

# SAS Macro RREst\_Trend

## Relative risk estimation with various trend estimates

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## 1 General remarks

This document describes the SAS macro RREst. It should be read together with the paper “Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category”. This document focuses on technical details of generating the table of effective frequencies, while the practical aspects of the method are discussed in the paper.

## 2 Discussion of the procedure

This section illustrates the problem and its solution by considering a case-control study with odds ratios and confidence intervals given for several levels of exposure to a risk factor. The other cases are handled analogously.

### 2.1 Problem and objectives

The following table describes the numbers of participants in a case-control study (this case corresponds to subsection 4.1):

| Exposure                     | Cases | Controls |
|------------------------------|-------|----------|
| Exposure level 0 (unexposed) | $A_0$ | $B_0$    |
| Exposure level 1             | $A_1$ | $B_1$    |
| ...                          | ...   | ...      |
| Exposure level $n$           | $A_n$ | $B_n$    |
| Total Cases/Controls         | $A$   | $B$      |

The frequencies  $A_0, \dots, A_n$  and  $B_0, \dots, B_n$  are not known. Instead, the following are known:

- the odds ratios  $R_i = \frac{A_i B_0}{A_0 B_i}$ ,  $i = 1, \dots, n$ , with  $(1 - \alpha)$ -confidence intervals  $(L_i, U_i)$ ,
- the initial (2 x 2)-table of overall frequencies given below, or at least an approximation to it:

|             | Cases     | Controls  |
|-------------|-----------|-----------|
| Unexposed   | $A_0$     | $B_0$     |
| All exposed | $A - A_0$ | $B - B_0$ |

From this table, the following two quantities are calculated:

- $P = B_0 / B$ , the proportion of unexposed subjects in the controls,
- $Z = B / A$ , the relative frequency of controls to cases overall

The confidence limits  $(L_i, U_i)$  are assumed to be based on the formula

$$\exp\left(\log(R_i) \pm z_{1-\alpha/2} \sqrt{V_i}\right) \text{ where } V_i = A_i^{-1} + A_0^{-1} + B_i^{-1} + B_0^{-1}.$$

The approximate variances  $V_i$  can therefore be calculated as

$$V_i = \left( \frac{\log(U_i / L_i)}{2 \cdot z_{1-\alpha/2}} \right)^2.$$

This yields a system of  $2(n+1)$  equations linking the  $2(n+1)$  input quantities  $(R_1, \dots, R_n, V_1, \dots, V_n, P, Z)$  to the same number of unknown quantities  $(A_0, \dots, A_n, B_0, \dots, B_n)$ .

## 2.2 Reduction to two dimensions

The given system of equations can be reduced to an optimisation problem in two dimensions by substitution. Assume  $A_0$  and  $B_0$  are known. Then the remaining unknown quantities are derived successively using the formulae:

$$\hat{A}_i = \frac{1 + A_0 R_i B_0^{-1}}{V_i - A_0^{-1} - B_0^{-1}} \quad i = 1, \dots, n$$

$$\hat{B}_i = \frac{1 + B_0 (A_0 R_i)^{-1}}{V_i - A_0^{-1} - B_0^{-1}} \quad i = 1, \dots, n$$

$$\hat{A} = A_0 + \hat{A}_1 + \dots + \hat{A}_n, \quad \hat{B} = B_0 + \hat{B}_1 + \dots + \hat{B}_n$$

$$\hat{P} = B_0 / \hat{B}, \quad \hat{Z} = \hat{B} / \hat{A}$$

Values  $A_0$  and  $B_0$ , which provide a solution to the problem, must therefore meet the following conditions:

$$\hat{P} = P \tag{1}$$

$$\hat{Z} = Z, \tag{2}$$

where  $\hat{P}$  and  $\hat{Z}$  are considered as functions  $\hat{P}(A_0, B_0)$ ,  $\hat{Z}(A_0, B_0)$  and  $P$  and  $Z$  are the values calculated from the initial 2x2 table.

