

Chapter 158

Tests for the Matched-Pair Difference of Two Proportions in a Cluster-Randomized Design

Introduction

Cluster-randomized designs are those in which whole clusters of subjects (classes, hospitals, communities, etc.) are sampled, rather than individual subjects. This sample size and power procedure is used for the case where the subject responses are binary (proportion outcome). To reduce the variation (and thus increase power), clusters are matched, with one cluster of each pair assigned to the control group, and the other assigned the treatment group. This procedure gives the number of pairs needed for the desired power requirement.

The formulas used here are based on Hayes and Bennett (1999) and Hayes and Moulton (2009). The methods are discussed in Donner and Klar (2000) and briefly in Campbell and Walters (2014).

Technical Details

Definition of Terms

The following table presents the various terms that are used.

Group	1 (Control)	2 (Treatment)
Sample size:	K	K
Proportions:	P_1	P_2

Coefficient of Variation: CV_M (within-pair coefficient of variation between clusters in the absence of intervention)

Number of cluster pairs: K ($2K$ is the total number of clusters)

Cluster size: M (Average number of individuals per cluster)

Hypotheses

The null and alternative hypotheses are

$$H_0: P_{Diff} = 0 \quad \text{vs.} \quad H_1: P_{Diff} \neq 0$$

Corresponding one-sided hypotheses may also be used. These hypotheses may be tested based on an appropriate paired difference test.

Sample Size and Power Calculations

Sample Size Calculation

The sample size calculation for the number of cluster pairs, as given in Hayes and Bennett (1999) and Hayes and Moulton (2009), is

$$K = 2 + (z_{\alpha/2} + z_{\beta})^2 \frac{P_1(1 - P_1)/M + P_2(1 - P_2)/M + CV_M^2(P_1^2 + P_2^2)}{(P_1 - P_2)^2}$$

Estimating CV_M

Hayes and Bennett (1999) suggest that CV_M may be estimated based on the following, if prior data is available:

Let P_{ij} represent the true proportion in the j^{th} cluster ($j = 1, 2$) of the i^{th} pair ($i = 1, \dots, M$) and p_{ij} represent the corresponding observed proportion. If the empirical variance of the i^{th} pair is called s_i^2 then define

$$s_m^2 = \sum s_i^2 / M$$

as the average of the within-pair variances.

CV_M may be estimated from

$$CV_M^2 = \frac{s_m^2 - Av(p_i(1 - p_i)/n_{ij})}{Av(p_i^2)}$$

where n_{ij} is the number of individuals in the i^{th} pair of the j^{th} cluster, and $Av()$ indicates the mean over all M clusters.

According to Hayes and Bennett (1999), "If only unmatched data are available, a conservative approach is to use [the coefficient of variation (SD/Mean) between clusters within each group] as an upper limit for CV_M ."

If no data is available, a series of plausible values, usually between 0 and 0.5, should be considered.

Power Calculation

The corresponding power calculation to the sample size calculation above is

$$Power = 1 - \Phi \left(\sqrt{\frac{(K - 2)(P_1 - P_2)^2}{P_1(1 - P_1)/M + P_2(1 - P_2)/M + CV_M^2(P_1^2 + P_2^2)}} - z_{\alpha/2} \right)$$

where $z_x = \Phi(x)$ is the standard normal distribution function.

Procedure Options

This section describes the options that are specific to this procedure. These are located on the Design tab. For more information about the options of other tabs, go to the Procedure Window chapter.

Design Tab

The Design tab contains most of the parameters and options that you will be concerned with.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. The parameters that may be selected are *Power*, *K*, *M*, and *P2*.

Under most situations, you will select either *Power* to calculate power or *K* to calculate the number of cluster pairs. Occasionally, you may want to fix the number of clusters and find the necessary cluster size.

The value selected here always appears as the vertical axis on the charts (when applicable).

When searching for *M*, some scenarios with small *K*'s are not feasible.

Test

Alternative Hypothesis

Specify whether the test is one-sided or two-sided. The one-sided option specifies a one-tailed test.

Power and Alpha

Power

This option specifies one or more values for power. Power is the probability of rejecting a false null hypothesis, and is equal to one minus beta. Beta is the probability of a type-II error, which occurs when a false null hypothesis is not rejected.

Values must be between zero and one. Historically, the value of 0.80 (beta = 0.20) was used for power. Now, 0.90 (beta = 0.10) is commonly used.

