

Chapter 454

Meta-Analysis of Two Proportions

Introduction

This module performs a meta-analysis of a set of two-group, binary-event studies. These studies each have a treatment group (arm) and a control group. The results of each study may be summarized as counts in a 2-by-2 table. The program provides numeric reports and plots to allow the investigation and summarization of the studies. Diagnostic plots include the *forest plot*, *radial plot*, *L'Abbe plot*, and *funnel plot*. Both fixed and random effect models are available for analysis with a variety of settings.

Meta-Analysis refers to methods for the systematic review of a set of individual studies with the aim to combine their results. Meta-analysis has become popular for a number of reasons:

1. The adoption of evidence-based medicine which requires that all reliable information is considered.
2. The desire to avoid narrative reviews which are often misleading.
3. The desire to interpret the large number of studies that may have been conducted about a specific treatment.
4. The desire to increase the statistical power of the results by combining many small-size studies.

The goals of meta-analysis may be summarized as follows. A meta-analysis seeks to systematically review all pertinent evidence, provide quantitative summaries, integrate results across studies, and provide an overall interpretation of these studies.

We have found many books and articles on meta-analysis. In this chapter, we briefly summarize the information in Schwarzer et al (2015), Chen and Peace (2021), Harrer et al (2022), Sutton et al (2000), and Palmer and Sterne (2016). Refer to those sources for more details about the meta-analysis formulas used.

For a great introduction we recommend Chapter 10 of the Cochrane Handbook. The reference for this chapter is Deeks, Higgins, and Altman (2021).

Treatment Effects

Suppose you have obtained the results for k studies, labeled $i = 1, \dots, k$. Each study consists of a treatment group (1) and a control group (2). The results of each study are summarized by four counts:

- A_i the number of subjects in the treatment group having the event of interest.
- B_i the number of subjects in the treatment group not having the event of interest.
- C_i the number of subjects in the control group having the event of interest.
- D_i the number of subjects in the control group not having the event of interest.

Occasionally, one of these counts will be zero which causes calculation problems. To avoid this, the common procedure is to add a small value such as 0.5 or 0.25 to all counts so that zero counts do not occur.

Proportions (Risks) for an Individual Study

These counts may be used to calculate estimates of the event-risk in the treatment group as

$$\hat{p}_{1i} = \frac{A_i}{A_i + B_i}$$

and in the control group as

$$\hat{p}_{2i} = \frac{C_i}{C_i + D_i}$$

Based on these risks, three measures of treatment effect may be defined and used in the meta-analysis. These are the odds ratio, the risk ratio, and the risk difference.

Odds Ratio for an Individual Study

The odds ratio is the most commonly used measure of treatment effect. It is defined as follows.

$$OR_i = \frac{\frac{p_{1i}}{1 - p_{1i}}}{\frac{p_{2i}}{1 - p_{2i}}} = \frac{A_i D_i}{B_i C_i}$$

For statistical analysis, the logarithm of the odds ratio is usually used because its distribution is more accurately approximated by the normal distribution for smaller sample sizes. The variance of the sample log odds ratio is estimated by

$$V(\ln(\widehat{OR}_i)) = \frac{1}{A_i} + \frac{1}{B_i} + \frac{1}{C_i} + \frac{1}{D_i}$$

Risk Ratio or Relative Risk for an Individual Study

The risk ratio is calculated as follows.

$$RR_i = \frac{p_{1i}}{p_{2i}}$$

Like the odds ratio, the logarithm of the risk ratio is usually used because its distribution is more accurately approximated by the normal distribution for smaller sample sizes. The variance of the sample log risk ratio is estimated by

$$V(\ln(\widehat{RR}_i)) = \frac{1}{A_i} - \frac{1}{A_i + B_i} + \frac{1}{C_i} - \frac{1}{C_i + D_i}$$

Risk Difference for an Individual Study

The risk difference is calculated as follows.

$$RD_i = p_{1i} - p_{2i}$$

The estimated variance of the sample risk difference is given by

$$V(\widehat{RD}_i) = \frac{p_{1i}(1 - p_{1i})}{A_i + B_i} + \frac{p_{2i}(1 - p_{2i})}{C_i + D_i}$$

Confidence Interval for Effect Measures of an Individual Study

Let θ_i represent an effect measure created from the 2-by-2 table. In this procedure, the effect measure may be an odds ratio, risk ratio, or risk difference. The ratios are usually transformed so that the analysis is performed on the log odds ratio or log risk ratio.

Let $\hat{\theta}_i$ represent the estimate of θ_i from the study. Confidence intervals for each individual study based on the normal distribution may be defined for θ_i as follows.

$$\hat{\theta}_i \pm z_{1-\alpha/2} \sqrt{V(\hat{\theta}_i)}$$

In the case of the odds ratio and the risk ratio, the confidence interval is created on the logarithmic scale and then transformed back to the original scale.

It will be useful to make the following definition for the weights w_i .

$$v_i = V(\hat{\theta}_i)$$

$$w_i = 1/v_i$$

Hypothesis Tests for Combined Studies

Several hypothesis tests have been developed to test various aspects about the variation in the effects. This variation is referred to as heterogeneity. Three statistical tests have been devised to test the overall null hypothesis that all treatment effects are the same.

Test Name	Null Hypothesis	Alternative Hypothesis	Test Statistic	Distribution
Nondirectional	$H_0 : \theta_i = 0 \quad i = 1, \dots, k$	$H_1 : \theta_i \neq 0 \quad \text{for some } i$	$X_{ND} = \sum_{i=1}^k w_i \hat{\theta}_i^2$	χ_k^2
Directional	$H_0 : \theta_i = \theta \quad i = 1, \dots, k$	$H_1 : \theta_i \neq \theta \neq 0 \quad \text{for some } i$	$X_D = \frac{(\sum_{i=1}^k w_i \hat{\theta}_i)^2}{\sum_{i=1}^k w_i}$	χ_1^2
Cochran's Q	$H_0 : \theta_i = \theta \quad i = 1, \dots, k$	$H_1 : \theta_i \neq \theta \neq 0 \quad \text{for some } i$	$Q = \sum_{i=1}^k w_i (\hat{\theta}_i - \hat{\theta})^2$ $\hat{\theta} = \frac{\sum_{i=1}^k w_i \hat{\theta}_i}{\sum_{i=1}^k w_i}$	χ_{k-1}^2

Cochran's Q is sometimes called the *heterogeneity test*.

Measures to Quantify Heterogeneity

Several statistics have been proposed to help quantify and interpret the heterogeneity that is found in a particular meta-analysis.

H Index

Higgins and Thompson (2002) (see also Chen and Peace (2021) page 157) present a heterogeneity measure which is based on the fact that $E(Q) = k - 1$. This leads to

$$H = \sqrt{\frac{Q}{k - 1}}$$

The reference interval for H is

$$LL_H = \exp \left\{ \ln(H) - \left| z_{\frac{\alpha}{2}} \right| SE_{\ln(H)} \right\}$$

$$UL_H = \exp \left\{ \ln(H) + \left| z_{\frac{\alpha}{2}} \right| SE_{\ln(H)} \right\}$$

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where

$$SE_{\ln(H)} = \begin{cases} \frac{\ln(Q) - \ln(k-1)}{2 \left(\sqrt{2Q - \sqrt{2k-3}} \right)} & \text{if } Q > k \\ \sqrt{\left(\frac{1}{2k-4} \right) \left(1 - \frac{1}{3(k-2)^2} \right)} & \text{if } Q \leq k \end{cases}$$

If $LL_H > 1$, H is statistically significant.

I^2 Index

Higgins and Thompson (2002) (see also Chen and Peace (2021) page 158) present an *inconsistency* measure called I^2

$$I^2 = 100\% \frac{\hat{\tau}^2}{\hat{\tau}^2 + s^2}$$

where s^2 is a 'typical' estimate of the within-study variance given by Bowden *et al.* (2011) page 3 as

$$s^2 = \frac{(k-1) \sum w_i}{(\sum w_i)^2 - \sum w_i^2}$$

This measure is related to H^2 as follows

$$I^2 = 100\% \frac{(H^2 - 1)}{H^2}$$

Thus, a reference interval for I^2 can be derived from the reference interval for H^2 as

$$LL_{I^2} = 100\% \left(\frac{LL_H^2 - 1}{LL_H^2} \right)$$

$$UL_{I^2} = 100\% \left(\frac{UL_H^2 - 1}{UL_H^2} \right)$$

Higgins *et al.* (2003) explain that this index does not depend on the number of studies as do other heterogeneity measures. They suggest that 25%, 50%, and 75% are reasonable cutoffs for low, medium, and high values of the index.

A generalized version of the I^2 index, which we call I_{PM}^2 , along with its reference interval, can then be found by inserting τ_{PM}^2 and its two reference limits into the equation

$$I^2 = 100\% \left(\frac{\hat{\tau}^2}{\hat{\tau}^2 + s^2} \right)$$

which was given above. Similar to results hold for H^2 .

Effects Model

Two types of models have been adopted to allow the testing of various hypotheses and creating confidence intervals for the studies in the meta-analysis. The simplest model is the *fixed effects model*. It is used when the studies in the analysis all have similar characteristics. A second model, the *random effects model*, is a little more complicated but is usually more realistic in its assumptions. These models are described next.

Fixed Effects Model

The fixed effects model is given by

$$\hat{\theta}_i = \theta + \sigma e_i$$

where $e_i = N(0,1)$ so that $\hat{\theta}_i \sim N(\theta, \sigma^2)$.

If the effects are assumed to be equal (homogeneous) except for a small random error, the *fixed effects model* may be used to construct a combined confidence interval. The fixed effects model assumes homogeneity of study results. That is, it assumes that a common population effect θ for all i . This assumption may not be realistic when combining studies with different patient pools, protocols, follow-up strategies, doses, durations, etc.

