Chapter 525

Mantel-Haenszel Test

Introduction

The Mantel-Haenszel test compares the odds ratios of several 2-by-2 tables. Each table is of the form:

	Disease		
Exposure	**Yes (Cases)**	**No (Controls)**	**Total**
Yes	A	B	m_1
No	C	D	m_2
Total	n_1	n_2	n

where *A, B, C,* and *D* are counts of individuals.

The odds of an exposed individual contracting the disease is:

$$o_1 = \frac{p_1}{1-p_1} = \frac{A/m_1}{B/m_1} = \frac{A}{B}$$

The odds of an unexposed individual contracting the disease is:

$$o_2 = \frac{p_2}{1-p_2} = \frac{C/m_2}{D/m_2} = \frac{C}{D}$$

The odds ratio, ψ, is calculated using the equation:

$$\psi = \frac{o_1}{o_2} = \frac{AD}{BC}$$

This is the ratio of the odds of exposed individuals contracting a disease to the odds of unexposed individuals contracting a disease. It is closely related to the risk ratio which is:

$$Risk = \frac{p_1}{p_2}$$

When the probability of the disease is rare, $1-p_1 \approx 1$ and $1-p_2 \approx 1$. Hence, in this case, the odds ratio is almost identical to the risk ratio.

The above 2-by-2 table may be partitioned according to one or more variables into several 2-by-2 tables. Each individual table is referred to as a stratum. For example, consider the following data presented by Schlesselman (1982) for a case-control study investigating the relationship among lung cancer (the disease variable), employment in shipbuilding (exposure to asbestos), and smoking:

Mantel-Haenszel Test

Smoking	Shipbuilding	Cancer	Control	Odds Ratio
Minimal	Yes	11	35	
	No	50	203	1.28
Moderate	Yes	70	42	
	No	217	220	1.69
Heavy	Yes	14	3	
	No	96	50	2.43

These data are contained in the SMOKING database. We see that the odds ratios steadily increase as the amount of smoking increases.

The Mantel-Haenszel analysis provides two closely related pieces of information. First, it provides statistical tests of whether the odds ratios are equal (homogeneous) or unequal (heterogeneous) across strata. Second, it provides an estimate of the odds ratio of the exposure variable, adjusted for the strata variable. In this example, it provides estimates of the odds ratio of asbestos exposure to lung cancer after removing the influence of smoking.

Assumptions

Two basic assumptions should be considered when using this procedure.

1. *Observations are independent from each other*. In practice, this means that each observation comes from a different subject, that the subjects were randomly selected from the population of interest, and that no specific group of subjects is purposefully omitted.

2. *All observations are identically distributed*. This means that they are obtained in the same way. For example, you could not mix the results of a telephone survey with those of a door-to-door survey.

Data Structure

The data may be entered in either raw or summarized form. In either case, each variable represents a factor and each row of data represents a cell. An optional variable may be used to give the count (frequency) of the number of individuals in that cell. When the frequency variable is left blank, each row receives a frequency of one. The following table shows how the above table was entered in the Smoking dataset.

Smoking dataset

Smoking	Shipbuilding	Cancer	Count
1_Minimal	1_Yes	1_Yes	11
1_Minimal	2_No	1_Yes	50
1_Minimal	1_Yes	2_No	35
1_Minimal	2_No	2_No	203
2_Moderate	1_Yes	1_Yes	70
2_Moderate	2_No	1_Yes	217
2_Moderate	1_Yes	2_No	42
2_Moderate	2_No	2_No	220
3_Heavy	1_Yes	1_Yes	14
3_Heavy	2_No	1_Yes	96
3_Heavy	1_Yes	2_No	3
3_Heavy	2_No	2_No	50

You will note that we have used the phrase "1_Yes" instead of "Yes" and "2_No" instead of "No." We have done this so that the categories are sorted in the correct order. Normally, a "Yes" would be sorted after a "No." However, the data in the table must be arranged so that the upper-left cell (corresponding to the count *A*) refers to

individuals who are exposed to the risk factor and have the disease. Entering "1_Yes" and "2_No" causes the categories to be sorted in the proper order. An alternative way of accomplishing this would have been to enter a "1" for Yes and a "2" for No.

Procedure Options

This section describes the options available in this procedure.

Variables Tab

Specify the variables to be analyzed.

