symmetry — Symmetry and marginal homogeneity tests

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## Description

Title

symmetry performs asymptotic symmetry and marginal homogeneity tests, as well as an exact symmetry test on  $K \times K$  tables where there is a 1-to-1 matching of cases and controls (nonindependence). This testing is used to analyze matched-pair case-control data with multiple discrete levels of the exposure (outcome) variable. In genetics, the test is known as the transmission/disequilibrium test (TDT) and is used to test the association between transmitted and nontransmitted parental marker alleles to an affected child (Spieldman, McGinnis, and Ewens 1993). For  $2 \times 2$  tables, the asymptotic test statistics reduce to the McNemar test statistic, and the exact symmetry test produces an exact McNemar test; see [R] **Epitab**. For many exposure variables, symmetry can optionally perform a test for linear trend in the log relative risk.

symmetry expects the data to be in the wide format; that is, each observation contains the matched case and control values in variables *casevar* and *controlvar*. Variables can be numeric or string.

symmi is the immediate form of symmetry. The symmi command uses the values specified on the command line; rows are separated by '\', and options are the same as for symmetry. See [U] 19 Immediate commands for a general introduction to immediate commands.

## Quick start

Symmetry and marginal homogeneity tests for 1-to-1 matched case-control studies symmetry case control

Same as above

symmetry control case

Exact test of table symmetry

symmetry case control, exact

Report the contribution from each off-diagonal pair to the overall  $\chi^2$ -statistic symmetry control case, contrib

Test for a linear trend in the log of the relative risk symmetry control case, trend

Request marginal homogeneity statistics that do not require the inversion of the variance-covariance matrix

symmetry case control, mh

Using frequency weight variable wvar

symmetry case control [fweight=wvar]

### Menu

### symmetry

Statistics > Epidemiology and related > Other > Symmetry and marginal homogeneity test

#### symmi

Statistics > Epidemiology and related > Other > Symmetry and marginal homogeneity test calculator

## Syntax

Symmetry and marginal homogeneity tests

```
symmetry casevar controlvar [if] [in] [weight] [, options]
```

Immediate form of symmetry and marginal homogeneity tests

```
symmi \#_{11} \#_{12} [...] \setminus \#_{21} \#_{22} [...] [ \...] [ if ] [ in ] [, options ]
```

options	Description
Main	
<u>not</u> able	suppress output of contingency table
<u>con</u> trib	report contribution of each off-diagonal cell pair
exact	perform exact test of table symmetry
mh	perform two marginal homogeneity tests
trend	perform a test for linear trend in the (log) relative risk (RR)
cc	use continuity correction when calculating test for linear trend

collect is allowed with symmetry; see [U] **11.1.10 Prefix commands**. fweights are allowed; see [U] **11.1.6 weight**.

# Options

Main

notable suppresses the output of the contingency table. By default, symmetry displays the  $n \times n$  contingency table at the top of the output.

contrib reports the contribution of each off-diagonal cell pair to the overall symmetry  $\chi^2$ .

exact performs an exact test of table symmetry. This option is recommended for sparse tables. CAUTION: The exact test requires substantial amounts of time and memory for large tables.

mh performs two marginal homogeneity tests that do not require the inversion of the variance-covariance matrix.

By default, symmetry produces the Stuart-Maxwell test statistic, which requires the inversion of the nondiagonal variance-covariance matrix, V. When the table is sparse, the matrix may not be of full rank, and then the command substitutes a generalized inverse  $V^*$  for  $V^{-1}$ . mh calculates optional marginal homogeneity statistics that do not require the inversion of the variance-covariance matrix. These tests may be preferred in certain situations. See *Methods and formulas* and Bickeböller and Clerget-Darpoux (1995) for details on these test statistics.

- trend performs a test for linear trend in the (log) relative risk (RR). This option is allowed only for numeric exposure (outcome) variables, and its use should be restricted to measurements on the ordinal or the interval scales.
- cc specifies that the continuity correction be used when calculating the test for linear trend. This correction should be specified only when the levels of the exposure variable are equally spaced.

## **Remarks and examples**

### stata.com

symmetry and symmi may be used to analyze 1-to-1 matched case-control data with multiple discrete levels of the exposure (outcome) variable.

### Example 1

Consider a survey of 344 individuals (BMDP 1990, 267–270) who were asked in October 1986 whether they agreed with President Reagan's handling of foreign affairs. In January 1987, after the Iran-Contra affair became public, these same individuals were surveyed again and asked the same question. We would like to know if public opinion changed over this period.