## 2.3 Existence and uniqueness of a solution

It can be shown by elementary algebraic transformations that (1) is equivalent to

$$\sum_{i=1}^n \frac{A_0 + B_0 / R_i}{V_i A_0 B_0 - A_0 - B_0} - \frac{1-P}{P} = 0 \tag{3}$$

and (2) is equivalent to

$$\sum_{i=1}^n \frac{-ZR_i A_0^2 + (1-Z)A_0 B_0 + R_i^{-1} B_0^2}{V_i A_0 B_0 - A_0 - B_0} - ZA_0 + B_0 = 0. \quad (4)$$

Multiplying by the common denominator  $\prod_{i=1}^n (V_i A_0 B_0 - A_0 - B_0)$  results in a representation of two polynomials of order  $2n+1$  and  $2(n+1)$  in  $A_0$  and  $B_0$ . The problem at hand thus consists in finding a common root of two polynomials. Certain additional constraints have thereby to be met, so that all  $A_i$  and  $B_i$  be positive (in the case of case-control studies considered here, this requirement is ensured if  $A_0$  and  $B_0$  are positive; however, this does not hold in all cases). No general result about the existence and uniqueness of a solution in this situation is known.

## 2.4 Reparametrisation and formulation as a optimisation on the unit square

For convenience, the problem is reparameterised in order to convert it into an optimisation task on the unit square. Define

$$\beta_1 = \frac{A_0^{-1} + B_0^{-1}}{V_{\min}} \quad \text{where } V_{\min} = \min \{V_1, \dots, V_n\},$$

$$\beta_2 = \frac{A_0}{A_0 + B_0}.$$

Each  $(\beta_1, \beta_2) \in (0,1) \times (0,1)$  represents a table of the kind given in 2.1, accounting for the conditions  $A_0 > 0$ ,  $B_0 > 0$  and  $A_0^{-1} + B_0^{-1} < V_{\min}$  (the latter condition is implied by the fact that all  $V_i = A_i^{-1} + A_0^{-1} + B_i^{-1} + B_0^{-1}$  must be positive). Conversely, each table meeting these requirements is represented by a pair of  $\beta$ 's on the unit square: for a given

$(\beta_1, \beta_2) \in (0,1) \times (0,1)$ , the corresponding table frequencies are derived by first calculating

$$A_0 = \frac{B_0 \beta_2}{1 - \beta_2} \quad \text{and} \quad B_0 = (\beta_1 \beta_2 V_{\min})^{-1},$$

and all other table frequencies can be calculated using the equations given in 2.2.