Fixed Study Weights

During the analysis, weights w_i are assigned to each study. These weights are often created from the variance as follows.

$$v_i = \hat{V}(\hat{\theta}_i)$$

$$w_i = 1/v_i$$

Inverse Variance Method for Combining Studies

If the fixed effects model is adopted, the *inverse variance* method, described by Sutton (2000) page 58, is often used to calculate combined confidence intervals and significance tests for θ . The basic formula used for combining confidence interval is

$$\hat{\theta} \pm z_{1-\alpha/2} \sqrt{V(\hat{\theta})}$$

where

$$\hat{\theta} = \frac{\sum_{i=1}^k w_i \hat{\theta}_i}{\sum_{i=1}^k w_i}$$

is the chosen effect measure type (log odds ratio, log risk ratio, or risk difference), $z_{1-\alpha/2}$ is the appropriate percentage point from the standardized normal distribution, and

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$$V(\hat{\theta}) = \frac{1}{\sum_{i=1}^k w_i}$$

is the variance of the estimated effect measure. The weights, w_i , are calculated using

$$w_i = \frac{1}{V(\hat{\theta}_i)}$$

The individual formulas for $V(\hat{\theta}_i)$ for each of the effect measures are given in the individual sections above. For example, for the odds ratio, the formula is

$$V(\ln(\widehat{OR}_i)) = \frac{1}{A_i} + \frac{1}{B_i} + \frac{1}{C_i} + \frac{1}{D_i}$$

Mantel-Haenszel Method for Combining Studies

The Mantel-Haenszel method is often suggested for combining studies with a confidence interval and significance tests for θ . In this case, the basic formula used for combining confidence interval is

$$\hat{\theta}_{MH} \pm z_{1-\alpha/2} \sqrt{V(\hat{\theta}_{MH})}$$

where

$$\hat{\theta}_{MH} = \frac{\sum_{i=1}^k w_i \hat{\theta}_i}{\sum_{i=1}^k w_i}$$

is the chosen effect measure type (log odds ratio, log risk ratio, or risk difference) and $z_{1-\alpha/2}$ is the appropriate percentage point from the standardized normal distribution. The weights and variances are calculated differently for each of the effect measures.

Odds Ratios

For odds ratios, Mantel-Haenszel estimator of the odds ratio in the natural scale (see Chen and Peace (2021) page 90) is given by

$$\widehat{OR}_{MH} = \frac{L_1}{L_2}$$

The confidence intervals in the log scale have been shown to be more accurate, so the confidence interval is given in that scale. The variance of the log odds ratio is given by (see Schwarzer et al. (2015) page 72-76).

$$V\{\ln(\widehat{OR}_{MH})\} = \frac{L_3}{2L_1^2} + \frac{L_4 + L_5}{2L_1L_2} + \frac{L_6}{2L_2^2}$$

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where

$$L_1 = \sum_i \frac{A_i D_i}{N_i}$$

$$L_2 = \sum_i \frac{B_i C_i}{N_i}$$

$$L_3 = \sum_i \frac{(A_i + D_i) A_i D_i}{N_i^2}$$

$$L_4 = \sum_i \frac{(A_i + D_i) B_i C_i}{N_i^2}$$

$$L_5 = \sum_i \frac{(B_i + C_i) A_i D_i}{N_i^2}$$

$$L_6 = \sum_i \frac{(B_i + C_i) B_i C_i}{N_i^2}$$

The confidence interval is then given by

$$\ln(\widehat{OR}_{MH}) \pm z_{1-\alpha/2} \sqrt{V(\ln(\widehat{OR}_{MH}))}.$$

This interval is then re-scaled back to the natural scale using exponentiation.

Note that study tables with zero cells need not be adjusted by adding 0.5 in this case. However, this adjustment is used when presenting the individual study results.

Risk Ratios

For risk ratios, the weights are

$$w_i = (A_i + B_i) C_i / N_i$$

and the individual study risk ratios are

$$\widehat{RR}_i = \frac{\left(\frac{A_i}{A_i + B_i} \right)}{\left(\frac{C_i}{C_i + D_i} \right)}$$

Hence, the final estimate of RR in the natural scale is

$$\widehat{RR}_{MH} = \frac{\sum_{i=1}^k w_i \widehat{RR}_i}{\sum_{i=1}^k w_i}$$

Note that study tables with zero cells need to be adjusted by adding 0.5 (or 0.01 or 0.1) to all four cells.

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The variance of the log of the risk ratio is given by (see Schwarzer et al. (2015) page 72-76).

$$V\{\ln(\widehat{RR}_{MH})\} = \frac{G_1}{G_2 G_3}$$

where

$$G_1 = \sum_i \frac{(A_i + B_i)(C_i + D_i)(A_i + C_i) - A_i C_i N_i}{N_i^2}$$

$$G_2 = \sum_i \frac{A_i(C_i + D_i)}{N_i}$$

$$G_3 = \sum_i \frac{C_i(A_i + B_i)}{N_i}$$

Risk Differences

For risk differences, the weights are

$$w_i = (A_i + B_i)(C_i + D_i)/N_i$$

The variance of the risk difference is given by

$$V(\widehat{RD}_{MH}) = \frac{J_1}{J_2^2}$$

where

$$J_1 = \sum_i \frac{A_i B_i (C_i + D_i)^3 + C_i D_i (A_i + B_i)^3}{(A_i + B_i)(C_i + D_i) N_i^2}$$

$$J_2 = \sum_i \frac{(A_i + B_i)(C_i + D_i)}{N_i}$$

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Peto Method for Combining Studies

For the Peto method, the individual study odds ratio is given by (see Schwarzer et al. (2015) page 72-76).

$$\widehat{OR}_i = \exp[\{A_i - E(A_i)\}/v_i]$$

where

$$E(A_i) = \frac{(A_i + B_i)(A_i + C_i)}{N_i}$$

The variance of the log odds ratio is given by

$$V\{\ln(\widehat{OR}_i)\} = \frac{1}{v_i}$$

where

$$v_i = \frac{\{(A_i + B_i)(C_i + D_i)(A_i + C_i)(B_i + D_i)\}}{\{N_i^2(N_i - 1)\}}$$

These individual studies are combined using

$$\widehat{OR}_{Peto} = \exp\left\{\frac{\sum w_i \ln(\widehat{OR}_i)}{\sum w_i}\right\}$$

where

$$w_i = v_i$$

The variance of the log Peto odds ratio is given by

$$V\{\ln(\widehat{OR}_{Peto})\} = \frac{1}{\sum w_i}$$

The heterogeneity test in this case is

$$Q_{Peto} = \sum_{i=1}^k w_i \left\{ (\ln(\widehat{OR}_i))^2 - (\ln(\widehat{OR}_{Peto}))^2 \right\}$$

Random Effects Model

The random effects model assumes that the individual θ_i are normally distributed with mean θ and between-study variance τ^2 . Palmer and Sterne (2016) page 25 indicate that either the Mantel-Haenszel or the Inverse-Variance estimate may be used for the combined estimate. For the odds ratio and the risk ratio, the In OR and In risk ratio is used. For the risk difference, no transformation is applied.

The random effects model is given by

$$\hat{\theta}_i = \theta + t_i + \sigma_i e_i$$

where t_i and e_i are independent. Note that $t_i \sim N(0, \tau^2)$ and $e_i = N(0,1)$ so that $\hat{\theta}_i \sim N(\theta, \tau^2 + \sigma^2)$.

Random Study Weights

The individual study weights for the random effects model are

$$w_i^* = \frac{1}{V(\hat{\theta}_i) + \tau^2}$$

where τ^2 is estimated using one of the techniques shown next.

τ^2 Estimation

A very important quantity in meta-analysis is the between-study variance τ^2 . **NCSS** provides two estimators of this quantity, one called the DerSimonian and Laird (DL) estimator and the other called the Paule and Mandel (PM) estimator. The PM estimator has been recommended by several recent articles.

DerSimonian and Laird Estimator of τ^2

The between-study variance τ^2 can be estimated by the DerSimonian and Laird estimator $\hat{\tau}_{DL}^2$ (see Higgins and Thompson (2002) page 1543 and Veroniki *et al.* (2016) pages 60 - 61).

$$\hat{\tau}_{DL}^2 = \max \left[0, \frac{Q - (k - 1)}{\sum w_i - \left(\frac{\sum w_i^2}{\sum w_i} \right)} \right]$$

Note that this formula uses the fixed effect weights w_i .

Using the definition of I^2 in terms of $\hat{\tau}^2$ (see below), a simple confidence interval for τ^2 can be derived by plugging in the I^2 reference limits LL_{I^2} and UL_{I^2} into the rearranged formula

$$\hat{\tau}^2 = s^2 \left(\frac{I^2}{100 - I^2} \right)$$

Random effect weights are

$$w_i^* = \frac{1}{V(\hat{\theta}_i) + \hat{\tau}_{DL}^2}$$

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The combined estimate of the effect measure is

$$\hat{\theta}_{DL} = \frac{\sum w_i^* \hat{\theta}_i}{\sum w_i^*}$$

The variance of this estimate is

$$V(\hat{\theta}_{DL}) = \frac{1}{\sum w_i^*}$$

The formulas used for the confidence interval are of the form

$$\hat{\theta}_{DL} \pm z_{1-\alpha/2} \sqrt{V(\hat{\theta}_{DL})}$$

where $z_{1-\alpha/2}$ is the appropriate percentage point from the standardized normal distribution .

The formula used for the one degree-of-freedom heterogeneity test is

$$z = \frac{\hat{\theta}_{DL}}{\sqrt{V(\hat{\theta}_{DL})}}$$

Paule and Mandel Estimator of τ^2

The between-study variance τ^2 can be estimated by the Paule and Mandel Q-profile estimator $\hat{\tau}_{PM}^2$ (see Bowden *et al.* (2011) page 3 and Veroniki *et al.* (2016) pages 63 - 64). Paule and Mandel proposed that the generalized Q-statistic be iterated for various values of τ^2 until $Q_{gen}(\tau^2) = k - 1$, its expected value.

$$Q_{gen}(\tau^2) = \sum_{i=1}^k u_i (\hat{\theta}_i - \tilde{\theta}_{PM})^2$$

where

$$u_i = \frac{1}{V(\hat{\theta}_i) + \tau^2}$$

$$\tilde{\theta}_{PM} = \frac{\sum u_i \hat{\theta}_i}{\sum u_i}$$

The variance of this estimate is

$$V(\tilde{\theta}_{PM}) = \frac{1}{\sum u_i}$$

Viechtbauer (2007) proposed that an α -level confidence set for τ_{PM}^2 is found by iterating the same generalized Q-statistic, this time solving for the values of τ^2 which make $Q_{gen}(\tau^2) = \chi_{k-1, 1-\alpha/2}^2$ and $Q_{gen}(\tau^2) = \chi_{k-1, \alpha/2}^2$. The two resulting values of τ^2 form a non-symmetric confidence interval for τ_{PM}^2 .

Knapp-Hartung Adjustment

The Knapp-Hartung adjustment, Knapp and Hartung (2003), is recommended when using a random effects model. See, for example, IntHout *et al.* (2014). This procedure requires the following two adjustments.

1. A Student's-t distribution with $k-1$ degrees of freedom replaces the normal distribution in the confidence intervals and significance tests.
2. The variance of the estimated effect measure is now

$$V(\hat{\theta}_{KH}) = \frac{\sum w_i (\hat{\theta}_i - \hat{\theta}_{DL})^2}{(k-1) \sum w_i}$$

Graphical Displays

A number of plots have been devised to display the information in a meta-analysis. These include the forest plot, the radial plot, and the L'Abbe plot. More will be said about each of these plots in the Output section.

