

Chapter 635

Meta-Analysis of Tests for the Risk Ratio of Two Proportions using a Random-Effects Model

Introduction

This procedure calculates power and number of studies for fixed-effect meta-analyses of parallel group studies that are summarized by the risk ratios in two group proportions. The sample size formulas used by this procedure were published in Hedges and Pigott (2001) and Harrer *et al.* (2022).

Meta-Analysis

Meta-analysis refers to the systematic assessment of a group of two or more individual studies (experiments or clinical trials). The studies must be similar so that their results may be numerically compared. For example, in this procedure all studies must have as their outcome two group proportions whose risk ratio is used to compare their values.

By combining the results of several studies, their individual results may be summarized and assessed. The power of the combined test will be increased since it represents a larger sample.

Fixed-Effects versus Random-Effects Models

The *fixed-effects model*, which is assumed by another procedure, assumes that all studies have the same true effect size. That is, it assumes that all factors that might influence the effect size are the same so that the true effect size for all studies is the same. Therefore, only the *within study variability* needs to be considered since the effect size variation occurs because of random error.

The *random-effects model*, which is assumed by this procedure, assumes that the studies in the analysis are similar, but not to the extent that they all have the same true effect size. Instead, it is assumed that each study has its own true effect size and that the particular outcome of the study is a sample from a distribution with that proportion. The random-effects model must not only account for the *within study variability*, but it must also account for the *between study variability*.

Technical Details

The Meta-Analysis of the Risk Ratio of Two Proportions

The sample size formulas used by this procedure were published in Harrer *et al.* (2022).

A series of K studies are assumed to each have an effect size OR which is the risk ratio between two group proportions. The results of these individual studies may be combined into one overall statistical test that draws a more precise conclusion.

Test Statistic

Suppose each study has two populations from which dichotomous (binary) responses are recorded. The probability (or risk) of obtaining the event of interest in population 1 (the treatment group) is p_1 and in population 2 (the control group) is p_2 . The corresponding failure proportions are given by $q_1 = 1 - p_1$ and $q_2 = 1 - p_2$.

An assumption is made that the responses from each group follow a binomial distribution. This means that the event probability, p_i , is the same for all subjects within the group and that the response from one subject is independent of that of any other subject.

Random samples of m and n individuals are obtained from these two populations. The data from these samples can be displayed in a 2-by-2 contingency table as follows

Group	Success	Failure	Total
Treatment	a	c	m
Control	b	d	n
Total	s	f	N

The following alternative notation is sometimes used.

Group	Success	Failure	Total
Treatment	x_{11}	x_{12}	n_1
Control	x_{21}	x_{22}	n_2
Total	m_1	m_2	N

The binomial proportions, p_1 and p_2 , are estimated from these data using the formulae

$$\hat{p}_1 = \frac{a}{m} = \frac{x_{11}}{n_1} \quad \text{and} \quad \hat{p}_2 = \frac{b}{n} = \frac{x_{21}}{n_2}$$

Risk Ratio

The risk ratio is computed as

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

Meta-Analysis for the Risk Ratio of Proportions

The formulas presented in this section are given Harrer *et al.* (2022) pages 404 and 446.

Suppose the individual tables are summarized into one 2-by-2 table whose individual cells now contain the corresponding cell averages which are still named a , b , c , and d . These counts can be reparametrized using the two group proportions $P1$ and $P2$ and the two average-group sample sizes $N1$ and $N2$. The average cell counts are then given by

$$a = (P1)(N1)$$

$$b = (P2)(N2)$$

$$c = (1 - P1)(N1)$$

$$d = (1 - P2)(N2)$$

Using these summary statistics, an effect size called the *log odds ratio* can be calculated using

$$\log(RR) = \log\left(\frac{P1}{P2}\right)$$

along with an estimate of the within-group variance

$$V_W = \frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d}$$

For planning purposes, the between-group variance is estimated as a multiple of the within-group variance as follows

$$V_B = RV_W$$

Hedges and Pigott (2001) recommend using 0.333 for a *small* value, 0.667 for a *medium* value, and 1.0 for a *large* value of R . Note that the fixed-effect results is achieved when R is set to 0.

I^2 - Heterogeneity Index

Some authors measure the amount of heterogeneity in the meta-analysis using the heterogeneity index I^2 (also called the *degree of heterogeneity* or *inconsistency*) instead of R . This value is related to R as follows. Note that often this value is presented as a percentage.

$$I^2 = \frac{V_B}{V_B + V_W}$$

This value is related to R using the relationship

$$R = \frac{I^2}{1 - I^2}$$

Random-Effects Standard Error

The final random-effects standard error used in the power calculation is

$$SE_{\log RR} = \sqrt{\frac{V_W + V_B}{K}}$$

The meta-analysis z-test is then calculated as

$$Z = \frac{\log(RR) - \log(RR_0)}{SE_{\log RR}}$$

which is based on the six parameters $P1$, $P2$, $N1$, $N2$, R , and RR_0 .