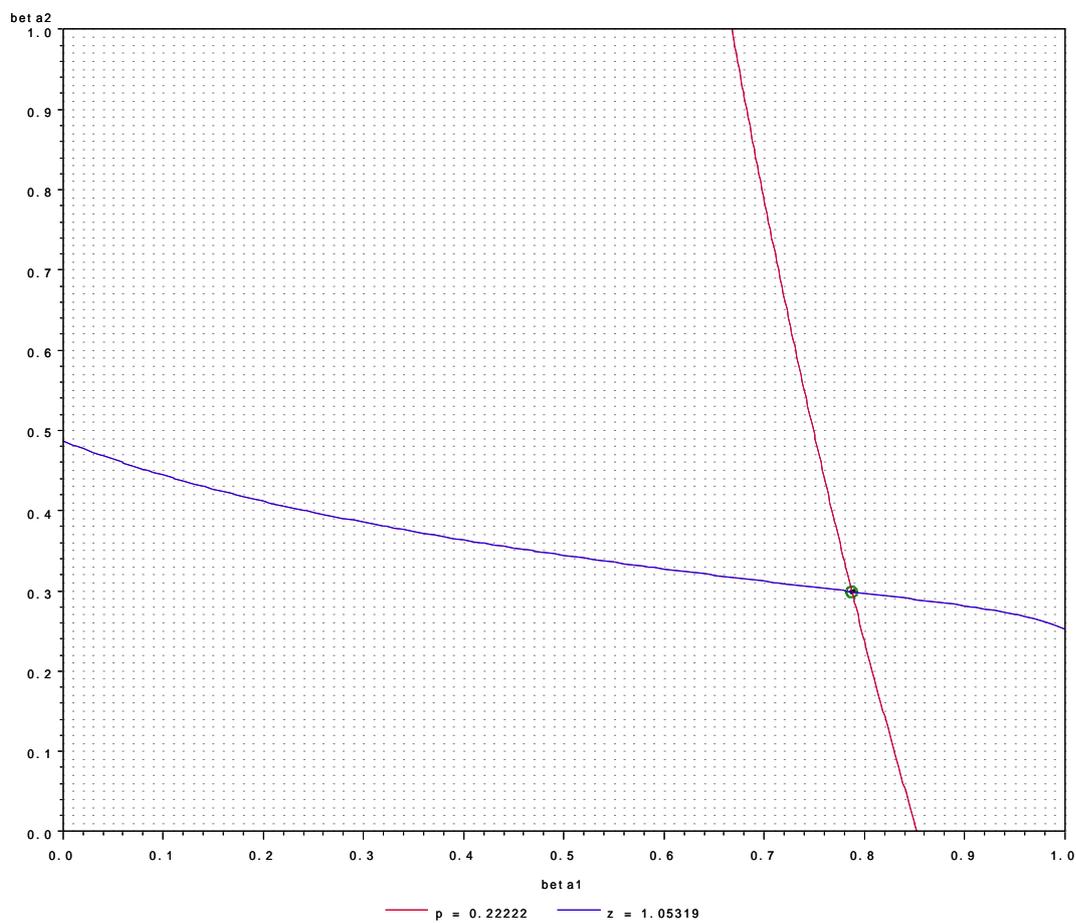
The problem now consists in finding a minimum of the objective function

$$F(\beta_1, \beta_2) = \frac{(P - \hat{P})^2}{P^2} + \frac{(Z - \hat{Z})^2}{Z^2}$$

in which the function's value is 0, i.e. values  $\hat{\beta}_1$  and  $\hat{\beta}_2$  with  $F(\hat{\beta}_1, \hat{\beta}_2) = 0$ . A suitable starting point for the iterative process is found by calculating the value of the objective

function at every point of a grid on the unit square and choosing the point with the lowest value. An iterative gradient method then searches for a minimum. If this process ends in a point where  $F = 0$ , we have succeeded in finding a potential solution.

Figure 1 illustrates the problem and its solution for the example Smith et al. discussed in the paper. The two lines are the contours corresponding to the conditions  $\hat{P}(\beta_1, \beta_2) = 0.2222$  and  $\hat{Z}(\beta_1, \beta_2) = 1.053$  respectively. The intersection of the two lines is the solution of the problem. There is little doubt that there is a unique solution in this instance.



**Figure 1: Solution finding with the data from Smith et al..**

### 3 Concepts

The macro RREst handles the following four cases distinguished by study type, categorisation of the results:

- case-control study with odds ratios given for various exposure groups versus an unexposed group,
- case-control study with odds ratios given for various disease categories versus a control group,
- prospective (cohort) study with risk ratios given for various exposure groups versus an unexposed group,
- prospective (cohort) study with risk ratios given for various disease categories versus the group of subjects without disease.

This section discusses some general features of the macro. An outline of the different cases and some case-specific detailed information follow in section 4.

#### 3.1 Parametrisation

An appropriate parametrisation  $(\beta_1, \beta_2) \in (0,1) \times (0,1)$  has to be found for each of the four cases separately. An attempt was made to find, whenever possible, a parametrisation corresponding to a one-to-one mapping between the unit square and the set of all possible frequency tables meeting the restrictions imposed by the input data. In all cases but one, such a parametrisation was found. In case 4.4, only a parametrisation yielding a one-to-one mapping between the set of possible tables and *a subset of* the unit square was found. Attention has therefore to be paid to ensure that the macro does not produce an assumed solution featuring negative cell frequencies.