Data Structure

The data are entered into a dataset using one row per study. The four counts of the study's 2-by-2 table are entered into four columns. In addition to these, an additional variable is usually used to hold a short label. Another variable may be needed to hold a grouping variable.

As an example, we will use data referred to in Sutton (2000) as the cholesterol-lowering intervention dataset. This data set reviews 34 randomized clinical trials that were conducted to study the effects of three cholesterol-lowering treatments: diet, drug, and surgery. The mortality of patients in a treatment arm and a control arm were recorded. These data are contained in the SUTTON22 database. You should load this database to see how the data are arranged.

Example 1 – Meta-Analysis of Proportions

This section presents an example of how to analyze the data contained in the Sutton22 dataset. This dataset contains data for 34 randomized clinical trials that were conducted to study the effects of three cholesterol-lowering treatments: diet, drug, and surgery. The mortality of patients in a treatment arm and a control arm were recorded.

In this analysis we will ignore the three treatments.

Setup

To run this example, complete the following steps:

1 Open the Sutton22 example dataset

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Select **Sutton22** and click **OK**.

2 Specify the Meta-Analysis of Two Proportions procedure options

- Find and open the **Meta-Analysis of Two Proportions** procedure using the menus or the Procedure Navigator.
- The settings for this example are listed below and are stored in the **Example 1** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Variables Tab

Type of Data Input	Enter Variables for the First and Second Columns of the 2 x 2 Tables
Count Variable A.....	TDeath
Count Variable B.....	CDeath
Count Variable C	TSurvive
Count Variable D	CSurvive
Row Label Variable.....	StudyId
Subgroup Variable	<Empty>
Combination Method.....	Mantel-Haenszel
Knapp-Hartung Adjustment	Used
Outcome Measure	Odds Ratio (O1 / O2)
τ^2 Method	Paule and Mandel (PM)
I^2 and H^2 Method.....	DerSimonian and Laird (DL)
Adjustment Method.....	Add ϵ to all cells in tables with 1 zero cell (Recommended)
ϵ (Zero Count Adjustment Value).....	0.5

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Reports Tab

Run Summary.....	Checked
Data Summary.....	Checked
Analysis (Combined Only).....	Unchecked
Analysis (Combined, Individual).....	Checked
Q Heterogeneity Reports.....	Checked
τ^2 Between-Study Variation.....	Checked
s^2 Within-Study Variation.....	Checked
I^2 Inconsistency Index.....	Checked
H^2 Relative Excess in Heterogeneity.....	Checked
Confidence Level.....	95

Plots Tab

Forest Plot.....	Checked
Radial Plot.....	Checked
L'Abbe Plot.....	Checked
Horizontal Funnel Plot.....	Checked
Vertical Funnel Plot.....	Unchecked

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

Run Summary**Run Summary**

Parameter	Variable	Parameter	Value
A	TDeath	Rows Processed	34
B	CDeath	Rows Filtered Out	0
C	TSurvive	Rows with Missing Values*	0
D	CSurvive	Rows with Too Many Zeroes†	0
Row Label	StudyId	Rows Analyzed	34
Subgroup	None	Number of Observations	57076
		Number of Subgroups	1
		Adjustment Method	Add ϵ to all cells in tables with 1 zero cell
		ϵ (Adjustment Value)	0.5

* Rows are excluded when they have missing values, negative counts, or text for numeric values.

† Rows are excluded when the table includes zero cell counts that are not adjusted (see 'Adjustment Method' option).

This report records the variables that were used and the number of rows that were processed.

Data Summary

Data Summary									
StudyId	Group 1 Counts			Group 2 Counts			Group Proportions		Odds Ratio OR
	Response		Total N1	Response		Total N2	P1	P2	
	1 A	2 B		1 C	2 D				
S1	28	51	79	176	151	327	0.3544	0.5382	0.4710
S2	70	38	108	215	109	324	0.6481	0.6636	0.9339
S3	37	40	77	119	79	198	0.4805	0.6010	0.6141
S4	2	3	5	86	27	113	0.4000	0.7611	0.2093
S5	0	3	3	30	30	60	0.0000	0.5000	0.1429
S6	61	82	143	218	194	412	0.4266	0.5291	0.6620
S7	41	55	96	165	151	316	0.4271	0.5222	0.6822
S8	20	24	44	103	105	208	0.4545	0.4952	0.8495
S9	111	113	224	907	902	1809	0.4955	0.5014	0.9769
S10	81	27	108	346	116	462	0.7500	0.7489	1.0058
S11	31	51	82	213	202	415	0.3780	0.5133	0.5765
S12	17	12	29	33	38	71	0.5862	0.4648	1.6313
S13	23	20	43	24	28	52	0.5349	0.4615	1.3417
S14	0	4	4	30	56	86	0.0000	0.3488	0.2058
S15	1025	723	1748	4527	2066	6593	0.5864	0.6866	0.6470
S16	174	178	352	250	244	494	0.4943	0.5061	0.9541
S17	28	31	59	171	163	334	0.4746	0.5120	0.8610
S18	42	48	90	308	319	627	0.4667	0.4912	0.9063
S19	4	5	9	75	73	148	0.4444	0.5068	0.7787
S20	37	48	85	1112	1081	2193	0.4353	0.5071	0.7493
.
.
.
Total	2601	2216	4817	30087	22172	52259			

This report shows the input data. You should scan it for any mistakes. The 'Total' line provides the combined totals of all studies.

Group 1 and Group 2 Counts

These are the count values that were read from the database.

P1 and P2

This is the estimated event proportions in the treatment and control groups. Note these do not use the Zero Count Adjustments.

Odds Ratio (or Risk Ratio or Risk Difference)

This is the estimated value of the odds ratio. Note that it depends not only on the data, but also on the Zero Adjustment value used.

Odds Ratio Analysis

Odds Ratio Analysis

Method used to Combine Studies: Mantel-Haenszel
 Knapp-Hartung Adjustment: Active
 τ^2 Method: Paule and Mandel
 Confidence Limits Method: Q-Profile
 Zero Cell Count Adjustment Method: Add ϵ (0.5) to all cells in tables with 1 zero cell

StudyId	Odds Ratio	Log(Odds Ratio)		95.0% CI of OR		Test (OR = 1)		Percent Weight		Q
		Value	Std Err	Lower	Upper	Value	P-Value	Fixed	Random	
Combined										
Fixed Model	0.8474	-0.1656	0.0322	0.7956	0.9026	-5.143	0.0000	100.0		89.608
Random Model	0.8862	-0.1208	0.0627	0.7800	1.0068	-1.926	0.0628		100.0	
Studies										
S1	0.4710	-0.7528	0.2601	0.2829	0.7842	-2.895	0.0038	2.1	3.4	5.100
S2	0.9339	-0.0684	0.2333	0.5912	1.4753	-0.293	0.7694	1.8	3.9	0.173
S3	0.6141	-0.4876	0.2703	0.3615	1.0431	-1.804	0.0713	1.7	3.3	1.419
S4	0.2093	-1.5640	0.9391	0.0332	1.3188	-1.665	0.0959	0.2	0.4	2.217
S5*	0.1429	-1.9459	1.5334	0.0071	2.8849	-1.269	0.2044	0.2	0.2	1.348
S6	0.6620	-0.4125	0.1958	0.4510	0.9717	-2.107	0.0351	3.1	4.6	1.591
S7	0.6822	-0.3824	0.2351	0.4304	1.0814	-1.627	0.1038	2.1	3.8	0.851
S8	0.8495	-0.1631	0.3330	0.4423	1.6317	-0.490	0.6243	0.9	2.5	0.000
S9	0.9769	-0.0234	0.1417	0.7400	1.2895	-0.165	0.8689	4.8	5.8	1.007
S10	1.0058	0.0058	0.2468	0.6201	1.6314	0.023	0.9814	1.6	3.6	0.482
S11	0.5765	-0.5509	0.2480	0.3545	0.9373	-2.221	0.0263	2.1	3.6	2.414
S12	1.6313	0.4894	0.4458	0.6808	3.9088	1.098	0.2724	0.4	1.6	2.158
S13	1.3417	0.2939	0.4134	0.5968	3.0164	0.711	0.4771	0.5	1.8	1.236
S14*	0.2058	-1.5807	1.5076	0.0107	3.9513	-1.049	0.2944	0.1	0.2	0.881
S15	0.6470	-0.4354	0.0554	0.5805	0.7211	-7.866	0.0000	37.6	7.8	23.770
S16	0.9541	-0.0470	0.1395	0.7258	1.2541	-0.337	0.7361	5.0	5.9	0.722
S17	0.8610	-0.1497	0.2828	0.4947	1.4986	-0.529	0.5965	1.3	3.1	0.003
S18	0.9063	-0.0984	0.2259	0.5821	1.4110	-0.436	0.6630	2.0	4.0	0.088
S19	0.7787	-0.2502	0.6907	0.2011	3.0148	-0.362	0.7172	0.2	0.8	0.015
S20	0.7493	-0.2886	0.2229	0.4841	1.1599	-1.295	0.1955	2.2	4.1	0.305
.
.
.

Q The 'Q' column gives the contribution of this study (or group of studies) to Q, the test statistic for heterogeneity. The overall value of Q is given in the first line.

* A continuity correction was made to this study by adding 0.5 to all cells.

This report displays results for the odds ratio outcome measure. The report gives you the combined results first followed by the individuals results of each study.

Odds Ratio

This is the odds ratio for each study. The first two lines are the combined results for all studies using either the Fixed-Effects Model or the Random Effects Model. In this example, the Mantel-Haenszel method was used to combine the individual studies and the Knapp-Hartung Adjustment of the random-effects model was used.

The rows with starred labels (StudyId) had row counts modified because a zero cell count was detected.

Meta-Analysis of Two Proportions

Log(Odds Ratio)

These two columns contain the log of the odds ratio and the associated standard error.

95.0% CI of OR (Confidence Limits)

These are the lower and upper confidence limits in the original (not logged) scale. The first two lines are the combined results for all studies using either the Fixed-Effects Model or the Random Effects Model. In this example, the Mantel-Haenszel method was used to combine the individual studies and the Knapp-Hartung Adjustment of the random-effects model was used.

Test (OR = 1)

These two columns give the result of a hypothesis test of whether the odds ratio is one.

Percent Weight

These two columns give percent of the total of the individual weight that was used by this row. You can see how the model choice impacts the distribution of the weights.

