}$ .</u>

### 2.2. Two-tailed test.

The <u>classic statistic</u> is the chi-square statistic with the <u>Yates</u> c.c. So the p-value is given by  $P_Y = 2 \times \{1 - F(\chi_Y)\}$ . But this gives rise to a very conservative test [8].

The <u>optimal statistic</u> [9] is that of Yates but using the <u>Mantel</u> precaution [8]. The p-value is given by  $P_{III} = \{1-F(\chi_Y)\}+\{1-F(\chi_{Y'})\}$ , where  $\chi_{Y'}^2$  refers to the value of  $\chi_Y^2$  in the table with  $x'_1 = [2E_{II}-x_I]$ , where  $E_{11}=n_Ia_I/n$  and [x] refers to the rounding of x in the sense of moving away from the value of  $E_{11}$  ([x]= $E_{II}$  if  $x=E_{11}$ ; [x] = "the integral part of x" if  $x < E_{11}$ ; [x] = "the smallest integer not less than x" if  $x > E_{11}$ ). When  $x'_1 > s = \min(n_I, a_I)$  or  $x'_1 < r = \max(0, a_I - n_2)$ , then  $1-F(\chi_{Y'})=0$ . This test is always valid (since  $E^*=0$ ).

# **3.** Calculating the asymptotic p-value under the Model *II* (only the row marginal totals are fixed).

The <u>classic statistic</u> is the chi-square statistic with the <u>Yates</u> c.c. So the p-value is given by  $P_Y = 1 - F(\chi_Y)$  for the one-tailed test and  $P_Y = 2 \times \{1 - F(\chi_Y)\}$  for the two-tailed test. But this produces a very conservative test [10].

The optimal statistic is Pearson's chi-square statistic with the c.c. of Martín et el. [10]:

$$\chi_{II}^{2} = \frac{\left\{ \left| x_{1}y_{2} - x_{2}y_{1} \right| - c \right\}^{2}}{a_{1}a_{2}n_{1}n_{2}} (n-1) \text{ where } c = \begin{cases} 2 & \text{if } n_{1} = n_{2} \\ 1 & \text{if } n_{1} \neq n_{2} \end{cases}$$
(4)

The p-values for the one- and two-tailed tests then are  $P_{II} = 1 - F(\chi_{II})$  and  $P_{II} = 2 \times \{1 - F(\chi_{II})\}$  respectively.

For the test to be valid, it is necessary that:

$$E > E^* = \frac{1}{K+1} \left[ \frac{n}{2} \left\{ 1 - \sqrt{\frac{C}{C+4y}} \right\} \right]^- \text{ where } \begin{cases} C = \frac{n^2}{n-1} \\ y = \begin{cases} 9.743 + 14.786x \text{ for the one-tailed test} \\ 16.315 + 14.889x \text{ for the two-tailed test} \end{cases}$$

$$K = \frac{(K-1)^2}{K} \\ K = \frac{\max(n_1, n_2)}{\min(n_1, n_2)} \\ [z]^- = \text{ the integral part of } z \end{cases}$$
(5)

<u>A universal</u> (and conservative) <u>condition</u> is  $E^*=14.8$  (14.9) for the case of one (two) tails. <u>The universal condition when  $n \le 500$  is reduced to  $E^*=7.2$  (7.7) for the case of one (two) tails.</u>

## 4. Calculating the asymptotic p-value under the Model *I* (no fixed marginal).

The <u>classic statistic</u> is the chi-square statistic with the <u>Yates</u> c.c. Hence the p-value is given by  $P_Y = 1 - F(\chi_Y)$  for the one-tailed test and  $P_Y = 2 \times \{1 - F(\chi_Y)\}$  for the two-tailed test. But this gives rise to a very conservative test [10].