#### 3.2 Graphical Illustration

An example of an illustration of the solving process was given in section 2.4. The macro automatically generates this type of graphic containing the following elements:

- The points  $(\beta_1, \beta_2)$  of a grid on the unit square (determined by the macro parameter `grid`), drawn as gray dots. If some of the points correspond to a table with negative table frequencies, these grid points are marked by a black 'x'. This mainly occurs in case 4.4. In other cases it can happen for grid points lying next to the edge of the unit square, due to numerical instability.

- Two contours lines, each (approximately) indicating the set of points corresponding to frequency tables meeting one of the two additional conditions  $\hat{P} = P$  and  $\hat{Z} = Z$ . The red contour corresponds to the first equation, the blue one to the second.
- The course of the iteration process. In many instances, the starting and ending point of the process are very close, so that this feature is hardly visible.
- The point where the iterations stopped (and hopefully converged), marked by a green circle.

### 3.3 Checking the solution

After the iterative process has been completed and the contour plot created, the resulting frequency table is subject to the following checks:

- If SAS PROC NLIN does not return the convergence status “Converged”, a warning message is written to the log and the remaining steps of the macro (tests and contrast) are cancelled.
- The same happens if negative cell frequencies occur.
- The relative errors in the two equations are calculated as

$$\frac{\hat{P} - P}{P} \text{ and } \frac{\hat{Z} - Z}{Z}$$

If the absolute value of this error is greater than 0.001 for either of the two equations, the remaining steps are carried out but a warning message is written to the log at the end of the macro execution.

Note that the contour plot and the estimated table frequencies are output whether the checks have revealed possible errors or not.

### 3.4 Tests for homogeneity and trend (Breslow 1980)

A test for homogeneity and, if requested, a test for the significance of the trend are performed on the table of effective frequencies. The trend estimate depends on the dose values supplied. The resulting test statistics and their p-values are written to the SAS output window. The formulae are given in Appendix C of the document describing the Excel implementation (available at [www.pnlee.co.uk/software.htm](http://www.pnlee.co.uk/software.htm)).

### 3.5 Trend: rate of increase per unit dose

Two set of results are provided, one based on the dose values supplied and the other based on the Uniform scale. Both use the method described by Berlin et al. 1993 with correction for

non-independence of results by exposure level given by Greenland and Longnecker 1992 together with the modifications necessary for prospective studies described by Orsini et al. 2012. The results based on the supplied dose values can be used when a mean exposure value (dose) can be estimated for each exposure level. When a study uses a non-quantitative measure, such as ‘None’, ‘A little’ and ‘A lot’ this method cannot be used because the exposure cannot be quantified. However, the Uniform scale can be used to provide a trend result that is comparable across similar studies. See the documentation for the Excel implementation, especially Appendices D and E (available at [www.pnlee.co.uk/software.htm](http://www.pnlee.co.uk/software.htm)).

Goodness of fit tests are applied to both of these trend estimates. The method used to derive the fitted numbers of cases for these tests is described in the document “Goodness-of-fit tests for fitted RRs”, available at [www.pnlee.co.uk/software.htm](http://www.pnlee.co.uk/software.htm).

## 4 Symbols and formulae

### 4.1 Case-control study, results given by exposure level

**Frequency table:**

| Exposure                        | Cases | Controls |
|---------------------------------|-------|----------|
| Exposure level 0<br>(unexposed) | $A_0$ | $B_0$    |
| Exposure level 1                | $A_1$ | $B_1$    |
| ...                             | ...   | ...      |
| Exposure level $n$              | $A_n$ | $B_n$    |

**Measure of relative risk:** Odds ratio

**Point estimates:**  $R_i = \frac{A_i B_0}{A_0 B_i}$

**Confidence intervals:**

$\exp(\log(R_i) \pm z_{1-\alpha/2} \sqrt{V_i})$  where  $V_i = A_i^{-1} + A_0^{-1} + B_i^{-1} + B_0^{-1}$