Q

This column gives the contribution of each row to the heterogeneity Q value. This is useful in hunting for outliers. In this example, we note the rows 15 and 31 had unusually large contributions to Q and should be evaluated very carefully.

Heterogeneity Tests**Heterogeneity Tests**

Rows	Cochran's Test			Directional Test			Nondirectional Test		
	Q	DF	P-Value	χ^2_D	DF	P-Value	χ^2_{ND}	DF	P-Value
Combined	89.608	33	0.0000	27.8	1	0.0000	117.4	34	0.0000

Q	This statistic (sometimes called 'The heterogeneity test') tests the null hypothesis that all effects are equal (homogeneous effects) versus the alternative that at least one effect had a different effect (heterogeneous effects).
χ^2_D	This statistic tests the null hypothesis that all effects are equal (homogeneous effects) versus the alternative that at least one effect had a different effect (heterogeneous effects).
χ^2_{ND}	This statistic tests the null hypothesis that all effects are zero versus the alternative that at least one effect is non-zero.

This reports the results of three chi-square tests designed to test whether all treatment effects are equal.

Cochran's Test

Q tests the null hypothesis that all effects are equal versus the alternative that at least one effect had a different effect (heterogeneous effects) than the rest. This is the computed chi-square value for this test. The formula was presented earlier.

Directional Test

This statistic tests the null hypothesis that all effects are equal versus the alternative that at least one effect had a different effect.

Nondirectional Test

This statistic tests the null hypothesis that all effects are zero versus the alternative that at least one effect is non-zero.

τ^2 Between-Study Variation

τ^2 Between-Study Variation

τ^2 Method: Paule and Mandel
Confidence Limits Method: Q-Profile

τ^2	Variance		τ	Standard Deviation	
	95.0% CI			95.0% CI	
	Lower	Upper		Lower	Upper
0.047	0.012	0.185	0.218	0.109	0.430

This report shows the estimated between-study variance with a confidence interval. This value might be compared with the estimated within-study variance given in the next report.

s^2 Within-Study Variation

s^2 Within-Study Variation

Variance	Standard Deviation
s^2	s
0.041	0.202

This report shows the estimated within-study variance. This value might be compared with the estimated between-study variance given in the last report.

I^2 Inconsistency Index

I^2 Inconsistency Index

I^2 Method: DerSimonian and Laird
Confidence Limits Method: Transform C.I. of Hbl

I^2	I^2 Index	
	95.0% CI	
	Lower	Upper
63.173	46.808	74.503

The I^2 index may be interpreted as the proportion of total variation of treatment effects that is due to heterogeneity between studies.

H² Relative Excess in Heterogeneity

H² Relative Excess in Heterogeneity

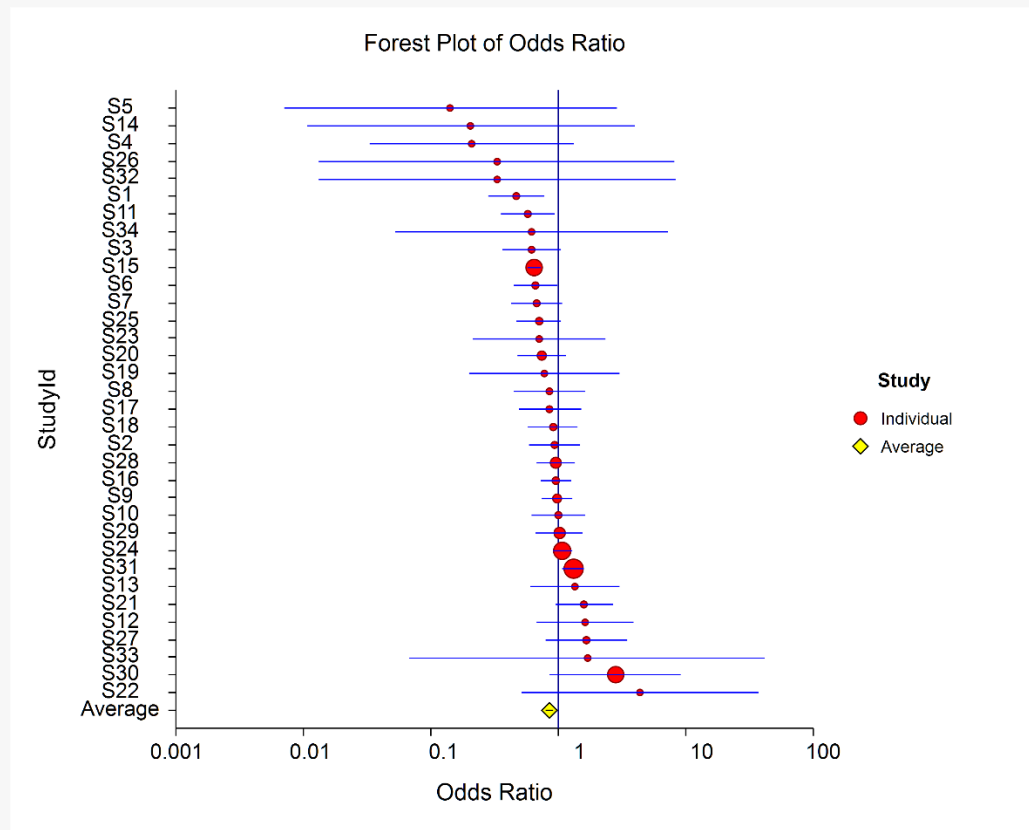
H² Method: DerSimonian and Laird
 Confidence Limits Method: Transform C.I. of HDL

H ² Index			H Index		
95.0% CI			95.0% CI		
H ²	Lower	Upper	H	Lower	Upper
2.715	1.880	3.922	1.648	1.371	1.980

The index H^2 is the ratio of Q (the heterogeneity) with its expected value. The minimum value of this index is one which occurs when there is no heterogeneity. A test heterogeneity is obtained by determining if the lower limit of the confidence interval is greater than one.

Forest Plot

Forest Plot



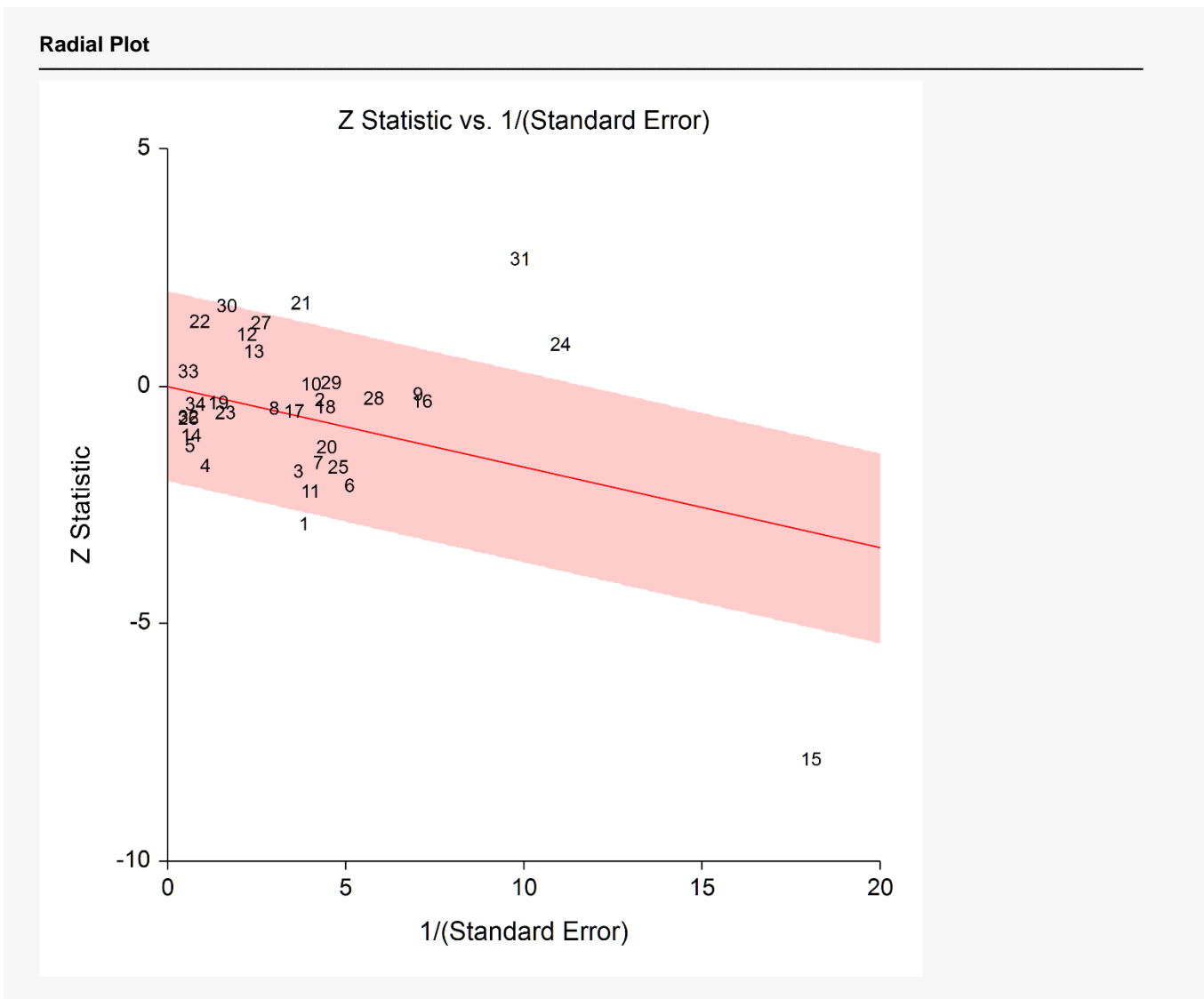
This plot presents the results for each study on one plot. The size of the plot symbol is proportional to the sample size of the study. The points on the plot are sorted by group and by the odds ratio. The lines

Meta-Analysis of Two Proportions

represent the confidence intervals about the odds ratios. Note that the narrower the confidence limits, the better.

