Chapter 639

Meta-Analysis of Tests for Paired Means using a Random-Effects Model

Introduction

This procedure calculates power and number of studies for random-effects meta-analyses of paired-response studies (e.g., pre-post designs) that are summarized by the difference in paired means. The sample size formulas used by this procedure were published in Hedges and Pigott (2001) and Cooper *et al.* (2019).

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 measurement paired-variable means whose difference 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 mean. 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 Difference of Paired Means

The sample size formulas used by this procedure were published in Hedges and Pigott (2001) and Cooper *et al.* (2019).

A series of *K* studies are assumed to each have an effect size δ which is the standardized difference between paired means. The results of these individual studies may be combined into one overall statistical test that draws a more precise conclusion.

Test Statistic

Suppose the ith study yields a sample size of *N* as well as a *standardized paired-mean difference d_i* which is calculated as

$$d_i = \frac{\bar{X}_{1i} - \bar{X}_{2i}}{S_{Within_i}}$$

where

$$S_{Within_i} = \frac{S_{Difference_i}}{\sqrt{2(1-r)}}$$

$S_{Difference_i}$ is the estimated standard deviation of the *N* differences between the paired response variables in the study.

The variance of d_i is given by

$$V_d = \left(\frac{1}{N} + \frac{d^2}{2N}\right) 2(1-r)$$

where *r* is the correlation between the paired variables X_1 and X_2.

Using a random-effects model, these results may be summarized and tested using the statistic

$$Z = \frac{\bar{d} - \delta_0}{S_{\bar{D}}}$$

where $\bar{D}$ is a weighted average of the individual d_i and $S_{\bar{D}}$ is a weighted estimate of its standard deviation that includes an estimate of the between-study variation.

We assume that Z follows the standard normal distribution and so it can be used to test the null hypothesis $H_0: \delta = \delta_0$ at significance level of α.

Hypotheses

Three statistical hypotheses commonly used are

$$H_0: \delta \leq \delta_0 \quad \text{vs.} \quad H_1: \delta > \delta_0$$

$$H_0: \delta \geq \delta_0 \quad \text{vs.} \quad H_1: \delta < \delta_0$$

$$H_0: \delta = \delta_0 \quad \text{vs.} \quad H_1: \delta \neq \delta_0$$

Power Calculation

The power of a one-tailed test that $\delta = \delta_0$ is given by

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

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

$$\lambda = \frac{\delta - \delta_0}{\sqrt{V_{\bar{d}}}}$$

$$V_F = \left(\frac{1}{N} + \frac{\delta^2}{2N}\right)2(1 - r)$$

$$V_{\bar{d}} = \frac{1}{K}(V_F + RV_F)$$

Here V_F represents the within-study variance and R is the heterogeneity ratio. This ratio allows us to specify the between-study variance, V_B, as a multiple of V_F. 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. Setting R to 0 results in the fixed-effects result.

The power of a two-tailed test that $\delta = \delta_0$ 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.

I² - Heterogeneity Index

Some authors state the amount of heterogeneity in the study using the heterogeneity index I^2 (also called the *degree of heterogeneity* or *inconsistency*) instead of R. This value is related to R using the relationship

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

Example 1 – Calculating Sample Size

Researchers wish to determine a reasonable number of studies for a meta-analysis with the following characteristics: pre-post design, two-sided significance level of 0.05 and a power of 0.9, average sample size of all studies is 25, $\delta_1 = 0.2, 0.3, 0.4$, and $\delta_0 = 0.0$. The value of R is set to 0.667. The correlation between the pre and post variables is assumed to be 0.3.