**Initial 2x2 table:**

|             | Cases               | Controls            |
|-------------|---------------------|---------------------|
| Unexposed   | $A_0$               | $B_0$               |
| All exposed | $A_1 + \dots + A_n$ | $B_1 + \dots + B_n$ |

**Definition of P and Z:**

$$P = \frac{B_0}{B_0 + B_1 + \dots + B_n}, Z = \frac{B_0 + \dots + B_n}{A_0 + \dots + A_n}$$

**Resulting formulae for  $A_i$  and  $B_i$ :**

$$A_i = \frac{1 + A_0 R_i B_0^{-1}}{V_i - A_0^{-1} - B_0^{-1}}, B_i = \frac{1 + B_0 (A_0 R_i)^{-1}}{V_i - A_0^{-1} - B_0^{-1}}$$

**Constraints on  $A_0$  and  $B_0$ :**

$$A_0 > 0, B_0 > 0 \text{ and } A_0^{-1} + B_0^{-1} < V_{\min}$$

**Parametrisation used:**

$$\beta_1 = \frac{A_0^{-1} + B_0^{-1}}{V_{\min}}, \beta_2 = \frac{A_0}{A_0 + B_0} \text{ where } V_{\min} = \min \{V_1, \dots, V_n\}.$$

Solved for  $A_0$  and  $B_0$ :

$$B_0 = (\beta_1 \beta_2 V_{\min})^{-1}, A_0 = \frac{B_0 \beta_2}{1 - \beta_2}$$

## 4.2 Case-control study, results given by disease category

**Frequency table:**

| Disease Category     | Exposed | Unexposed |
|----------------------|---------|-----------|
| Control              | $A_0$   | $B_0$     |
| Disease Category 1   | $A_1$   | $B_1$     |
| ...                  | ...     | ...       |
| Disease Category $n$ | $A_n$   | $B_n$     |

**Measure of relative risk: Odds ratio**

**Point estimates:**  $R_i = \frac{A_i B_0}{A_0 B_i}$

**Confidence intervals:**

$$\exp\left(\log(R_i) \pm z_{1-\alpha/2} \sqrt{V_i}\right) \text{ where } V_i = A_i^{-1} + A_0^{-1} + B_i^{-1} + B_0^{-1}$$

**Initial 2x2 table:**

|  |         |           |
|--|---------|-----------|
|  | Exposed | Unexposed |
|--|---------|-----------|

|           |                     |                     |
|-----------|---------------------|---------------------|
| Controls  | $A_0$               | $B_0$               |
| All Cases | $A_1 + \dots + A_n$ | $B_1 + \dots + B_n$ |

**Definition of  $P$  and  $Z$ :**

$$P = \frac{B_0}{B_0 + B_1 + \dots + B_n}, \quad Z = \frac{B_0 + \dots + B_n}{A_0 + \dots + A_n}$$

**Resulting formulae for  $A_i$  and  $B_i$ :**

$$A_i = \frac{1 + A_0 R_i B_0^{-1}}{V_i - A_0^{-1} - B_0^{-1}}, \quad B_i = \frac{1 + B_0 (A_0 R_i)^{-1}}{V_i - A_0^{-1} - B_0^{-1}}$$

**Constraints on  $A_0$  and  $B_0$ :**

$$A_0 > 0, \quad B_0 > 0 \quad \text{and} \quad A_0^{-1} + B_0^{-1} < V_{\min}$$

**Parametrisation used:**

$$\beta_1 = \frac{A_0^{-1} + B_0^{-1}}{V_{\min}}, \quad \beta_2 = \frac{A_0}{A_0 + B_0} \quad \text{where} \quad V_{\min} = \min \{V_1, \dots, V_n\}.$$

Solved for  $A_0$  and  $B_0$ :

$$B_0 = (\beta_1 \beta_2 V_{\min})^{-1}, \quad A_0 = \frac{B_0 \beta_2}{1 - \beta_2}$$

Note that the formulae in 4.1 and 4.2 are identical, although the underlying sampling schemes differ.