Binary Response Variable

Disease Variable

This is the binary response variable. The lowest value represents having the response. The highest value represents individuals who do not have the response. In a case-control study, this is the variable that separates the cases from the controls. The cases must receive the lowest value when the two categories are sorted, while the controls must be associated with the highest value.

Count Variable

Count Variable

This optional variable contains the count (frequency) of each cell in the table. If this variable is left blank, the frequency or each row in the database is assumed to be one.

Exposure Variable

Exposure Variable

This is the binary variable representing the risk factor. The lowest value represents individuals who have the risk factor. The highest value represents individuals who do not have the risk factor.

Delta

Delta

This value is added to each cell count when zeroes are present in the table. If there are no zeroes in the table, then this value is ignored. This option lets you analyze data with zero counts. The traditional value is 0.5. Recent simulation studies have indicated that 0.25 produces better results under certain situations. Specific statistics that are impacted are indicated later. The Mantel-Haenszel statistic, for example, does not use this delta value in its calculation.

Strata Specification

Stratum (1-4) Variable

At least one factor variable must be specified. Examples of factor variables are gender, age groups, "yes" or "no" responses, etc.

A factor's categories need not be consecutive integers. However, the program will display results in sorted order.

You may use text or numeric identification codes. The treatment of text variables is specified for each variable by the Data Type option on the Variable Info sheet.

Report Options

Alpha

This option specifies the significance level (alpha) used in calculating confidence limits.

Precision

Specify the precision of numbers in the report. Single precision will display seven-place accuracy, while double precision will display thirteen-place accuracy.

Variable Names

This option lets you select whether to display variable names, variable labels, or both.

Value Labels

Indicate whether to display the data values or their labels.

Example 1 – Mantel-Haenszel Test

This section presents an example of how to run an analysis of the data contained in the Smoking dataset.

You may follow along here by making the appropriate entries or load the completed template **Example 1** by clicking on Open Example Template from the File menu of the Mantel-Haenszel Test window.

1   Open the Smoking dataset.
- From the File menu of the NCSS Data window, select **Open Example Data**.
- Click on the file **Smoking.NCSS**.
- Click **Open**.

2   Open the Mantel-Haenszel Test window.
- On the menus, select **Analysis**, then **Proportions**, then **Mantel-Haenszel Test**. The Mantel-Haenszel Test procedure will be displayed.
- On the menus, select **File**, then **New Template**. This will fill the procedure with the default template.

3   Specify the variables.
- On the Mantel-Haenszel Test window, select the **Variables tab**.
- Double-click in the **Disease Variable** text box. This will bring up the variable selection window.
- Select **Cancer** from the list of variables and then click **Ok**. "Cancer" will appear in the Disease Variables box.
- Double-click in the **Count Variable** text box. This will bring up the variable selection window.
- Select **Count** from the list of variables and then click **Ok**. "Count" will appear in the Count Variable box.
- Double-click in the **Exposure Variable** text box. This will bring up the variable selection window.
- Select **Shipbuilding** from the list of variables and then click **Ok**. "Shipbuilding" will appear in the Exposure Variables box.
- Double-click in the **Stratum 1 Variable** text box. This will bring up the variable selection window.
- Select **Smoking** from the list of variables and then click **Ok**. "Smoking" will appear in the Stratum 1 Variables box.

4   Run the procedure.
- From the Run menu, select **Run Procedure**. Alternatively, just click the green Run button.

Strata Count Section

Strata Count Section

Strata	Smoking	A	B	C	D	Sample Odds Ratio
1	1_Minimal	11	35	50	203	1.2760
2	2_Moderate	70	42	217	220	1.6897
3	3_Heavy	14	3	96	50	2.4306

A: Shipbuilding = 1_Yes, Cancer = 1_Yes
B: Shipbuilding = 1_Yes, Cancer = 2_No
C: Shipbuilding = 2_No, Cancer = 1_Yes
D: Shipbuilding = 2_No, Cancer = 2_No

This report presents the data that were input. Each row of the report represents an individual 2-by-2 table. The definitions of the four letters (A, B, C, and D) are shown immediately below the report. Thus A is the number of individuals with Disease = Yes and Exposure = Yes.

Sample Odds Ratio

This is the odds ratio calculated for the 2-by-2 table listed on this row. The formula is

$$\psi = \frac{AD}{BC}$$

The sample odds ratio is not calculated when any of the four cell counts is zero. Note that this value is different from the Corrected Odds Ratio report in the Strata Detail Section.