The <u>optimal statistic</u> [11] is the <u>Pearson's</u> chi-square statistic with the c.c. of <u>Pirie and Hamdan</u> [12]:

$$\chi_I^2 = \frac{\left\{ \left| x_1 y_2 - x_2 y_1 \right| - 0.5 \right\}^2}{a_1 a_2 n_1 n_2} (n-1)$$
(6)

The p-values for the one- and two-tailed tests then are  $P_{II}=1-F(\chi_I)$  y  $P_{II}=2\times\{1-F(\chi_I)\}$  respectively.

For the test to be valid it is necessary that:

$$E > E^{*} = \frac{1}{K+1} \left[ \frac{n}{2} \left\{ 1 - \sqrt{\frac{C}{C+4y}} \right\} \right]^{-} \text{ where } \begin{cases} C = \frac{n^{4}}{(n-2)^{2}(n-1)} \\ y = \begin{cases} 7.318 + 3.899x \text{ for the one-tailed test} \\ 7.612 + 6.120x \text{ for the two-tailed test} \end{cases} \\ x = \frac{(K-1)^{2}}{K} \\ K = \begin{cases} \frac{\max(n_{1},n_{2})}{\min(n_{1},n_{2})} \text{ if } |n_{2}-n_{1}| \le |a_{2}-a_{1}| \\ \frac{\max(a_{1},a_{2})}{\min(a_{1},a_{2})} \text{ if } |n_{2}-n_{1}| > |a_{2}-a_{1}| \\ \left[z\right]^{-} = \text{ the integral part of } z \end{cases}$$
(7)

<u>A universal (and conservative) condition</u> is  $E^*=3.9$  (6.2) for the case of one (two) tails. The universal condition when  $n \le 500$  is reduced to  $E^*=3.0$  (3.9) for the case of one (two) tails.

#### REFERENCES

- Martín Andrés, A.; Sánchez Quevedo, M. J.; Tapia García, J.M. and Silva Mato, A. (2005). On the validity condition of the chi-squared test in 2×2 tables. *Test* 14 (1), 1-30.
- Fisher, R.A. (1935). The logic of inductive inference. *Journal of the Royal Statistical Society A 98*, 39-54.
- 3. Barnard, G.A. (1947). Significance tests for 2×2 tables. *Biometrika 34*, 123-138.
- Martín Andrés, A.; Silva Mato, A.; Tapia García, J.M. and Sánchez Quevedo, M. J. (2004). Comparing the asymptotic power of exact tests in 2×2 tables. *Computational Statistics and Data Analysis* 47 (4), 745-756.

- 5. Greenwood, P.E. and Nikulin, M.S. (1996). *A Guide to Chi-Squared Testing*, 1d ed., ed.Wiley Series in Probability and Statistics. New York, 1996.
- 6. Martín Andrés, A. and Herranz Tejedor, I. (1997). On condition for validity of the approximations to Fisher's exact test. *Biometrical Journal 39*, 935-54.
- Conover, W.J. (1974). Some reasons for not using the Yates' continuity corrections on 2×2 contingency tables. *Journal of the American Stat. Assoc.* 69, 374-376.
- 8. Mantel, N. (1974). Comment and a Suggestion. Journal of the American Stat. Assoc. 69, 378-380.
- Martín Andrés, A., Herranz Tejedor, I. and Luna del Castillo, J.D. (1992). Optimal correction for continuity in the chi-squared test in 2×2 tables (conditioned method). *Commun. Statist. - Simula. and Comp. 21 (4)*, 1077-1101.
- Martín Andrés, A.; Sánchez Quevedo, M. J. and Silva Mato, A. (2002). Asymptotical tests in 2×2 comparative trials (unconditional approach). *Computational Statistics and Data Analysis* 40 (2), 339-354.
- 11. Martín Andrés, A. and Tapia Garcia, J. M. (2004). Optimal unconditional asymptotic test in 2×2 multinomial trials. *Commun. Statist. -Simula. and Comp. 33 (1)*, 83-97.
- Pirie, W.R. and Hamdan, M.A. (1972). Some revised continuity corrections for discrete distributions. *Biometrics* 28, 693-701.