We first describe the dataset and list a few observations.

. use https	://www.stat	a-press.com	n/data/r18/	iran	
. describe					
Contains da Observatio		ps://www.st 344	ata-press.	com/data/r18/iran.dta	
Variables:		2		29 Jan 2022 02:37	
Variable	Storage	Display	Value		
name	type	format	label	Variable label	
before	byte	%8.0g	vlab	Public opinion before IC	
after	byte	%8.0g	vlab	Public opinion after IC	

Sorted by:

```
. list in 1/5
```

	before	after
1.	Agree	Agree
2.	Agree	Disagree
3.	Agree	Unsure
4.	Disagree	Agree
5.	Disagree	Disagree

Each observation corresponds to one of the 344 individuals. The data are in wide form so that each observation has a before and an after measurement. We now perform the test without options.

Public opinion	Pı	ublic opinio	on after IC	;		
before IC	Agree	Disagree	Unsure	Total		
Agree	47	56	38	141		
Disagree	28	61	31	120		
Unsure	26	47	10	83		
Total	101	164	79	344		
				chi2	df	Prob>chi2
Symmetry (as	symptotic	)		14.87	3	0.0019
Marginal hor	nogeneity	(Stuart-Mag	xwell)	14.78	2	0.0006

. symmetry before after

The test first tabulates the data in a  $K \times K$  table and then performs Bowker's (1948) test for table symmetry and the Stuart–Maxwell (Stuart 1955; Maxwell 1970) test for marginal homogeneity.

Both the symmetry test and the marginal homogeneity test are highly significant, thus indicating a shift in public opinion.

An exact test of symmetry is provided for use on sparse tables. This test is computationally intensive, so it should not be used on large tables. Because we are working on a fast computer, we will run the symmetry test again and this time include the exact option. We will suppress the output of the contingency table by specifying notable and include the contrib option so that we may further examine the cells responsible for the significant result.

. symmetry before after, contrib exact mh notable Contribution to symmetry Cells chi-squared n1\_2 & n2\_1 9.3333 n1\_3 & n3\_1 2.2500 n2\_3 & n3\_2 3.2821 df Prob>chi2 chi2 Symmetry (asymptotic) 14.87 3 0.0019 Marginal homogeneity (Stuart-Maxwell) 2 14.78 0.0006 2 Marginal homogeneity (Bickenboller) 13.53 0.0012 Marginal homogeneity (no diagonals) 15.25 2 0.0005 Symmetry (exact significance probability) 0.0018

The largest contribution to the symmetry  $\chi^2$  is due to cells  $n_{12}$  and  $n_{21}$ . These correspond to changes between the agree and disagree categories. Of the 344 individuals, 56 (16.3%) changed from the agree to the disagree response, whereas only 28 (8.1%) changed in the opposite direction.

For these data, the results from the exact test are similar to those from the asymptotic test.

## Example 2

Breslow and Day (1980, 163) reprinted data from Mack et al. (1976) from a case–control study of the effect of exogenous estrogen on the risk of endometrial cancer. The data consist of 59 elderly women diagnosed with endometrial cancer and 59 disease-free control subjects living in the same community as the cases. Cases and controls were matched on age, marital status, and time living in the community. The data collected included information on the daily dose of conjugated estrogen therapy. Breslow and Day analyzed these data by creating four levels of the dose variable. Here are the data as entered into a Stata dataset:

- . use https://www.stata-press.com/data/r18/bd163
- . list, noobs divider

case	control	count
0 0 0 0.1-0.299	0 0.1-0.299 0.3-0.625 0.626+ 0	6 2 3 1 9
0.1-0.299 0.1-0.299 0.1-0.299 0.3-0.625 0.3-0.625	0.1-0.299 0.3-0.625 0.626+ 0 0.1-0.299	4 2 1 9 2
0.3-0.625 0.3-0.625 0.626+ 0.626+ 0.626+	0.3-0.625 0.626+ 0 0.1-0.299 0.3-0.625	3 1 12 1 2
0.626+	0.626+	1

This dataset is in a different format from that of the previous example. Instead of each observation representing one matched pair, each observation represents possibly multiple pairs indicated by the count variable. For instance, the first observation corresponds to six matched pairs where neither the case nor the control was on estrogen, the second observation corresponds to two matched pairs where the case was not on estrogen and the control was on 0.1 to 0.299 mg/day, etc.