Strata Detail Section

Strata Detail Section

Strata	Lower 95.0% C.L.	1/2-Corrected Odds Ratio	Upper 95.0% C.L.	Exact Test	Proportion Exposed	Proportion Diseased
1	0.5653	1.2909	2.8335	0.5516	0.1538	0.2040
2	1.0805	1.6857	2.6465	0.0194	0.2040	0.5228
3	0.6127	2.2891	11.2098	0.1870	0.1043	0.6748

Each line on this report presents results for an individual 2-by-2 table. The strata number provides the identity of particular 2-by-2 table, since the tables in this report are listed in the same order as those in the Strata Count Section report described previously.

Strata

The row number.

1/2-Corrected Odds Ratio

This odds ratio is computed using the formula:

$$\psi' = \frac{(A + \delta)(D + \delta)}{(B + \delta)(C + \delta)}$$

where δ is the Delta value that was entered (usually, 0.5 or 0.25). Note that this odds ratio is defined when one or more cell counts are zero.

Lower, Upper 100(1-Alpha)% C.L.

The odds ratio confidence limits are calculated from those based on the Log Odds Ratio using the following procedure.

1. Compute the corrected odds ratio ψ' using the formula above.

2. Compute the logarithm of the odds ratio using:

$$L' = \ln(\psi')$$

3. Compute the standard error of L' using:

$$s_{L'} = \sqrt{\frac{1}{(A+\delta)} + \frac{1}{(B+\delta)} + \frac{1}{(C+\delta)} + \frac{1}{(D+\delta)}}$$

4. Compute the $100(1-\alpha)\%$ confidence limits for L using the fact that L' is approximately normally distributed for large samples:

$$L' \pm z_{\alpha/2} s_{L'}$$

   where $z_{\alpha/2}$ is the appropriate value from the standard normal distribution.

5. Transform the above confidence limits back to the original scale using:

$$\psi_{lower} = e^{L'-z_{\alpha/2}s_{L'}}$$

$$\psi_{upper} = e^{L'+z_{\alpha/2}s_{L'}}$$

6. Compute the quantities X, Y, W, F, U, and V using the formulas:

$$X = \psi(m_1 + n_1) + (m_2 - n_1)$$

$$Y = \sqrt{X^2 - 4m_1 n_1 \psi(\psi-1)}$$

$$W = \frac{1}{N_{11}} + \frac{1}{N_{12}} + \frac{1}{N_{21}} + \frac{1}{N_{22}}$$

$$F = \left(A - N_{11} - \tfrac{1}{2}\right)^2 W - z_{\alpha/2}^2$$

$$U = \frac{1}{N_{12}^2} + \frac{1}{N_{21}^2} - \frac{1}{N_{11}^2} - \frac{1}{N_{22}^2}$$

$$V = T\left[\left(A - N_{11} - \tfrac{1}{2}\right)^2 U - 2W\left(A - N_{11} - \tfrac{1}{2}\right)\right]$$

   where

$$N_{11} = \frac{X-Y}{2(\psi-1)}$$

$$N_{12} = m_1 - N_{11}$$

$$N_{21} = n_1 - N_{11}$$

$$N_{22} = n_2 - m_1 + N_{11}$$

$$T = \frac{1}{2(\psi - 1)^2}\left(Y - n - \frac{\psi - 1}{Y}\left[X(m_1 + n_1) - 2m_1 n_1(2\psi - 1)\right]\right)$$

Finally, use the updating equation below to calculate a new value for the odds ratio.

$$\psi^{(k+1)} = \psi^{(k)} - \frac{F}{V}$$

7. Continue iterating (computing the values in step 6) until the value of F is arbitrarily close to zero (say, if its absolute value is less than 0.0000001).

This procedure is used separately for the upper and lower confidence limits of the odds ratio.

Exact Test

This is the probability (significance) level of Fisher's exact test versus a two sided alternative. Reject the hypothesis that $\psi = 1$ when this value is less than a small value, say 0.05.

Proportion Exposed

This is the overall proportion of those in the table that were exposed to the risk factor. The calculation is:

$$m_1 / n$$

This figure may or may not estimate this proportion in the population depending on the sampling design that was used to obtain the data.

Proportion Diseased

This is the overall proportion of those in the table that were diseased. The calculation is:

$$n_1 / n$$

This figure may or may not estimate this proportion in the population depending on the sampling design that was used to obtain the data.