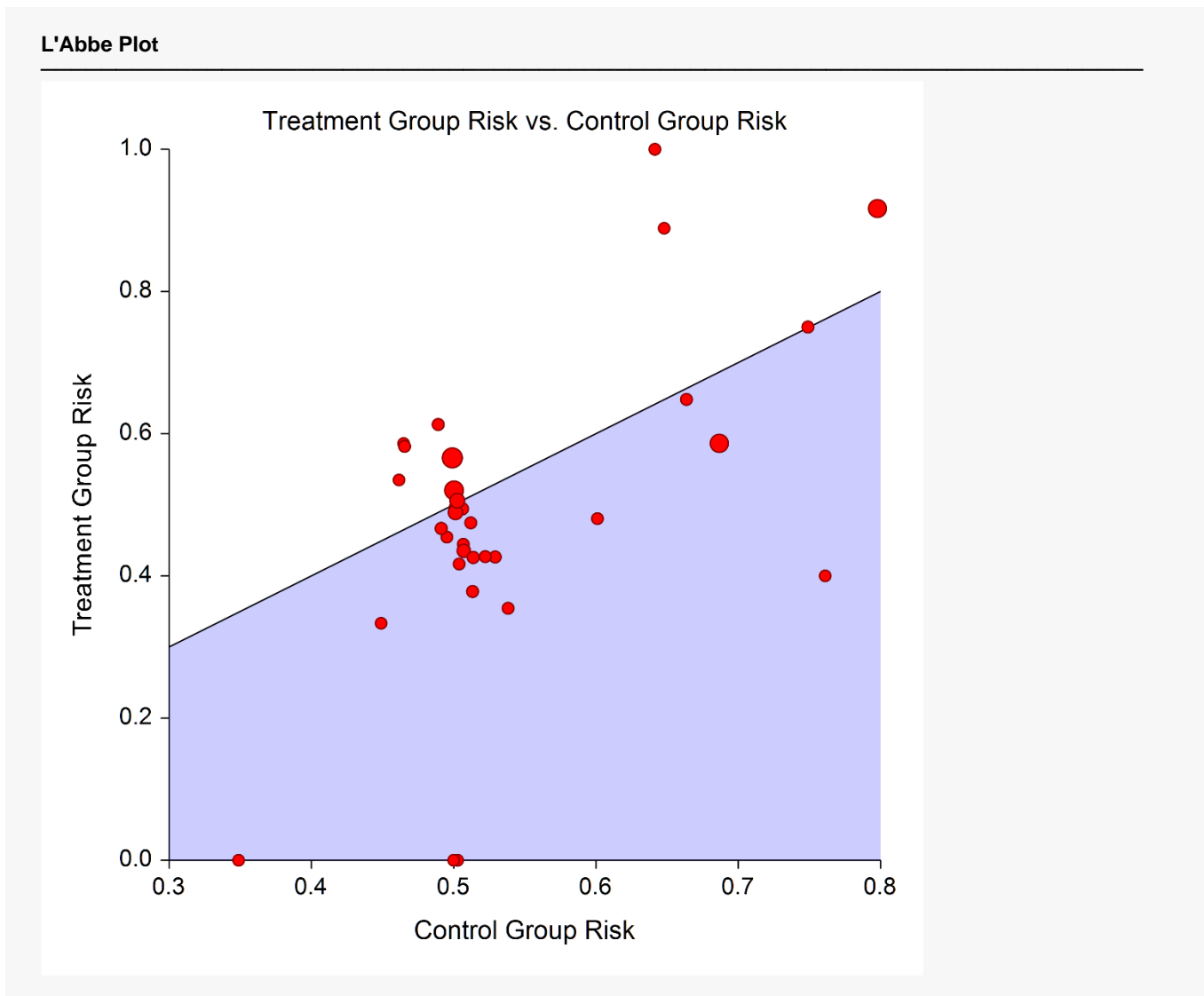
By studying this plot, you can determine the main conclusions that can be drawn from the set of studies. For example, you can determine how many studies were significant (the confidence limits do not intersect the vertical line at 1.0). You can see if there were different conclusions for the different groups.

Radial Plot



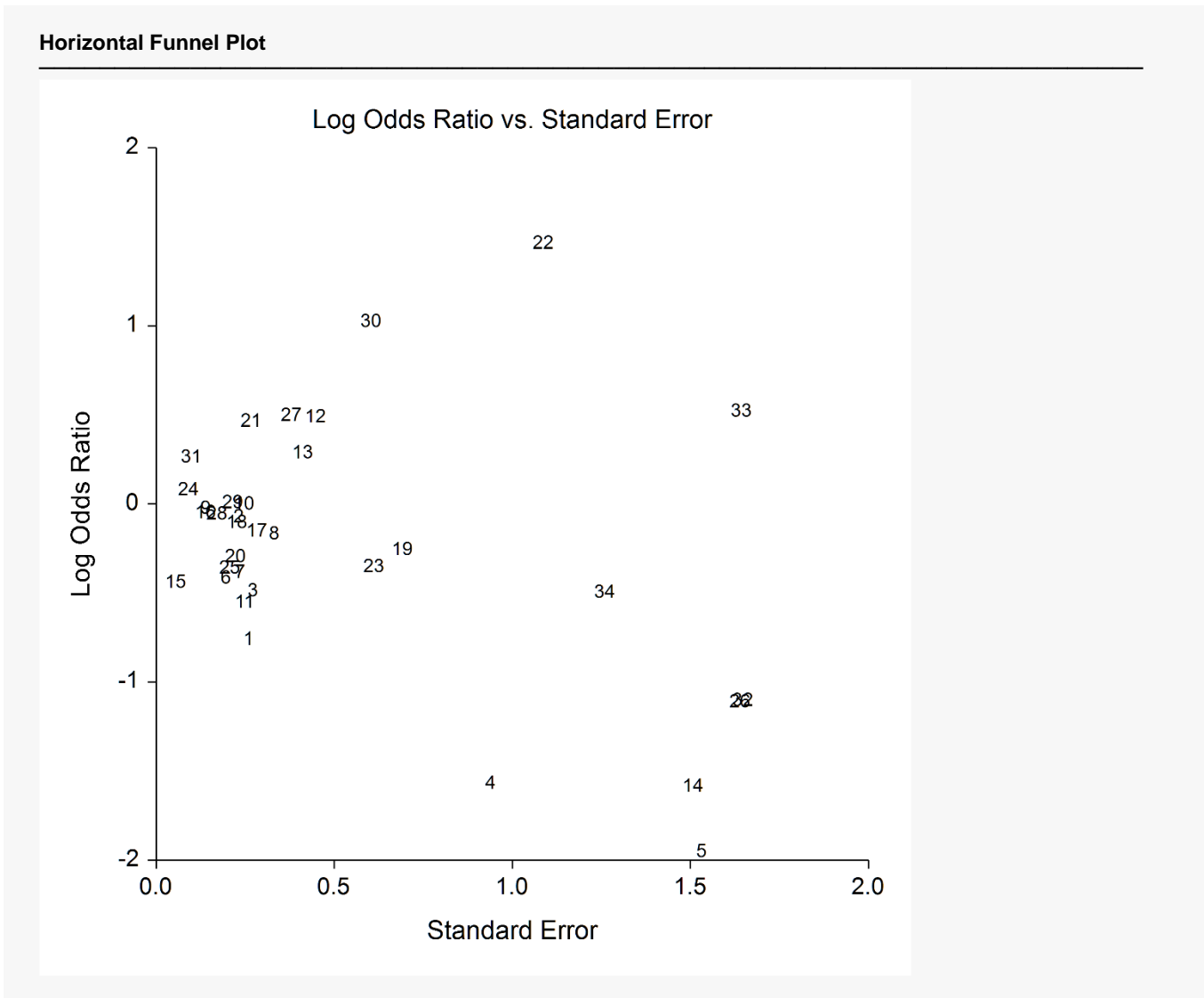
The radial (or Galbraith) plot shows the z-statistic (outcome divided by standard error) on the vertical axis and a measure of weight on the horizontal axis. Studies that have the largest weight are closest to the Y axis. Studies within the limits are interpreted as homogeneous. Studies outside the limits may be outliers.

L'Abbe Plot



The L'Abbe plot displays the treatment risk on vertical axis versus the control risk on the horizontal axis. Homogenous studies will be arranged along the diagonal line. This plot is especially useful in determining if the relationship between the treatment group and the control group is the same for all values of the control group risk.

Horizontal Funnel Plot



The funnel plot is often recommended to assess the publication bias in the meta-analysis. A plot with no bias opens out like a funnel to the right. Bias will appear as no studies in the upper right.

Several authors discouraged the use of the familiar triangle-shaped reference lines (not shown here) because they actually distract from the diagnosis.

We chose the horizontal orientation because it allows you to add various reference lines to the plot such as prediction limits and loess curve. However, the question of bias is probably most easily answered from the simple scatter plot shown here.

Example 2 – Meta-Analysis of Proportions with Subgroups

This section presents an example of how to analyze the data contained in the Sutton22 dataset, including the groups that are supplied. This dataset contains data for 34 randomized clinical trials that were conducted to study the effects of three cholesterol-lowering treatments: diet, drug, and surgery. The mortality of patients in a treatment arm and a control arm were recorded.

Setup

To run this example, complete the following steps:

1 Open the Sutton22 example dataset

- From the File menu of the NCSS Data window, select **Open Example Data**.
- Select **Sutton22** and click **OK**.

2 Specify the Meta-Analysis of Two Proportions procedure options

- Find and open the **Meta-Analysis of Two Proportions** procedure using the menus or the Procedure Navigator.
- The settings for this example are listed below and are stored in the **Example 2** settings file. To load these settings to the procedure window, click **Open Example Settings File** in the Help Center or File menu.

Variables Tab

Type of Data Input	Enter Variables for the First and Second Columns of the 2 x 2 Tables
Count Variable A.....	TDeath
Count Variable B.....	CDeath
Count Variable C	TSurvive
Count Variable D	CSurvive
Row Label Variable.....	StudyId
Subgroup Variable	Treatment
Combination Method.....	Mantel-Haenszel
Knapp-Hartung Adjustment	Used
Outcome Measure	Risk Ratio (P1 / P2)
τ^2 Method	Paule and Mandel (PM)
I^2 and H^2 Method.....	DerSimonian and Laird (DL)
Adjustment Method.....	Add ϵ to all cells in tables with 1 zero cell (Recommended)
ϵ (Zero Count Adjustment Value).....	0.5

Meta-Analysis of Two Proportions

Reports Tab

Run Summary.....	Checked
Data Summary.....	Checked
Analysis (Combined Only).....	Unchecked
Analysis (Combined, Individual).....	Checked
Q Heterogeneity Reports.....	Checked
τ^2 Between-Study Variation.....	Checked
s^2 Within-Study Variation.....	Checked
I^2 Inconsistency Index.....	Checked
H^2 Relative Excess in Heterogeneity.....	Checked
Confidence Level.....	95

Plots Tab

Forest Plot.....	Checked
Radial Plot.....	Checked
L'Abbe Plot.....	Checked
Horizontal Funnel Plot.....	Checked
Vertical Funnel Plot.....	Unchecked

3 Run the procedure

- Click the **Run** button to perform the calculations and generate the output.