We assume that Z follows the standard normal distribution and so it can be used to test the null hypothesis $H_0: RR = RR_0$ at significance level of α .

Hypotheses

Three statistical hypotheses commonly used are

$$H_0: RR \leq RR_0 \quad \text{vs.} \quad H_1: RR > RR_0$$

$$H_0: RR \geq RR_0 \quad \text{vs.} \quad H_1: RR < RR_0$$

$$H_0: RR = RR_0 \quad \text{vs.} \quad H_1: RR \neq RR_0$$

Power Calculation

The power of a one-tailed test that $RR = RR_0$ is given by

$$Power = 1 - \Phi(c_\alpha - \lambda)$$

where OR is set by the alternative hypothesis, c_α is the $1 - \alpha$ quantile of the standard normal distribution, and

$$\lambda = \frac{\log(RR) - \log(RR_0)}{SE_{\log RR}}$$

The power of a two-tailed test that $RR = RR_0$ is given by

$$Power = 1 - \Phi(c_{\alpha/2} - \lambda) + \Phi(-c_{\alpha/2} - \lambda)$$

These formulas can be used in search algorithms to determine the necessary number of studies required to achieve a desired level of power.

Meta-Analysis of Tests for the Risk Ratio of Two Proportions using a Random-Effects Model

Note that the values of $P_{1.0}$ (P1 assuming H_0) and $P_{1.1}$ (P1 assuming H_1) can be obtained from the risk ratios using

$$P_{1.0} = RR_0 P_2$$

and

$$P_{1.1} = RR_1(P_2)$$

where RR_1 is the risk ratio at which the power is calculated.

Example 1 – Calculating Sample Size

Researchers wish to determine a reasonable number of studies for a meta-analysis based on the risk ratio with the following characteristics: two-group, equal-allocation trials, two-sided significance level of 0.05, a power of 0.9, average group size of all studies is 25, $P_2 = 0.4$, $R = 0.667$, $RR_1 = 1.25$ 1.5 1.75, and $RR_0 = 1.0$.

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters 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.

Design Tab

Solve For	Number of Studies
Alternative Hypothesis	Two-Sided (H1: RR ≠ RR0)
Power.....	0.90
Alpha.....	0.05
N1 (Average Sample Size of Group 1).....	25
N2 (Average Sample Size of Group 2).....	N1
RR0 (Risk Ratio H0)	1.0
RR1 (Risk Ratio H1)	1.25 1.5 1.75
P2 (Group 2 Proportion).....	0.4
Calculate Between-Study Variance From	R (Between-Study Var / Within-Study Var)
R (Between-Study Var / Within-Study Var)	0.667

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Reports

Numeric Results

Solve For: **Number of Studies**
 Hypotheses: H0: RR = RR0 vs. H1: RR ≠ RR0
 Between-Study Variance Input: R (Between-Study / Within-Study Variances)

Power	Average Sample Size Per Study			Number of		Risk Ratio		Proportion			Between-Study Variance Calculation		
	Group 1 N1	Group 2 N2	Total N	Studies K	Subjects KN	RR H0 RR0	RR H1 RR1	P1 H0 P1.0	P1 H1 P1.1	Control P2	R	I ²	Alpha
0.90144	25	25	50	28	1400	1	1.25	0.4	0.5	0.4	0.667	0.40012	0.05
0.92123	25	25	50	10	500	1	1.50	0.4	0.6	0.4	0.667	0.40012	0.05
0.93356	25	25	50	7	350	1	1.75	0.4	0.7	0.4	0.667	0.40012	0.05

- Power The probability of rejecting a false null hypothesis about the risk ratio. This is the power calculated at the actual risk ratio.
- N1, N2, N The average sample sizes of groups 1 and 2 along with the total of both groups calculated on all studies included in the meta-analysis.
- K The number of studies included in the meta-analysis.
- KN The number of subjects included in the meta-analysis. KN = K x N.
- RR0 The value of the risk ratio assumed by the null hypothesis, H0.
- RR1 The value of the risk ratio assumed by the alternative hypothesis, H1. This is the risk ratio at which the power is calculated.
- P1.0 The value of the response proportion of group 1 assumed by the null hypothesis, H0.
- P1.1 The value of the response proportion of group 1 assumed by the alternative hypothesis, H1.
- P2 The value of the response proportion of group 2 assumed by both H0 and H1.
- R The value of the heterogeneity ratio used to specify the between study variance. The formula is (Between Study Variance) = R x (Within Study Variance). The following values are often used: Small = 0.333, Medium = 0.667, Large = 1.000.
- I² The value of the heterogeneity index used to specify the Between Study variance. The formula is (Between Study Variance) = I² / (1 - I²) x (Within Study Variance). The following values are often used: Small = 0.25, Medium = 0.5, Large = 0.75.
- Alpha The probability of rejecting a true null hypothesis.