### 4.3 Cohort study, results given by exposure level

**Frequency table:**

| Exposure                        | Events | At Risk |
|---------------------------------|--------|---------|
| Exposure level 0<br>(unexposed) | $A_0$  | $B_0$   |
| Exposure level 1                | $A_1$  | $B_1$   |
| ...                             | ...    | ...     |
| Exposure level $n$              | $A_n$  | $B_n$   |

**Measure of relative risk:** Risk ratio

**Point estimates:**  $R_i = \frac{A_i B_0}{B_i A_0}$

**Confidence intervals:**

$\exp(\log(R_i) \pm z_{1-\alpha/2} \sqrt{V_i})$  where  $V_i = A_i^{-1} - B_i^{-1} + A_0^{-1} - B_0^{-1}$

**Initial 2x2 table:**

|             | Events              | At Risk             |
|-------------|---------------------|---------------------|
| Unexposed   | $A_0$               | $B_0$               |
| All exposed | $A_1 + \dots + A_n$ | $B_1 + \dots + B_n$ |

**Definition of P and Z:**

$$P = \frac{B_0}{B_0 + B_1 + \dots + B_n}, \quad Z = \frac{B_0 + \dots + B_n}{A_0 + \dots + A_n}$$

**Resulting formulae for  $A_i$  and  $B_i$ :**

$$A_i = \frac{1 - A_0 R_i B_0^{-1}}{V_i - A_0^{-1} + B_0^{-1}}, \quad B_i = \frac{1 + B_0 (A_0 R_i)^{-1}}{V_i - A_0^{-1} + B_0^{-1}}$$

**Constraints on  $A_0$  and  $B_0$ :**

$$0 < A_0 < B_0,$$

$$A_0^{-1} - B_0^{-1} < V_{\min} \text{ where } V_{\min} = \min \{V_1, \dots, V_n\},$$

$$\frac{R_i A_0}{B_0} < 1$$

**Parametrisation used:**

$$\beta_1 = 1 - \frac{100}{100 + B_0 - (R_{\max} - 1)/V_{\min}}, \quad \beta_2 = \frac{R_{\max} \{A_0 (1 + B_0 V_{\min}) - B_0\}}{B_0 (1 + B_0 V_{\min} - R_{\max})}$$

where  $R_{\max} = \max \{R_1, \dots, R_n, 1\}$  and  $V_{\min} = \min \{V_1, \dots, V_n\}$ .

Solved for  $A_0$  and  $B_0$ :

$$B_0 = \frac{100 \beta_1}{1 - \beta_1} + \frac{R_{\max} - 1}{V_{\min}}, \quad A_0 = B_0 \left( \frac{1 - \beta_2}{1 + B_0 V_{\min}} + \frac{\beta_2}{R_{\max}} \right)$$

#### 4.4 Cohort study, results given by disease category

Frequency table:

| Disease Category     | Exposed | Unexposed |
|----------------------|---------|-----------|
| Total (At Risk)      | $A_0$   | $B_0$     |
| Disease Category 1   | $A_1$   | $B_1$     |
| ...                  | ...     | ...       |
| Disease Category $n$ | $A_n$   | $B_n$     |

Measure of relative risk: Risk ratio

Point estimates:  $R_i = \frac{A_i B_0}{A_0 B_i}$

Confidence intervals:

$$\exp\left(\log(R_i) \pm z_{1-\alpha/2} \sqrt{V_i}\right) \text{ where } V_i = -A_0^{-1} - B_0^{-1} + A_i^{-1} + B_i^{-1}$$

Initial 2x2 table:

|              | Exposed             | Unexposed           |
|--------------|---------------------|---------------------|
| At Risk      | $A_0$               | $B_0$               |
| All diseased | $A_1 + \dots + A_n$ | $B_1 + \dots + B_n$ |

Definition of  $P$  and  $Z$ :

$$P = \frac{B_0}{B_0 + B_1 + \dots + B_n}, \quad Z = \frac{B_0 + \dots + B_n}{A_0 + \dots + A_n}$$