Run Summary**Run Summary**

Parameter	Variable	Parameter	Value
A	TDeath	Rows Processed	34
B	CDeath	Rows Filtered Out	0
C	TSurvive	Rows with Missing Values*	0
D	CSurvive	Rows with Too Many Zeroes†	0
Row Label	StudyId	Rows Analyzed	34
Subgroup	Treatment	Number of Observations	57076
		Number of Subgroups	3
		Adjustment Method	Add ϵ to all cells in tables with 1 zero cell
		ϵ (Adjustment Value)	0.5

* Rows are excluded when they have missing values, negative counts, or text for numeric values.

† Rows are excluded when the table includes zero cell counts that are not adjusted (see 'Adjustment Method' option).

This report records the variables that were used and the number of rows that were processed.

Data Summary

Data Summary									
[Treatment] StudyId	Group 1 Counts			Group 2 Counts			Group Proportions		Risk Ratio RR
	Response			Response			P1	P2	
	1 A	2 B	Total N1	1 C	2 D	Total N2			
[Diet]									
S1	28	51	79	176	151	327	0.3544	0.5382	0.6585
S7	41	55	96	165	151	316	0.4271	0.5222	0.8179
S8	20	24	44	103	105	208	0.4545	0.4952	0.9179
S9	111	113	224	907	902	1809	0.4955	0.5014	0.9883
S16	174	178	352	250	244	494	0.4943	0.5061	0.9768
S17	28	31	59	171	163	334	0.4746	0.5120	0.9270
S21	39	28	67	182	209	391	0.5821	0.4655	1.2505
S22	8	1	9	46	25	71	0.8889	0.6479	1.3720
S24	269	248	517	4272	4268	8540	0.5203	0.5002	1.0401
Subgroup Total	718	729	1447	6272	6218	12490			
[Drug]									
S2	70	38	108	215	109	324	0.6481	0.6636	0.9767
S3	37	40	77	119	79	198	0.4805	0.6010	0.7995
S4	2	3	5	86	27	113	0.4000	0.7611	0.5256
S5	0	3	3	30	30	60	0.0000	0.5000	0.2500
S6	61	82	143	218	194	412	0.4266	0.5291	0.8062
S10	81	27	108	346	116	462	0.7500	0.7489	1.0014
S11	31	51	82	213	202	415	0.3780	0.5133	0.7366
S12	17	12	29	33	38	71	0.5862	0.4648	1.2612
S13	23	20	43	24	28	52	0.5349	0.4615	1.1589
S15	1025	723	1748	4527	2066	6593	0.5864	0.6866	0.8540
S18	42	48	90	308	319	627	0.4667	0.4912	0.9500
S19	4	5	9	75	73	148	0.4444	0.5068	0.8770
S20	37	48	85	1112	1081	2193	0.4353	0.5071	0.8585
S23	5	7	12	66	65	131	0.4167	0.5038	0.8270
S26	0	1	1	94	93	187	0.0000	0.5027	0.4974
S27	19	12	31	292	305	597	0.6129	0.4891	1.2531
S28	68	71	139	1838	1829	3667	0.4892	0.5012	0.9760
S29	44	43	87	2007	1987	3994	0.5057	0.5025	1.0065
S30	33	3	36	6549	1660	8209	0.9167	0.7978	1.1490
S31	236	181	417	5095	5115	10210	0.5659	0.4990	1.1341
S32	0	1	1	48	48	96	0.0000	0.5000	0.5000
S33	1	0	1	93	52	145	1.0000	0.6414	1.1711
S34	1	2	3	22	27	49	0.3333	0.4490	0.7424
Subgroup Total	1837	1421	3258	23410	15543	38953			
[Surgery]									
S14	0	4	4	30	56	86	0.0000	0.3488	0.2852
S25	46	62	108	375	355	730	0.4259	0.5137	0.8291
Subgroup Total	46	66	112	405	411	816			
[Combined6]									
Grand Total	2601	2216	4817	30087	22172	52259			

Meta-Analysis of Two Proportions

This report shows the input data. You should scan it for any mistakes. The 'Total' line provides the combined totals of all studies.

Group 1 and Group 2 Counts

These are the count values that were read from the database.

P1 and P2

This is the estimated event proportions in the treatment and control groups. Note these do not use the Zero Count Adjustments.

Odds Ratio (or Risk Ratio or Risk Difference)

This is the estimated value of the odds ratio. Note that it depends not only on the data, but also on the Zero Adjustment value used.

Risk Ratio Analysis

Risk Ratio Analysis

Method used to Combine Studies: Mantel-Haenszel
 Knapp-Hartung Adjustment: Active
 τ^2 Method: Paule and Mandel
 Confidence Limits Method: Q-Profile
 Zero Cell Count Adjustment Method: Add ϵ (0.5) to all cells in tables with 1 zero cell

[Treatment] StudyId	Risk Ratio	Log(Risk Ratio)		95.0% CI of RR		Test (RR = 1)		Percent Weight		Q
		Value	Std Err	Lower	Upper	Value	P-Value	Fixed	Random	
[Combined]										
Fixed Model	0.9312	-0.0713	0.0142	0.9056	0.9575	-5.019	0.0000	100.0		100.620
Random Model	0.9723	-0.0281	0.0287	0.9171	1.0309	-0.976	0.3289		100.0	
[Diet]										
Fixed Model	0.9878	-0.0122	0.0290	0.9332	1.0456	-0.422	0.6733	25.8		26.627
Random Model	0.9858	-0.0143	0.0661	0.8464	1.1481	-0.217	0.8337		33.3	
S1	0.6585	-0.4178	0.1602	0.4810	0.9015	-2.607	0.0091	1.5	2.3	4.674
S7	0.8179	-0.2010	0.1299	0.6341	1.0550	-1.547	0.1218	1.7	3.0	0.997
S8	0.9179	-0.0856	0.1794	0.6458	1.3046	-0.477	0.6330	0.8	1.9	0.006
S9	0.9883	-0.0117	0.0714	0.8593	1.1367	-0.164	0.8695	4.3	5.3	0.697
S16	0.9768	-0.0235	0.0699	0.8518	1.1201	-0.336	0.7366	4.5	5.4	0.468
S17	0.9270	-0.0759	0.1470	0.6949	1.2366	-0.516	0.6059	1.1	2.6	0.001
S21	1.2505	0.2236	0.1168	0.9946	1.5724	1.913	0.0557	1.2	3.4	6.369
S22	1.3720	0.3163	0.1468	1.0290	1.8293	2.155	0.0312	0.2	2.6	6.972
S24	1.0401	0.0393	0.0436	0.9550	1.1329	0.903	0.3667	10.5	6.7	6.443

Meta-Analysis of Two Proportions

[Drug]										
Fixed Model	0.9145	-0.0894	0.0164	0.8856	0.9443	-5.456	0.0000	72.1		72.247
Random Model	0.9733	-0.0271	0.0327	0.9095	1.0416	-0.828	0.4167		63.2	
S2	0.9767	-0.0235	0.0812	0.8331	1.1452	-0.290	0.7719	2.3	4.9	0.346
S3	0.7995	-0.2237	0.1319	0.6174	1.0354	-1.697	0.0898	1.4	3.0	1.336
S4	0.5256	-0.6433	0.5503	0.1788	1.5453	-1.169	0.2424	0.2	0.3	1.080
S5*	0.2500	-1.3863	1.3291	0.0185	3.3825	-1.043	0.2969	0.1	0.0	0.979
S6	0.8062	-0.2154	0.1075	0.6530	0.9953	-2.004	0.0451	2.4	3.8	1.797
S10	1.0014	0.0014	0.0617	0.8873	1.1303	0.023	0.9813	2.8	5.8	1.388
S11	0.7366	-0.3057	0.1495	0.5495	0.9873	-2.045	0.0408	1.5	2.5	2.459
S12	1.2612	0.2321	0.2014	0.8499	1.8716	1.152	0.2491	0.4	1.6	2.269
S13	1.1589	0.1475	0.2065	0.7731	1.7372	0.714	0.4752	0.5	1.6	1.122
S15	0.8540	-0.1578	0.0217	0.8184	0.8912	-7.259	0.0000	41.0	7.6	15.838
S18	0.9500	-0.0513	0.1198	0.7512	1.2014	-0.428	0.6685	1.7	3.3	0.028
S19	0.8770	-0.1312	0.3814	0.4153	1.8521	-0.344	0.7308	0.2	0.5	0.025
S20	0.8585	-0.1526	0.1253	0.6715	1.0975	-1.218	0.2233	1.8	3.2	0.421
S23	0.8270	-0.1899	0.3524	0.4145	1.6500	-0.539	0.5899	0.2	0.6	0.113
S26*	0.4974	-0.6985	1.2269	0.0449	5.5081	-0.569	0.5692	0.0	0.1	0.261
S27	1.2531	0.2256	0.1487	0.9362	1.6772	1.517	0.1293	0.6	2.5	3.985
S28	0.9760	-0.0243	0.0882	0.8210	1.1603	-0.275	0.7832	2.9	4.5	0.284
S29	1.0065	0.0064	0.1071	0.8158	1.2417	0.060	0.9521	1.9	3.8	0.526
S30	1.1490	0.1389	0.0506	1.0406	1.2687	2.747	0.0060	1.2	6.4	17.287
S31	1.1341	0.1259	0.0440	1.0404	1.2363	2.859	0.0042	8.6	6.7	20.061
S32*	0.5000	-0.6931	1.2289	0.0450	5.5597	-0.564	0.5727	0.0	0.1	0.256
S33*	1.1711	0.1580	0.4129	0.5213	2.6308	0.383	0.7021	0.1	0.5	0.308
S34	0.7424	-0.2978	0.8317	0.1455	3.7896	-0.358	0.7203	0.1	0.1	0.074
[Surgery]										
Fixed Model	0.8111	-0.2094	0.1178	0.6439	1.0217	-1.778	0.0754	2.2		1.746
Random Model	0.8225	-0.1954	0.0921	0.2552	2.6510	-2.121	0.2804		3.5	
S14*	0.2852	-1.2544	1.3496	0.0203	4.0175	-0.929	0.3526	0.1	0.0	0.769
S25	0.8291	-0.1874	0.1174	0.6587	1.0436	-1.596	0.1104	2.1	3.4	0.978

Q The 'Q' column gives the contribution of this study (or group of studies) to Q, the test statistic for heterogeneity. The overall value of Q is given in the first line.

* A continuity correction was made to this study by adding 0.5 to all cells.

This report displays results for the risk-ratio outcome for each subgroup. The report gives you the combined results first (Fixed Model and Random Model), followed by the individuals results of each study.

Risk Ratio

This is the risk ratio for each study. The first two lines are the combined results for all studies using either the Fixed-Effects Model or the Random Effects Model. In this example, the Mantel-Haenszel method was used to combine the individual studies and the Knapp-Hartung Adjustment of the random-effects model was used.