Summary Statements

A collection of two-group studies will be used to test whether the Group 1 proportion is different from the Group 2 proportion (H0: RR = 1 versus H1: RR ≠ 1, RR = P1 / P2). The meta-analysis comparison will be made using a two-sided random-effects-model Z-test, with a Type I error rate (α) of 0.05. The response proportion of Group 2 (the control group) is assumed to be 0.4. The heterogeneity ratio used to create the between-study variance is assumed to be 0.667. With average study sample sizes of 25 for Group 1 and 25 for Group 2, to detect a risk ratio (RR) of 1.25 with 90% power, the number of needed studies will be 28.

References

Borenstein, M., Hedges, L.V., Higgins, J.P.T., and Rothstein, H.R. 2021. Introduction to Meta-Analysis, Second Edition. John Wiley and Sons.

Cooper, J., Hedges, L.V., Valentine, J.C. 2019. The Handbook of Research Synthesis and Meta-Analysis, Third Edition. Russell Sage Foundation.

Griffin, J.W. 2021. 'Calculating statistical power for meta-analysis using metapower', The Quantitative Methods for Psychology, Vol. 17, No. 1, pages 24-39.

Harrer, M., Cuijpers, P., Furukawa, T.A., and Ebert, D.D. 2022. Doing Meta-Analysis with R: A Hands-On Guide. CRC Press.

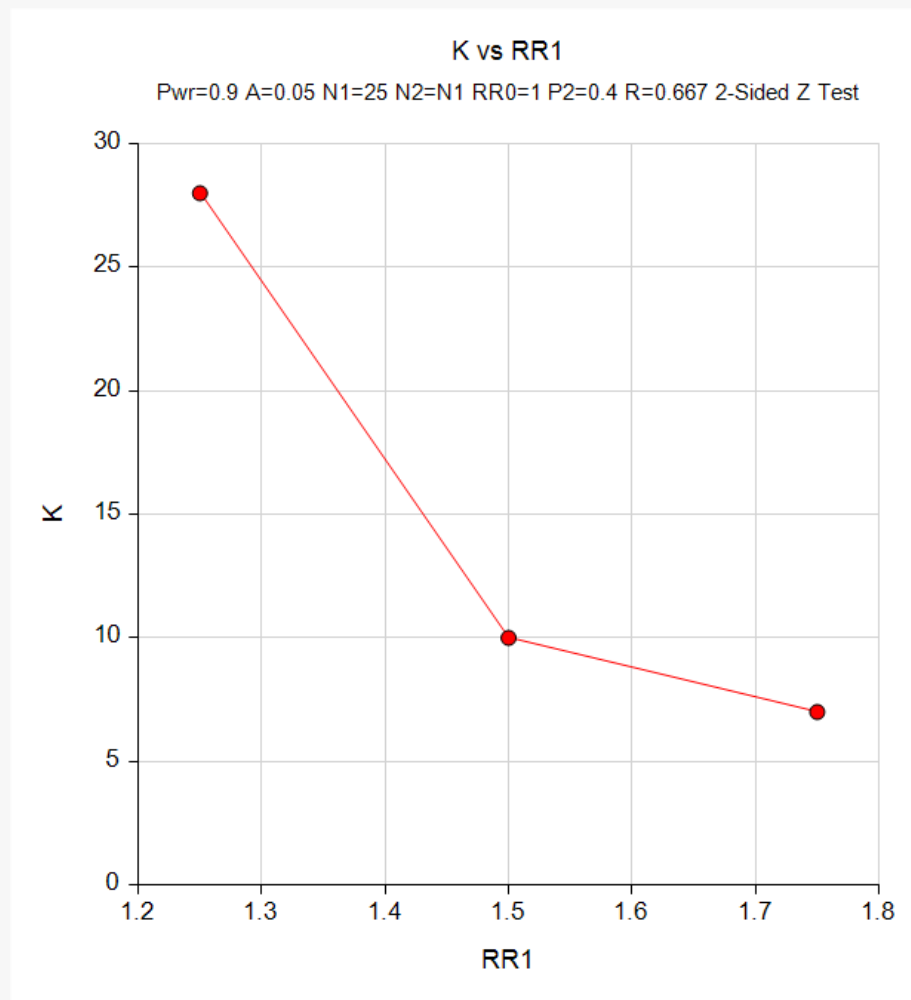
Hedges, L.V. and Pigott, T.D. 2001. 'The Power of Statistical Tests in Meta-Analysis', Psychological Methods, Volume 6, No. 3, pages 203-217.