Resulting formulae for  $A_i$  and  $B_i$ :

$$A_i = \frac{1 + A_0 R_i B_0^{-1}}{V_i + A_0^{-1} + B_0^{-1}}, \quad B_i = \frac{1 + B_0 (A_0 R_i)^{-1}}{V_i + A_0^{-1} + B_0^{-1}}$$

Constraints on  $A_0$  and  $B_0$ :

$$A_0 > 0, \quad B_0 > 0.$$

Parametrisation used:

$$\beta_1 = \frac{A_0}{A_0 + 100}, \quad \beta_2 = \frac{B_0}{B_0 + 100}$$

Solved for  $A_0$  and  $B_0$ :

$$A_0 = \frac{100 \cdot \beta_1}{1 - \beta_1}, B_0 = \frac{100 \cdot \beta_2}{1 - \beta_2}$$

Note that this parametrisation does not take into account the restrictions  $A_0 > A_1 + \dots + A_n$  and  $B_0 > B_1 + \dots + B_n$ , cf. section 3.1.

## 5 Parameters of the macro

Before calling the macro users can set their own main title by e.g. `title1` ‘This is the main title’. Other titles (`Title2`, `title3`, etc.), if used earlier, will be changed during macro execution and finally cancelled.

The macro `RREst` has 12 parameters:

- `ds1`      Name of first input data set containing risk measures, the limits of confidence intervals and definition of the contrast to be estimated.
- `ds2`      Name of second input data set containing the initial 2x2 frequency table.
- `type`      Study type: PR (for Prospective) CC (for Case Control) or XS (for cross-sectional).  
Default: CC
- `levels`    Categorisation of results: exposure or disease.  
Default: exposure
- `out`        Name of output data set containing the estimated table frequencies.  
Default: `_RREst_`
- `alpha`     Error probability for the confidence intervals.  
Default: 0.05 (equivalent to 95% CI)
- `trend`     Should a trend test be performed: 1=yes, 0=no.  
Default: 0
- `details`    Output of detailed results (see section 6.2 below): 1=yes, 0=no.  
Default: 0
- `grid`        Grid width on unit square for the data set that is used for searching a starting point for the iterative process and for drawing the contour plot.  
Default: 0.01
- `ini_beta`   Starting point for the iterative process. If this is given an empty string (the default), the starting point is determined in a search over the grid determined by the parameter `grid`.

ds1 and ds2 are positional parameters, the others are keyword parameters. The positional parameters must be specified in the order given above at every call to the macro. Specifying of keyword parameters is only necessary if they differ from the default value.

Examples:

```
%RREst (mydata1, mydata2)
```

Default values are used for all keyword parameters.

```
%RREst (mydata1, mydata2, type=PR)
```

Default values are used for all keyword parameters except `type`.

## 5.1 ds1

Each row of this input data set corresponds to an exposure group or a disease category group. Note the special role of the first row (unexposed, at risk or control depending on the study type and categorisation). The input data set must contain the following variables (with exactly the names given here):

`level` A label for the group (character variable)

`Est` Estimation of the relative risk or odds ratio, as appropriate (not read in first row)

`lower` Lower confidence limit of the relative risk (not read in first row)

`upper` Upper confidence limit of the relative risk (not read in first row)

If one of these variables is missing the macro stops executing and writes an error message to the log.

In addition `ds1` may contain a numeric dose or exposure variable named `dose` that is used for the trend test. It should be given a value in all rows including the first. If not included, dose values are assumed to be 0, 1, 2, and so on.

All additional numeric variables in the data set are considered to be *contrasts*. In each contrast, the groups with value 1 in the respective variable are compared to a baseline consisting of the groups with value 0. The groups with other values are not included in the comparison.

## 5.2 ds2

This input data set correspond to the initial (2 x 2)-table of overall frequencies as defined for the four cases in section 4. It is used to calculate the values of  $P$  and  $Z$ . Only two variables (columns) are of importance, which must be named depending on the case:

- case control, exposure groups: “Cases” and “Controls”
- case control, disease categories: “Exposed” and “Unexposed”
- prospective, exposure groups: “Cases” and “At\_Risk”
- prospective, disease categories: “Exposed” and “Unexposed”
- cross-sectional, exposure groups: “Cases” and “Non-cases”
- cross-sectional, disease categories: “Exposed” and “Unexposed”

Only the values of these two variables are read in the first two columns. Normally, the data set should have exactly two columns. However, this is not checked.