To use symmetry to analyze this dataset, we must specify fweight to indicate that in our data there are observations corresponding to more than one matched pair.

Dosage level for		Dosage	level for	control			
case	0	0.1-0.299	0.3-0.625	0.626	5+	Total	
0	6	2	3	1		12	
0.1-0.299	9	4	2	1		16	
0.3-0.625	9	2	3	1		15	
0.626+	12	1	2	1		16	
Total	36	9	10	4		59	
				chi2	df	Pro	b>chi2
Symmetry (asymptotic)				17.10	6		0.0089
Marginal ho	omogeneity	(Stuart-Maxw	rell)	16.96	3	1	0.0007

. symmetry case control [fweight=count]

Both the test of symmetry and the test of marginal homogeneity are highly significant, thus leading us to reject the null hypothesis that there is no effect of exposure to estrogen on the risk of endometrial cancer.

Breslow and Day perform a test for trend assuming that the estrogen exposure levels were equally spaced by recoding the exposure levels as 1, 2, 3, and 4.

We can easily reproduce their results by recoding our data in this way and by specifying the trend option. Two new numeric variables were created, ca and co, corresponding to the variables case and control, respectively. Below, we list some of the data and our results from symmetry:

- . encode case, gen(ca)
- . encode control, gen(co)
- . label values ca
- . label values co
- . list in 1/4

case	control	count	ca	со
0	0	6	1	1
0	0.1-0.299	2	1	2
0	0.3-0.625	3	1	3
0	0.626+	1	1	4
	case 0 0 0 0	0 0 0 0.1-0.299 0 0.3-0.625	0 0 6 0 0.1-0.299 2 0 0.3-0.625 3	0 0 6 1   0 0.1-0.299 2 1   0 0.3-0.625 3 1

. symmetry ca co [fw=count], notable trend cc

	chi2	df	Prob>chi2
Symmetry (asymptotic) Marginal homogeneity (Stuart-Maxwell)	17.10 16.96	6 3	0.0089 0.0007
Linear trend in the (log) RR	14.43	1	0.0001

We requested the continuity correction by specifying cc. Doing so is appropriate because our coded exposure levels are equally spaced.

The test for trend was highly significant, indicating an increased risk of endometrial cancer with increased dosage of conjugated estrogen.

You must be cautious: the way in which you code the exposure variable affects the linear trend statistic. If instead of coding the levels as 1, 2, 3, and 4, we had instead used 0, 0.2, 0.46, and 0.7

(roughly the midpoint in the range of each level), we would have obtained a  $\chi^2$  statistic of 11.19 for these data.

# Stored results

symmetry stores the following in r():

Scalars

r(N_pair) number of matched pairs	
r(chi2) asymptotic symmetry $\chi^2$	
r(df) asymptotic symmetry degrees of freedo	m
r(p) asymptotic symmetry <i>p</i> -value	
r(chi2_sm) MH (Stuart-Maxwell) $\chi^2$	
r(df_sm) MH (Stuart-Maxwell) degrees of freed	om
r(p_sm) MH (Stuart-Maxwell) p-value	
r(chi2_b) MH (Bickenböller) $\chi^2$	
r(df_b) MH (Bickenböller) degrees of freedom	
r(p_b) MH (Bickenböller) p-value	
r(chi2_nd) MH (no diagonals) $\chi^2$	
r(df_nd) MH (no diagonals) degrees of freedom	
r(p_nd) MH (no diagonals) p-value	
r(chi2_t) $\chi^2$ for linear trend	
r(p_trend) p-value for linear trend	
r(p_exact) exact symmetry p-value	

### Methods and formulas

Methods and formulas are presented under the following headings:

Asymptotic tests Exact symmetry test

### Asymptotic tests

Consider a square table with K exposure categories, that is, K rows and K columns. Let  $n_{ij}$  be the count corresponding to row i and column j of the table,  $N_{ij} = n_{ij} + n_{ji}$ , for i, j = 1, 2, ..., K, and  $n_{i,j}$  and let  $n_{jj}$  be the marginal totals for row i and column j, respectively. Asymptotic tests for symmetry and marginal homogeneity for this  $K \times K$  table are calculated as follows:

The null hypothesis of complete symmetry  $p_{ij} = p_{ji}$ ,  $i \neq j$ , is tested by calculating the test statistic (Bowker 1948)

$$T_{\rm cs} = \sum_{i < j} \frac{(n_{ij} - n_{ji})^2}{n_{ij} + n_{ji}}$$

which is asymptotically distributed as  $\chi^2$  with K(K-1)/2 - R degrees of freedom, where R is the number of off-diagonal cells with  $N_{ij} = 0$  as discussed in Hoenig, Morgan, and Brown (1995).