Valentine, J.C., Pigott, T.D., and Rothstein, H.R. 2010. 'How Many Studies Do You Need? A Primer on Statistical Power for Meta-Analysis', Journal of Education and Behavioral Statistics, Volume 35, No. 2, pages 215-247.

This report shows the sample sizes for the indicated scenarios.

Plots Section

Plots



This plot represents the required number of studies for various values of RR1.

Example 2 – Validation using Hand Calculations

We could not find a validation example for this procedure in the literature so we will validate the procedure using hand calculations.

Suppose a meta-analysis using the risk ratio is contemplated with the following characteristics: two-group, equal-allocation trials, two-sided significance level of 0.05, $K = 10$, average group size of all studies is 10, $P_2 = 0.5$, $R = 1$, $RR_1 = 1.5$, and $RR_0 = 1.0$. Calculate the power.

Step 1: Compute the value of P_1 .

$$P_1 = (RR_1)(P_2) = 1.5(0.5) = 0.75$$

Step 2: Compute the average cell counts.

$$a = (P_1)(N_1) = 0.75(10) = 7.5$$

$$b = (P_2)(N_2) = 0.5(10) = 5$$

$$c = (1 - P_1)(N_1) = 0.25(10) = 2.5$$

$$d = (1 - P_2)(N_2) = 0.5(10) = 5$$

Step 3: Compute the effect size.

$$\log(RR_1) = \log(1.5) = 0.4054651$$

Step 4: Compute the within-study variance component.

$$V_W = \frac{1}{a} + \frac{1}{c} - \frac{1}{a+b} - \frac{1}{c+d} = \frac{1}{7.5} + \frac{1}{2.5} - \frac{1}{7.5+5} - \frac{1}{2.5+5} = 0.3200000$$

Step 5: Compute the between-study variance component.

$$V_B = R(V_W) = 0.3200000$$

Step 6: Compute the standard error of the effect size.

$$SE_{\log RR} = \sqrt{\frac{V_W + V_B}{K}} = \sqrt{\frac{0.3200000 + 0.3200000}{10}} = 0.2529822$$

Step 7: Compute λ .

$$\lambda = \frac{\log(RR) - \log(OR)}{SE_{\log RR}} = \frac{0.4054651 - 0}{0.2529822} = 1.6027415$$

Step 8: Compute $c_{\alpha/2}$.

$$c_{\alpha/2} = \Phi(1 - 0.025) = 1.95996398$$

Step 9: Compute the power.

$$\begin{aligned}
 \text{Power} &= 1 - \Phi(c_{\alpha/2} - \lambda) + \Phi(-c_{\alpha/2} - \lambda) \\
 &= 1 - \Phi(1.95996398 - 1.6027415) + \Phi(-1.95996398 - 1.6027415) \\
 &= 1 - \Phi(0.3572224) + \Phi(-3.5627055) \\
 &= 1 - 0.63953734 + 0.000183526 \\
 &= 0.3606462
 \end{aligned}$$

Setup

If the procedure window is not already open, use the PASS Home window to open it. The parameters 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.

Design Tab

Solve For **Power**

Alternative Hypothesis **Two-Sided (H1: RR ≠ RR0)**

Alpha..... **0.05**

K (Number of Studies) **10**

N1 (Average Sample Size of Group 1)..... **10**

N2 (Average Sample Size of Group 2)..... **N1**

RR0 (Risk Ratio|H0) **1.0**

RR1 (Risk Ratio|H1) **1.5**

P2 (Group 2 Proportion)..... **0.5**

Calculate Between-Study Variance From **R (Between-Study Var / Within-Study Var)**

R (Between-Study Var / Within-Study Var) **1**

Output

Click the Calculate button to perform the calculations and generate the following output.

Numeric Results

Solve For: Power

Hypotheses: H0: RR = RR0 vs. H1: RR ≠ RR0

Between-Study Variance Input: R (Between-Study / Within-Study Variances)

Power	Average Sample Size Per Study			Number of		Risk Ratio		Proportion			Between-Study Variance Calculation		
	Group 1 N1	Group 2 N2	Total N	Studies K	Subjects KN	RR H0 RR0	RR H1 RR1	P1 H0 P1.0	P1 H1 P1.1	Control P2	R	I ²	Alpha
0.36065	10	10	20	10	200	1	1.5	0.5	0.75	0.5	1	0.5	0.05

PASS also calculates a power of 0.36065 which validates the procedure.