## 5.3 type

Valid values are CC, PR and XS, and are not case-sensitive. If an invalid value is entered, the macro stops executing and writes an error message to the log.

## 5.4 levels

Valid values are Exposure and Disease, and are not case-sensitive. Only the first two letters are read, i.e. `ex`, `di`, `exp`, `dis` etc. are understood. If an invalid value is entered, the macro stops executing and writes an error message to the log.

## 5.5 out

Any valid SAS-name, possibly of the kind `library.dataset`.

## 5.6 alpha

Valid values are any number between 0 and 1.

## 5.7 trend

If `trend=1`, a trend test is performed. If the variable `dose` is not in the input data set, the test assumes a dose or exposure of 1 in the first row, 2 in the second row, etc. It is crucial in this case that the exposure levels appear in order of increasing exposure intensity in `ds1`. If the results are given by disease category, then the variable labelled `dose` should express a measure of seriousness of the disease categories instead of exposure levels.

## 5.8 details

Setting `details=1` requests the macro to print some additional results to the output window. See section 6.2 for more information.

## 5.9 grid

Valid values are numbers between 0 and 1, preferably numbers that are reciprocal to an integer. If e.g. `grid=0.01` (the default), the grid contains the  $101^2=10,201$  points  $(0, 0)$ ,  $(0, 0.01)$ ,  $(0, 0.02)$ , ...,  $(0.99, 1)$ ,  $(1, 1)$ . Points lying on the edge of the unit square are moved towards the inside by  $1e^{-8}$ .

## 5.10 ini\_beta

This parameter forces the macro to start the iterative optimisation process in the point  $(\beta_1, \beta_2) \in (0,1) \times (0,1)$  specified (the starting point is determined automatically by default). For instance, enter `ini_beta=0.15 0.3` to let iterations start at  $(\beta_1, \beta_2) = (0.15, 0.3)$ . This parameter is useful if the contour plot suggests that there could be multiple solutions.

# 6 Output

## 6.1 Output data sets

The macro generates the following data sets:

- data set `&out`  
Contains the estimated frequencies of the table (as shown in section 4).
- data set `_iteration_`  
Contains the history of the iterative optimisation process.
- data set `_comparison_`  
Contains the relative errors as defined in section 3.3.
- data set `_test_`  
Contains the test statistics and p-values of the test for homogeneity and the trend test (if performed).

- data set `_TR_test_`  
Contains the test statistics for the estimates of rate of increase in risk per unit dose (for the specified dose values) and the equivalent results using the Uniform scale (instead of the specified dose values). Goodness of fit statistics are included for both types of trend result. This table is produced for data categorised by exposure (not for data categorised by disease type) when trend results have been requested.
- data set `_contrasts_`  
Contains the estimated contrasts and their confidence intervals.
- data sets `_InputData1_`, `_InputData2_`, `_prtInput_`, `_tempdata1_`, `_tempdata2_`, `_annotate_`  
These data sets are not of direct interest for the user.

Note that under certain circumstances, calculation of the `_test_` and `_contrast_data` sets is cancelled, cf. section 3.3.

## 6.2 Output written to the output window

By default, the following output is generated:

- The data set `_prtInput_`  
This data set summarises the two input datasets. It is printed for control purposes and should be checked by the user before examination of the results.
- The output data set `&out`
- The output data set `_test_`
- The output data set `_TR_test_`  
(only if trend tests were requested and the data are categorised by exposure)
- The output data set `_contrasts_`  
(only if there was at least one contrast specified in the first input data set)

If the macro parameter `details` is given the value 1, the following results are printed in addition:

- The output data set `_iteration_`
- The output data set `_comparison_`