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: δ ≠ δ0)**
Power..	**0.90**
Alpha..	**0.05**
N (Average Sample Size Per Study)............................	**25**
δ0 (Standardized Mean of Paired Differences|H0).........	**0.0**
δ1 (Standardized Mean of Paired Differences|H1).........	**0.2 0.3 0.4**
ρ (Correlation of the Observed Variables)	**0.3**
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: δ = δ0   vs.   H1: δ ≠ δ0
Between-Study Variance Input: R (Between-Study / Within-Study Variances)

Power		Average Sample Size Per Study	Number of		Standardized Mean of Paired Differences		Correlation of Paired Variables	Between-Study Variance Calculation		
Target	Actual	N	Studies K	Subjects KN	δ|H0 δ0	δ|H1 δ1	ρ	R	I²	Alpha
0.9	0.91067	25	26	650	0	0.2	0.3	0.667	0.40012	0.05
0.9	0.91424	25	12	300	0	0.3	0.3	0.667	0.40012	0.05
0.9	0.91513	25	7	175	0	0.4	0.3	0.667	0.40012	0.05

Target Power   The power desired. Power is the probability of rejecting a false null hypothesis.
Actual Power   The power actually achieved. Power is the probability of rejecting a false null hypothesis about the
                 standardized paired mean difference (SPMD). This is the power calculated at the actual SPMD.
N   The average sample size per study 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.
δ0   The value of the standardized paired-mean difference (SPMD) assumed by the null hypothesis. Note that δ =
                 [(µ1 - µ2) / σw] where σw is the within-subject standard deviation.
δ1   The value of the SPMD assumed by the alternative hypothesis, H1. This is the value of δ at which the power
                 is calculated.
ρ   The correlation coefficient between the paired observations on the same subject.
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 paired studies will be used to test whether the Group 1 mean is different from the Group 2 mean
(H0: δ = 0 versus H1: δ ≠ 0, δ = [µ1 - µ2] / σw). 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 heterogeneity ratio used to create the
between-study variance is assumed to be 0.667. The correlation between paired observations is assumed to be
0.3. With an average study sample size of 25 pairs, to detect a standardized mean of paired differences (δ) of 0.2
with 90% power, the number of needed studies will be 26.

References
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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.
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This report shows the number of studies needed for the indicated scenarios.

Plots Section

Plots
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K vs $\delta 1$

Pwr=0.9 A=0.05 N=25 $\delta 0$=0 ρ=0.3 R=0.667 2-Sided Z Test
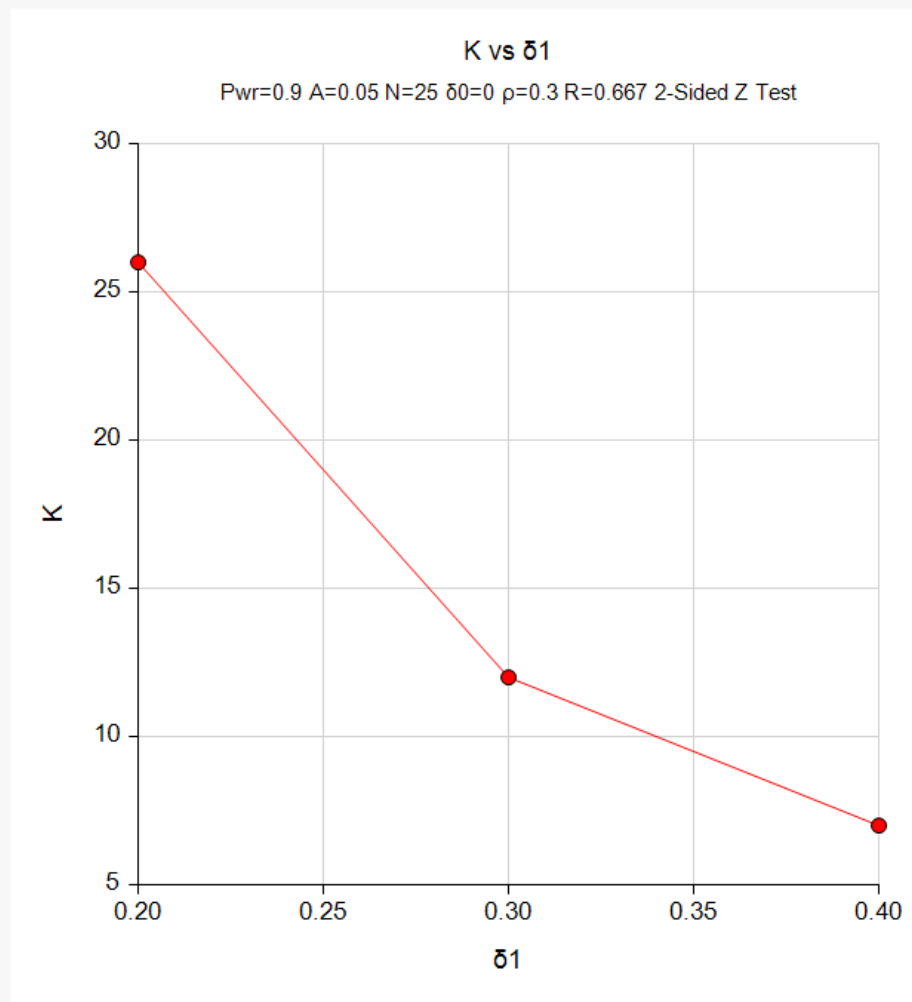
This plot shows the number of studies needed for the indicated scenarios.

