

### **Program Z\_EQUIV.EXE**

The program provides the asymptotical unconditional p-value (obtained with and without a continuity correction) for the comparison of two independent proportions ( $p_2$  and  $p_1$ ) by means of the z-pooled statistic  $Z = (\hat{d} - \delta \pm c)/s$  with:

- $x_i \sim$  two independent binomial ( $n_i, p_i$ );
- Sample 1 (2): standard (new) treatment;
- $\hat{d} = \hat{p}_2 - \hat{p}_1$  and  $\hat{p}_i = x_i/n_i$ ;
- $\delta =$  the value of  $d = p_2 - p_1$  under null hypotheses H;
- $c =$  the continuity correction (c.c. in the following) (see the Table);
- $s = \sqrt{\tilde{p}(1-\tilde{p})/n_1 + (\tilde{p}+\delta)(1-\tilde{p}-\delta)/n_2}$  = E.E. = the standard error of  $\hat{d}$  under H;
- $\tilde{p} =$  the estimator of maximum likelihood of  $p=p_1$  under H;
- $E =$  minimum expected quantity =  $\{n_1 \tilde{p}, n_1(1-\tilde{p}), n_2(\tilde{p}+\delta), n_2(1-\tilde{p}-\delta)\}$

The null (H) and alternative (K) hypotheses are:

<b>Hypotheses:</b>	<b>Null</b>	<b>Alternative</b>
For SG:	$d \leq \delta$	$d > \delta$
For IG:	$d \leq \delta$	$d < \delta$
For SDG:	$\delta_1 \leq d \leq \delta_2$	$d < \delta_1$ or $d > \delta_2$
For SD:	$ d  \leq \Delta$	$ d  > \Delta$
For SG2:	$d = \delta$	$d \neq \delta$
For PEG:	$d \leq \delta_1$ or $d \geq \delta_2$	$\delta_1 < d < \delta_2$
For PE:	$ d  \geq \Delta$	$ d  < \Delta$

To calculate the p-value, see the Table. For further details, see the paper:

Martín Andrés, A. and Herranz Tejedor, I. (2004). Asymptotical tests on the equivalence, substantial difference and non-inferiority problems with two proportions. *Biometrical Journal* 46 (3), 305-319.

**Table**

Case	p-value	c = Variable c.c. ( $\times 2$ if $n_1 = n_2$ )
<b>SG (IG)</b>	$P=F\left\{\frac{- \hat{d}+\delta +c}{s}\right\} \quad \left(F\left\{\frac{ \hat{d}-\delta +c}{s}\right\}\right)$	$[N(1-\delta)]^{-1}$ if $\delta \geq 0$ ( $\delta \leq 0$ ) $(1-\delta)[N\{2-(1+\delta)^2\}]^{-1}$ if $\delta < 0$ ( $\delta > 0$ )
<b>SDG</b>	$P=F\left\{\frac{- \hat{d}-\delta_1 +c}{s_o}\right\} + F\left\{\frac{- \hat{d}-\delta_2 +c}{s_o}\right\}$ if $\hat{d} \in \delta_1 + \delta_2 \pm 1$ $P=\max_{i=1,2} F\left\{\frac{- \hat{d}-\delta_i +c}{s_i}\right\}$ if $\hat{d} \notin \delta_1 + \delta_2 \pm 1$	$\frac{(1+\delta_1)+(1-\delta_2)}{N\{(1+\delta_1)^2+(1-\delta_2)^2\}}$ if $\delta_1 \leq 0 \leq \delta_2$ $\frac{2- \delta_2-\delta_1 }{N\{2-[1- \delta_2 ^2]-(1- \delta_1 ^2)\}}$ other case
<b>SD</b>	$P=F\left\{\frac{- \hat{d}+\Delta +c}{s_o}\right\} + F\left\{\frac{- \hat{d}-\Delta +c}{s_o}\right\}$	$\frac{1}{N(1-\Delta)}$
<b>SG2</b>	$P=2 \times F\left\{\frac{- \hat{d}-\delta +c}{s}\right\}$ if $\hat{d} \in 2\delta \pm 1$ $P=F\left\{\frac{- \hat{d}-\delta +c}{s}\right\}$ if $\hat{d} \notin 2\delta \pm 1$	$\frac{1}{N}$
<b>PEG</b>	$P=\max_{i=1,2} \left[ F\left\{\frac{\delta_r +  \hat{d}-\delta_o +c}{s_i}\right\} - F\left\{\frac{\delta_r -  \hat{d}-\delta_o -c}{s_i}\right\} \right]$ where $\delta_o=(\delta_1+\delta_2)/2$ and $\delta_r=(\delta_2-\delta_1)/2$	$\frac{\delta_2-\delta_1}{N\{2-(1+\delta_1)^2-(1-\delta_2)^2\}}$ if $\delta_1 < 0 < \delta_2$ $\left[N\{2- \delta_1 - \delta_2 \}\right]^{-1}$ other case
<b>PE</b>	$P=\max_{i=1,2} \left[ F\left\{\frac{\Delta+ \hat{d} +c}{s_i}\right\} - F\left\{\frac{\Delta- \hat{d} -c}{s_i}\right\} \right]$	$\frac{1}{N(2-\Delta)}$
<b>NOTES</b>		
<p>(1) s is the value of <math>\sqrt{\tilde{p}(1-\tilde{p})/n_1 + (\tilde{p}+\delta)(1-\tilde{p}-\delta)/n_2}</math> in the observed point and for the <math>\delta</math>-value of each case; when there are two value of <math>\delta</math> implied (<math>\delta_1</math> y <math>\delta_2</math>; <math>-\Delta</math> y <math>+\Delta</math>), the <math>\delta</math>-values are respectively <math>s_1</math> and <math>s_2</math>, whose maximum is <math>s_o</math>;</p> <p>(2) <math>F(\cdot)</math> is the distribution function of a normal typical distribution;</p> <p>(3) <math>N = (n_1+1) \times (n_2+1)</math>.</p> <p>(4) A continuity correction valid for all the cases is <math>c = 1/N</math> (<math>2/N</math> if <math>n_1 = n_2</math>): <b>Constant c.c.</b></p> <p>(5) The p-value <b>without</b> continuity correction is obtained for <math>c=0</math>.</p>		