Log(Risk Ratio)

These two columns contain the log of the odds ratio and the associated standard error.

95.0% CI of RR (Confidence Limits)

These are the lower and upper confidence limits in the original (not logged) scale. The first two lines are the combined results for all studies using either the Fixed-Effects Model or the Random Effects Model. In this example, the Mantel-Haenszel method was used to combine the individual studies and the Knapp-Hartung Adjustment of the random-effects model was used.

Meta-Analysis of Two Proportions

Test (RR = 1)

These two columns give the result of a hypothesis test of whether the risk ratio is one.

Percent Weight

These two columns give percent of the total of the individual weight that was used by this row. You can see how the model choice impacts the distribution of the weights.

Q

This column gives the contribution of each row to the heterogeneity Q value. This is useful in hunting for outliers. In this example, we note the rows 15 and 31 had unusually large contributions to Q and should be evaluated very carefully.

Heterogeneity Tests**Heterogeneity Tests**

Treatment	Cochran's Test			Directional Test			Nondirectional Test		
	Q	DF	P-Value	χ^2_D	DF	P-Value	χ^2_{ND}	DF	P-Value
Diet	19.378	8	0.0130	0.1	1	0.7685	18.9	9	0.0257
Drug	74.551	22	0.0000	17.2	1	0.0000	89.2	23	0.0000
Surgery	0.635	1	0.4256	2.8	1	0.0947	3.4	2	0.1816
Combined	100.620	33	0.0000	13.4	1	0.0002	111.6	34	0.0000

The individual group test values do not sum to the combined value because these group values are calculated using only the studies in the corresponding group.

- Q This statistic (sometimes called 'The heterogeneity test') tests the null hypothesis that all effects are equal (homogeneous effects) versus the alternative that at least one effect had a different effect (heterogeneous effects).
- χ^2_D This statistic tests the null hypothesis that all effects are equal (homogeneous effects) versus the alternative that at least one effect had a different effect (heterogeneous effects).
- χ^2_{ND} This statistic tests the null hypothesis that all effects are zero versus the alternative that at least one effect is non-zero.

This reports the results of three chi-square tests designed to test whether all treatment effects are equal.

τ^2 Between-Study Variation

τ^2 Between-Study Variation

τ^2 Method: Paule and Mandel
Confidence Limits Method: Q-Profile

[Subgroup] Treatment	Variance			Standard Deviation		
	τ^2	95.0% CI		τ	95.0% CI	
		Lower	Upper		Lower	Upper
Diet	0.026	0.001	0.150	0.161	0.035	0.388
Drug	0.007	0.002	0.033	0.086	0.044	0.182
Surgery	0.000	0.000	578.800	0.000	0.000	24.058
Combined	0.010	0.003	0.034	0.102	0.054	0.184

This report shows the estimated between-study variance with a confidence interval. This value might be compared with the estimated within-study variance given in the next report.

s^2 Within-Study Variation

s^2 Within-Study Variation

[Subgroup] Treatment	Variance s^2	Standard Deviation s
Diet	0.009	0.093
Drug	0.008	0.088
Surgery	0.918	0.958
Combined	0.008	0.087

This report shows the estimated within-study variance. This value might be compared with the estimated between-study variance given in the last report.

I² Inconsistency Index

I² Inconsistency Index

I² Method: DerSimonian and Laird
 Confidence Limits Method: Transform C.I. of HDL

[Subgroup] Treatment	I ² Index		
	I ²	95.0% CI	
		Lower	Upper
Diet	58.717	13.724	80.246
Drug	70.490	54.946	80.671
Surgery			
Combined	67.203	53.141	77.046

The I^2 index may be interpreted as the proportion of total variation of treatment effects that is due to heterogeneity between studies.

H² Relative Excess in Heterogeneity

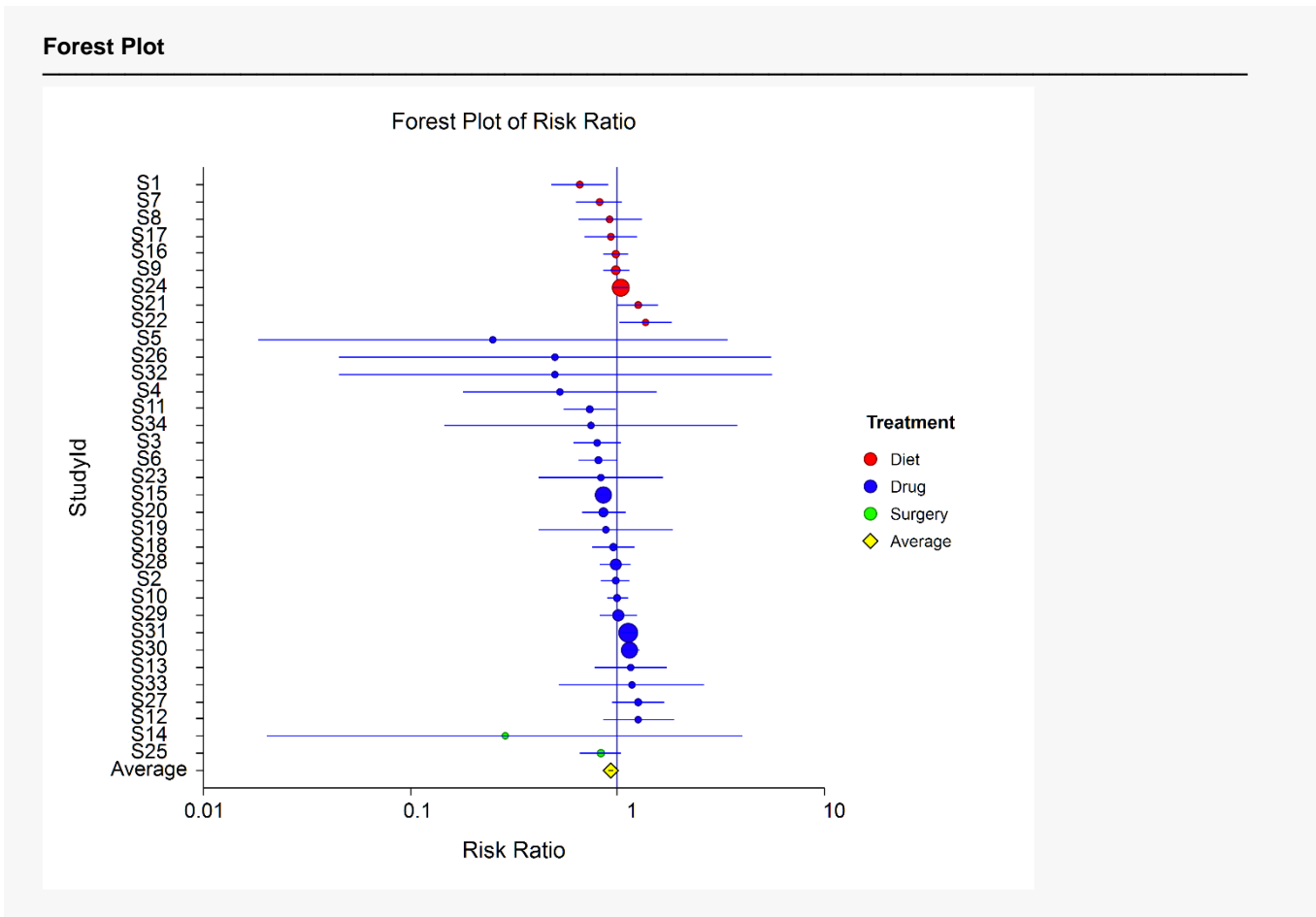
H² Relative Excess in Heterogeneity

H² Method: DerSimonian and Laird
 Confidence Limits Method: Transform C.I. of HDL

[Subgroup] Treatment	H ² Index			H Index		
	H ²	95.0% CI		H	95.0% CI	
		Lower	Upper		Lower	Upper
Diet	2.422	1.159	5.062	1.556	1.077	2.250
Drug	3.389	2.220	5.174	1.841	1.490	2.275
Surgery	1.000			1.000		
Combined	3.049	2.134	4.356	1.746	1.461	2.087

The index H^2 is the ratio of Q (the heterogeneity) with its expected value. The minimum value of this index is one which occurs when there is no heterogeneity. A test heterogeneity is obtained by determining if the lower limit of the confidence interval is greater than one.