Example 2 – Validation using Hand Calculations

Hedges and Pigott (2001) page 213 present an example of solving for power with a two-group, two-sided significance level of 0.05, average group sizes of 12 and 36 in groups 1 and 2, $\delta_1 = 0.2$, and $\delta_0 = 0.0$. The value of R is set to 0.333. The computed power is 0.4647.

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 is contemplated with the following characteristics: pre-post design, two-sided significance level of 0.05, K = 10, average sample size of all studies is 25, $\delta_1 = 0.2$, and $\delta_0 = 0.0$. The correlation between the pre and post variables is assumed to be 0.3. The value of R is set to 1.0.

Step 1: Compute the within-study variance.

$$V_F = \left(\frac{1}{N} + \frac{\delta^2}{2N}\right)2(1-r) = \left(\frac{1}{25} + \frac{0.2^2}{50}\right)2(1-0.3) = (0.04 + 0.0008)1.4 = 0.057120$$

Step 2: Compute the standard error of the effect size.

$$SE_d = \sqrt{\frac{V_F + RV_F}{K}} = \sqrt{\frac{0.057120 + 0.057120}{10}} = 0.1068831$$

Step 3: Compute λ.

$$\lambda = \frac{\delta_1 - \delta_0}{SE_d} = \frac{0.2 - 0}{0.1068831} = 1.871203$$

Step 4: Compute $c_{\alpha/2}$.

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

Step 5: Compute the power.

$$
\begin{aligned}
Power &= 1 - \Phi\big(c_{\alpha/2} - \lambda\big) + \Phi\big(-c_{\alpha/2} - \lambda\big) \\
&= 1 - \Phi(1.95996398 - 1.871203) + \Phi(-1.95996398 - 1.871203) \\
&= 1 - \Phi(0.0887610) + \Phi(-3.831167) \\
&= 1 - 0.5353640788 + 0.00006378 \\
&= 0.4646997
\end{aligned}
$$

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: δ ≠ δ0)**

Alpha..**0.05**

K (Number of Studies) **10**

N (Average Sample Size Per Study)..............**25**

δ0 (Standardized Mean of Paired Differences|H0).........**0.0**

δ1 (Standardized Mean of Paired Differences|H1).........**0.2**

ρ (Correlation of the Observed Variables) **0.3**

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
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Solve For: Power
Hypotheses: H0: δ = δ0   vs.   H1: δ ≠ δ0
Between-Study Variance Input: R (Between-Study / Within-Study Variances)
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Power	Average Sample Size Per Study N	Number of Studies K	Number of Subjects KN	δ|H0 δ0	δ|H1 δ1	Correlation of Paired Variables ρ	R	I²	Alpha
0.4647	25	10	250	0	0.2	0.3	1	0.5	0.05
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PASS also calculates a power that rounds to 0.4647 which validates the procedure.