The null hypothesis of marginal homogeneity,  $p_{i.} = p_{.i}$ , is tested by calculating the Stuart–Maxwell test statistic (Stuart 1955; Maxwell 1970),

$$T_{\rm sm} = \mathbf{d}' \mathbf{V}^{-1} \mathbf{d}$$

where **d** is a column vector with elements equal to the differences  $d_i = n_{i.} - n_{.i}$  for i = 1, 2, ..., K, and **V** is the variance–covariance matrix with elements

$$v_{ii} = n_{i.} + n_{.i} - 2n_{ii}$$
  
 $v_{ij} = -(n_{ij} + n_{ji}), \quad i \neq j$ 

 $T_{\rm sm}$  is asymptotically  $\chi^2$  with K-1 degrees of freedom.

This test statistic properly accounts for the dependence between the table's rows and columns. When the matrix V is not of full rank, a generalized inverse  $V^*$  is substituted for  $V^{-1}$ .

The Bickeböller and Clerget-Darpoux (1995) marginal homogeneity test statistic is calculated by

$$T_{\rm mh} = \sum_{i} \frac{(n_{i.} - n_{.i})^2}{n_{i.} + n_{.i}}$$

This statistic is asymptotically distributed, under the assumption of marginal independence, as  $\chi^2$  with K-1 degrees of freedom.

The marginal homogeneity (no diagonals) test statistic  $T_{\rm mh}^0$  is calculated in the same way as  $T_{\rm mh}$ , except that the diagonal elements do not enter into the calculation of the marginal totals. Unlike the previous test statistic,  $T_{\rm mh}^0$  reduces to a McNemar test statistic for  $2 \times 2$  tables. The test statistic  $\{(K-1)/2\}T_{\rm mh}^0$  is asymptotically distributed as  $\chi^2$  with K-1 degrees of freedom (Cleves, Olson, and Jacobs 1997; Spieldman and Ewens 1996).

Breslow and Day's test statistic for linear trend in the (log) of RR is

$$\frac{\left\{\sum_{i < j} (n_{ij} - n_{ji})(X_j - X_i) - cc\right\}^2}{\sum_{i < j} (n_{ij} + n_{ji})(X_j - X_i)^2}$$

where the  $X_j$  are the doses associated with the various levels of exposure and cc is the continuity correction; it is asymptotically distributed as  $\chi^2$  with 1 degree of freedom.

The continuity correction option is applicable only when the levels of the exposure variable are equally spaced.

#### Exact symmetry test

The exact test is based on a permutation algorithm applied to the null distribution. The distribution of the off-diagonal elements  $n_{ij}$ ,  $i \neq j$ , conditional on the sum of the complementary off-diagonal cells,  $N_{ij} = n_{ij} + n_{ji}$ , can be written as the product of K(K-1)/2 binomial random variables,

$$P(\mathbf{n}) = \prod_{i < j} {N_{ij} \choose n_{ij}} \pi_{ij}^{n_{ij}} (1 - \pi_{ij})^{n_{ij}}$$

where **n** is a vector with elements  $n_{ij}$  and  $\pi_{ij} = E(n_{ij}/N_{ij}|N_{ij})$ . Under the null hypothesis of complete symmetry,  $\pi_{ij} = \pi_{ji} = 1/2$ , and thus the permutation distribution is given by

$$P_0(\mathbf{n}) = \prod_{i < j} \binom{N_{ij}}{n_{ij}} \left(\frac{1}{2}\right)^{N_i}$$

The exact significance test is performed by evaluating

$$P_{\rm cs} = \sum_{n \in p} P_0(\mathbf{n})$$

where  $p = \{n : P_0(\mathbf{n}) < P_0(\mathbf{n}^*)\}$  and  $\mathbf{n}^*$  is the observed contingency table data vector. The algorithm evaluates  $p_{cs}$  exactly. For information about permutation tests, see Good (2005, 2006).

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### Also see

[R] **Epitab** — Tables for epidemiologists

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