Mantel-Haenszel Statistics Section

Mantel-Haenszel Statistics Section

Method	Lower 95.0% C.L.	Estimated Odds Ratio	Upper 95.0% C.L.	Chi-Square Value	DF	Prob Level
MH C.C.	1.1411	1.6438	2.3679	7.12	1	0.007616
MH	1.1545	1.6438	2.3404	7.60	1	0.005832
Robins	1.1558	1.6438	2.3378			
Woolf	1.1417	1.6291	2.3247	7.24	1	0.007137
Heterogeneity Test				0.81	2	0.667190

This report presents various odds ratio confidence limits and hypothesis tests. From what has been written in the statistical literature, we would recommend the following strategy when using this report.

For hypothesis testing, use the Heterogeneity Test to test the hypothesis that all odds ratios are equal. Use the MH C.C. hypothesis test to test the hypothesis test that all odds ratios are equal to one. Use the Robins confidence limits.

We will next discuss each row of this report.

MH C.C.

This row presents the Mantel-Haenszel confidence limits and hypothesis test with continuity correction. Generally speaking, the continuity correction is used to provide a closer approximation to the exact conditional test in which all marginal totals are assumed to be fixed.

Hypothesis Test

We will discuss the hypothesis test first. The Mantel-Haenszel chi-square value tests the null hypothesis that the individual stratum odds ratios are all equal to one versus the alternative hypothesis that at least one odds ratio is different from unity. Note that this is different from the Heterogeneity Test which does not test that the odds ratios are equal to one, just equal to each other.

The formula used for this test is:

$$
\chi^2_{mhcc} = \frac{\left(\left|\sum_{i=1}^{K} A_i - \sum_{i=1}^{K} E(A_i)\right| - \frac{1}{2}\right)^2}{\sum_{i=1}^{K} V(A_i)}
$$

where K is the number of strata and

$$
E(A_i) = \frac{n_{1i}m_{1i}}{n_i}
$$

$$
V(A_i) = \frac{n_{1i}n_{2i}m_{1i}m_{2i}}{n_i^2(n_i - 1)}
$$

This is a chi-square test with one degree of freedom. The probability level provides the upper tail probability of the test. Hence, when this value is less that your desired alpha level (say 0.05), reject the null hypothesis that all odds ratios are equal to one.

Confidence Limits for the Odds Ratio

The within-strata odds ratio is computed as follows:

$$
\psi_{mh} = \frac{\sum_{i=1}^{K} \frac{A_i D_i}{n_i}}{\sum_{i=1}^{K} \frac{B_i C_i}{n_i}}
$$

The test-based confidence limits for a 100(1-alpha)% confidence interval are given by

$$
\psi_{mhc,lower} = \exp\left(\left(1 - \frac{z_{\alpha/2}}{\sqrt{\chi^2_{mhcc}}}\right)\ln(\psi_{mh})\right)
$$

$$
\psi_{mhc,upper} = \exp\left(\left(1 + \frac{z_{\alpha/2}}{\sqrt{\chi^2_{mhcc}}}\right)\ln(\psi_{mh})\right)
$$

MH

This row presents the Mantel-Haenszel confidence limits and hypothesis test without continuity correction. Generally speaking, the uncorrected version of this test is used to provide a closer approximation to the unconditional chi-square test.

Hypothesis Test

We will discuss the hypothesis test first. The Mantel-Haenszel chi-square value tests the null hypothesis that the individual stratum odds ratios are all equal to one versus the alternative hypothesis that at least one odds ratio is different from unity. Note that this is different from the Heterogeneity Test which does not test that the odds ratios are equal to one, just equal to each other.

The formula used for this test is:

$$\chi^2_{mh} = \frac{\left(\left|\sum_{i=1}^{K} A_i - \sum_{i=1}^{K} E(A_i)\right|\right)^2}{\sum_{i=1}^{K} V(A_i)}$$

where K is the number of strata and

$$E(A_i) = \frac{n_{1i}m_{1i}}{n_i}$$

$$V(A_i) = \frac{n_{1i}n_{2i}m_{1i}m_{2i}}{n_i^2(n_i - 1)}$$

This is a chi-square test with one degree of freedom. The probability level provides the upper tail probability of the test. Hence, when this value is less that your desired alpha level (say 0.05), reject the null hypothesis that all odds ratios are equal to one.