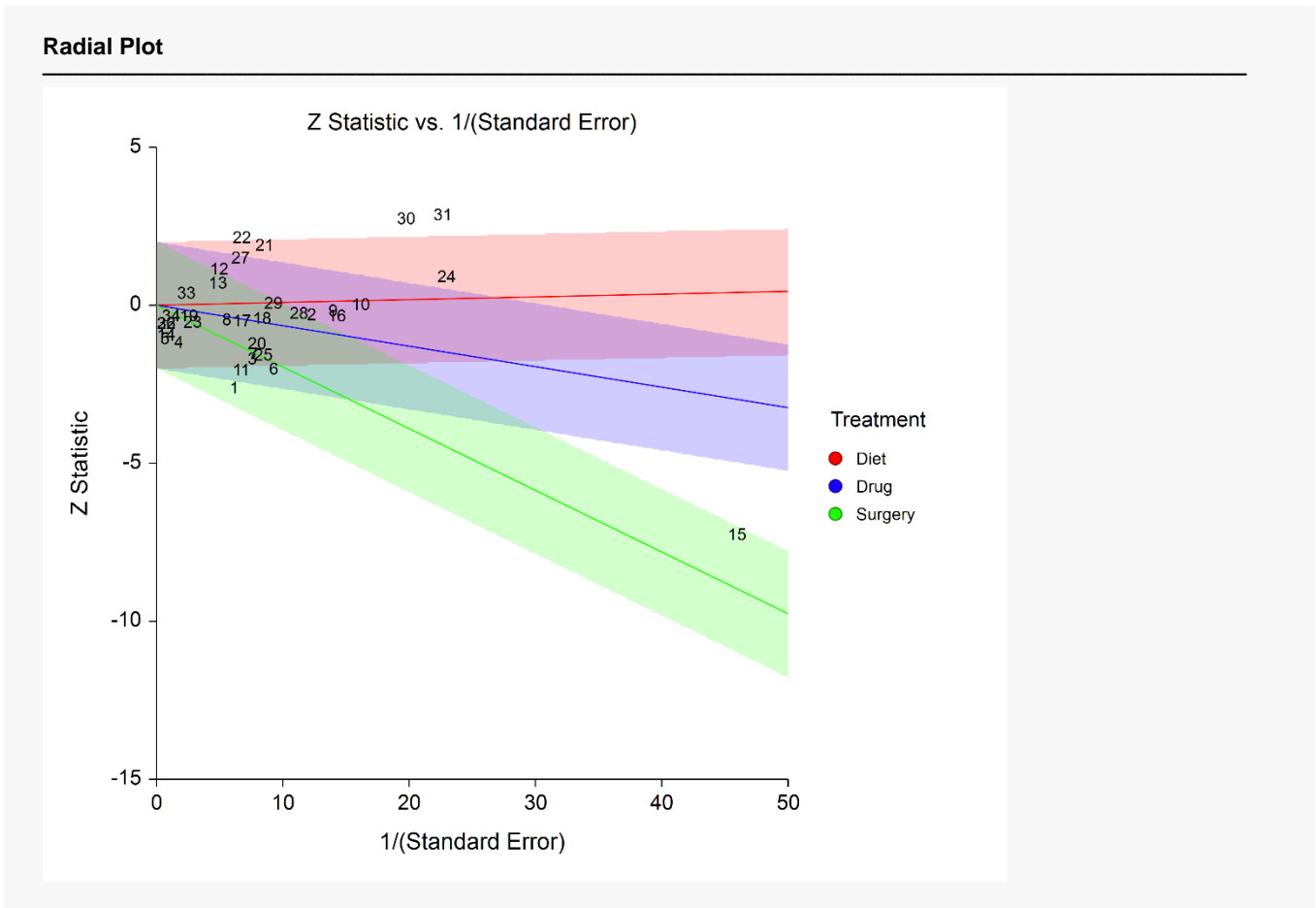
Forest Plot



This plot presents the results for each study on one plot. The size of the plot symbol is proportional to the sample size of the study. The points on the plot are sorted by group and by the odds ratio. The lines represent the confidence intervals about the odds ratios. Note that the narrower the confidence limits, the better.

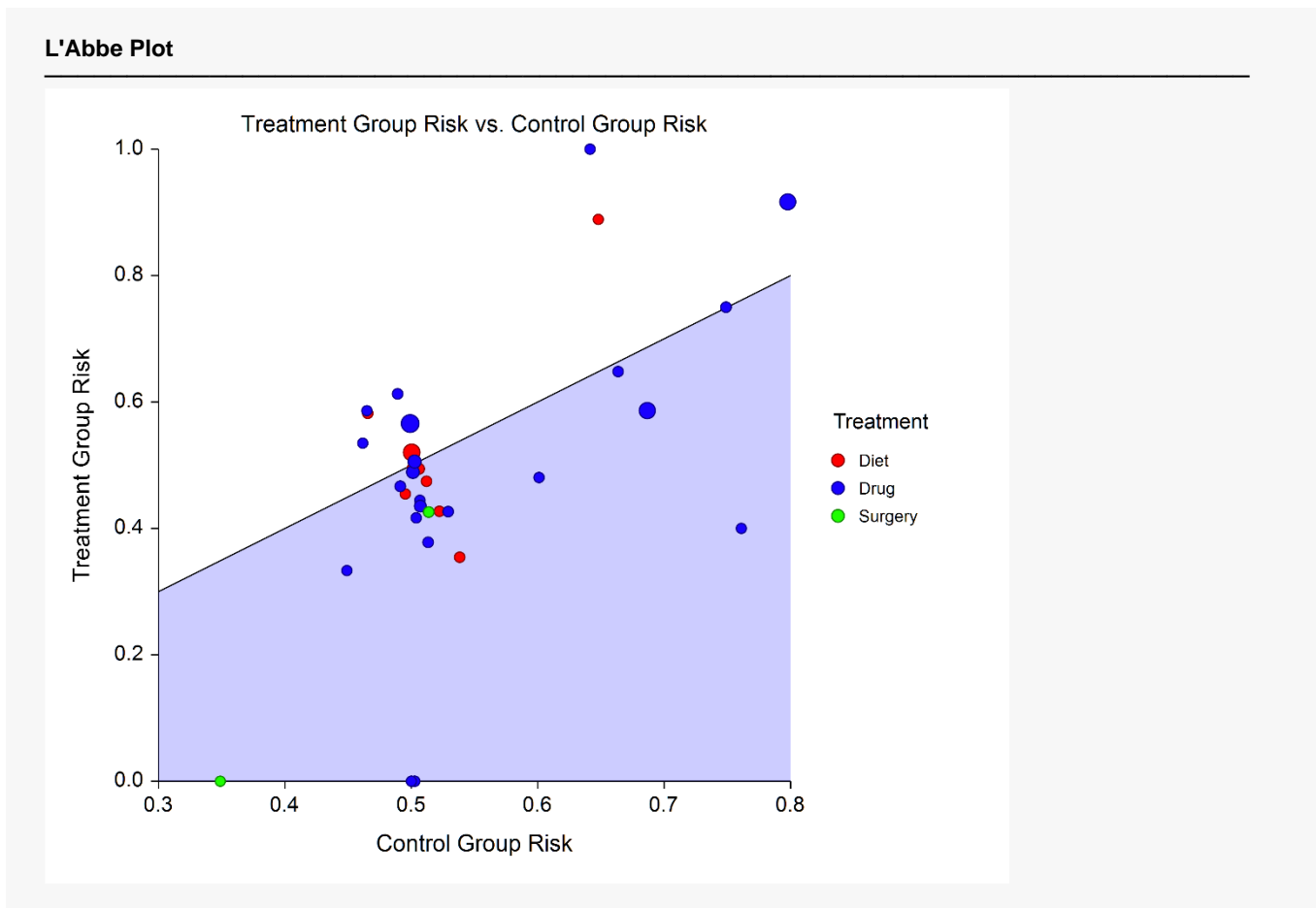
By studying this plot, you can determine the main conclusions that can be drawn from the set of studies. For example, you can determine how many studies were significant (the confidence limits do not intersect the vertical line at 1.0). You can see if there were different conclusions for the different groups.

Radial Plot



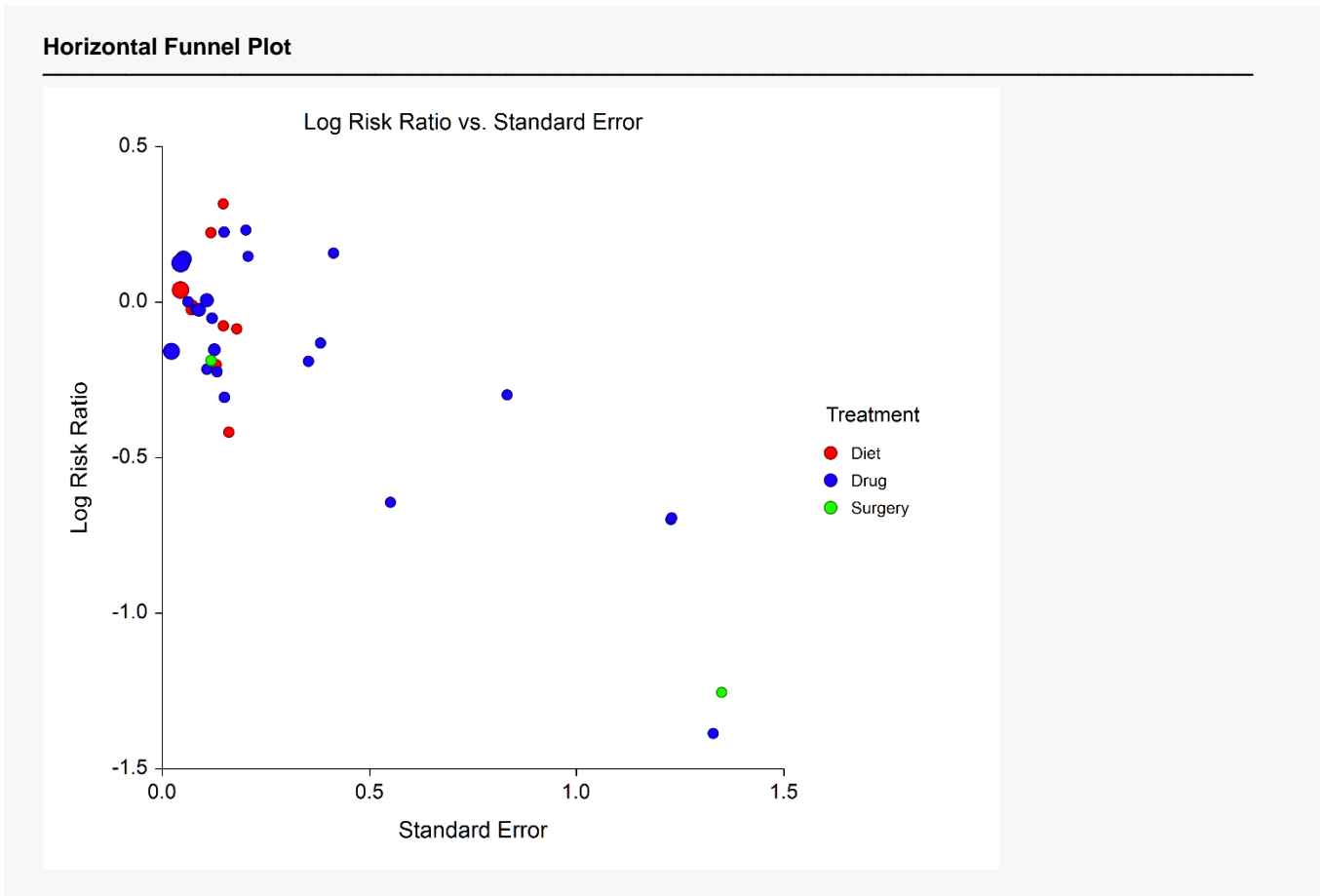
The radial (or Galbraith) plot shows the z-statistic (outcome divided by standard error) on the vertical axis and a measure of weight on the horizontal axis. Studies that have the largest weight are closest to the Y axis. Studies within the limits are interpreted as homogeneous. Studies outside the limits may be outliers.

L'Abbe Plot



The L'Abbe plot displays the treatment risk on vertical axis versus the control risk on the horizontal axis. Homogenous studies will be arranged along the diagonal line. This plot is especially useful in determining if the relationship between the treatment group and the control group is the same for all values of the control group risk.

Horizontal Funnel Plot



The funnel plot is often recommended to assess the publication bias in the meta-analysis. A plot with no bias opens out like a funnel to the right. Bias will appear as no studies in the upper right.

Several authors discouraged the use of the familiar triangle-shaped reference lines (no shown here) because they actually distract from the diagnosis.

We chose the horizontal orientation because it allows you to add various reference lines to the plot such as prediction limits and loess curve. However, the question of bias is probably most easily answer from the plain point plot shown here.