Confidence Limits for the Odds Ratio

The within-strata odds ratio is computed as follows:

$$\psi_{mh} = \frac{\sum_{i=1}^{K} \frac{A_i D_i}{n_i}}{\sum_{i=1}^{K} \frac{B_i C_i}{n_i}}$$

The test-based confidence limits for a 100(1-alpha)% confidence interval are given by

$$\psi_{mhc,lower} = \exp\left(\left(1 - \frac{z_{\alpha/2}}{\sqrt{\chi^2_{mh}}}\right)\ln(\psi_{mh})\right)$$

$$\psi_{mhc,upper} = \exp\left(\left(1 + \frac{z_{\alpha/2}}{\sqrt{\chi^2_{mh}}}\right)\ln(\psi_{mh})\right)$$

Robins

Robins (1986) presented an alternative formulation for the confidence limits which they have shown to be more accurate that any of the others presented. They did not make modifications to the hypothesis test, so no hypothesis test is printed on this line of the report.

Confidence Limits for the Odds Ratio

The within-strata odds ratio is computed as follows:

$$\psi_R = \frac{\sum_{i=1}^{K} \frac{A_i D_i}{n_i}}{\sum_{i=1}^{K} \frac{B_i C_i}{n_i}}$$

The confidence limits for a 100(1-alpha)% confidence interval are given by

$$\psi_{R,lower} = \exp\left(\left(\ln(\psi_R) - z_{\alpha/2}\sqrt{Vus}\right)\right)$$

$$\psi_{R,upper} = \exp\left(\left(\ln(\psi_R) + z_{\alpha/2}\sqrt{Vus}\right)\right)$$

where

$$Vus = \frac{\sum_{i=1}^{K} P_i R_i}{2\left(\sum_{i=1}^{K} R_i\right)^2} + \frac{\sum_{i=1}^{K} P_i S_i + Q_i R_i}{2\left(\sum_{i=1}^{K} R_i\right)\left(\sum_{i=1}^{K} S_i\right)} + \frac{\sum_{i=1}^{K} Q_i S_i}{2\left(\sum_{i=1}^{K} S_i\right)^2}$$

$$P_i = \frac{A_i + D_i}{n_i}$$

$$Q_i = \frac{B_i + C_i}{n_i}$$

$$R_i = \frac{A_i D_i}{n_i}$$

$$S_i = \frac{B_i C_i}{n_i}$$

Woolf

This row presents the confidence limits and hypothesis test developed by Woolf, as described by Schlesselman (1982). Recent studies have cast doubt on the usefulness of Woolf's tests, but they are provided anyway for completeness.

Confidence Limits for the Odds Ratio

The within-strata odds ratio is computed as follows:

$$\psi_w = \exp\left(\frac{\sum_{i=1}^{K} v_i^{-1} \ln \psi_i}{\sum_{i=1}^{K} v_i^{-1}}\right)$$

where

$$v_i = \frac{1}{A_i} + \frac{1}{B_i} + \frac{1}{C_i} + \frac{1}{D_i}$$

If any of the counts in a particular 2-by-2 table are zero, all counts in that table have delta (0.25 or 0.5) added to them.

Let W be calculated by:

$$W = \sum_{i=1}^{K} v_i^{-1}$$

The confidence limits are calculate using the equations:

$$\psi_{w,lower} = \psi_w \exp\left(-\frac{z_{\alpha/2}}{\sqrt{W}}\right)$$

$$\psi_{w,upper} = \psi_w \exp\left(\frac{z_{\alpha/2}}{\sqrt{W}}\right)$$

Hypothesis Test

Woolf's chi-square statistic tests the hypothesis that all odds ratios are equal to one.

The formula used for this test is:

$$\chi_w^2 = W\left(\ln \psi_w\right)^2$$

This is a chi-square test with one degree of freedom. The probability level provides the upper tail probability of the test. Hence, when this value is less that your desired alpha level (say 0.05), reject the null hypothesis that all odds ratios are equal to one.

Heterogeneity Test

This row presents a hypothesis test developed by Woolf, as described by Schlesselman (1982) for testing the more general hypothesis that all odds ratios are equal, but not necessarily equal to one.

Hypothesis Test

Woolf's chi-square statistic tests the hypothesis that all odds ratios are equal.

The formula used for this test is:

$$\chi_{wh}^2 = \sum_{i=1}^{K} v_i^{-1}\left(\ln \psi_i - \ln \psi_w\right)^2$$

This is a chi-square test with K-1 degrees of freedom. The probability level provides the upper tail probability of the test. Hence, when this value is less that your desired alpha level (say 0.05), reject the null hypothesis that all odds ratios are equal to one.