A single value may be entered or a range of values, such as *0.8 to 0.95 by 0.05*, may be entered.

Alpha

This option specifies one or more values for the probability of a type-I error. A type-I error occurs when a true null hypothesis is rejected.

Values must be between zero and one. Usually, the value of 0.05 is used for two-sided tests and 0.025 is used for one-sided tests.

You may enter a range of values such as *0.01 0.05 0.10* or *0.01 to 0.10 by 0.01*.

Sample Size – Number of Clusters & Cluster Size

K (Number of Cluster Pairs)

This is the number of cluster pairs. Each cluster pair consists of two clusters that are matched or paired based on one or more criteria. The total sample size is equal to the number of clusters times the cluster size. This value

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must be a positive number. You can enter a single value such as 20 or a series of values such as 10 20 30 or 10 to 30 by 5.

M (Cluster Size)

This is the average number of individuals or items per cluster. This value must be a positive number that is at least 1. It can be a decimal (fractional) number such as 20.7. You can enter a single value such as 50 or a series of values such as 40 50 60 or 40 to 60 by 5.

Effect Size

P1 (Proportion for Group 1)

Enter a value (or range of values) for the group 1 (control group) proportion. The value must be between zero and one. You can enter a single value such as 0.6 or a series of values such as 0.5 0.6 0.7 or 0.5 to 0.7 by 0.05.

Enter P2, Diff, or Ratio for Group 2

This option lets you indicate how P2 is entered. The options are

- **P2 (Proportion for Group 2)**
Enter the value of P2 directly.
- **Diff (Difference Between Proportions)**
Enter values for the difference between the proportions ($\text{Diff} = P2 - P1$). The value of P2 is equal to $P1 + \text{Diff}$.
- **Ratio (Ratio of Proportions)**
Enter values for the ratio of the proportions ($\text{Ratio} = P2 / P1$). The value of P2 is equal to $P1 * \text{Ratio}$. Note that the hypothesis still concerns the difference. This is just a convenient way of specifying a value.

P2 (Proportion for Group 2)

This option is displayed only if Enter P2, Diff, or Ratio for Group 2 = "P2 (Proportion of Group 2)."

Enter a value (or range of values) for the mean proportion in group 2 (treatment group). The value must be between zero and one and different from P1. You can enter a single value such as 0.6 or a series of values such as 0.5 0.6 0.7 or 0.5 to 0.7 by 0.05.

Diff (Difference Between Proportions)

This option is displayed only if Enter P2, Diff, or Ratio for Group 2 = "Diff (Difference Between Proportions)."

Enter values for the difference between the proportions ($\text{Diff} = P2 - P1$). The value of P2 is equal to $P1 + \text{Diff}$. The range is any positive or negative value other than 0 ($\text{Diff} \neq 0$), such that P2 is between zero and one. You can enter a single value such as 0.5 or a series of values such as 0.5 0.6 0.7 or 0.5 to 0.7 by 0.05.

Ratio (Ratio of Proportions)

This option is displayed only if Enter P2, Diff, or Ratio for Group 2 = "Ratio (Ratio of Proportions)."

Enter values for the ratio of the proportions ($\text{Ratio} = P2 / P1$) at which the power is to be calculated. The value of P2 is calculated using $P1 * \text{Ratio}$. The range is $\text{Ratio} > 0$, such that P2 is between zero and one, and $\text{Ratio} \neq 1$. Typically, Ratio is between 0.5 and 2.0. You can enter a single value such as 1.15 or a series of values such as 1.05 1.10 1.15 1.20 or 1.05 to 1.20 by 0.05.

CVM (Within-Pair Coefficient of Variation)

Enter a value or values for the within-pair coefficient of variation (SD/Mean) between clusters in the absence of intervention. See the documentation or references for suggestions for estimating CVM. If prior information is not available, Hayes and Bennett (1999) suggest that CVM is usually less than 0.25 and seldom greater than 0.50. You can enter a single value such as 0.15 or a series of values such as 0.05 0.10 0.15 0.20 or 0.05 to 0.30 by 0.05.

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Example 1 – Calculating Sample Size

One difficulty in calculating sample size for a matched-pair difference of two proportions in a cluster-randomized design is obtaining a value for CV_M , the within-pair coefficient of variation between clusters. This example shows how to enter a range of values to determine the effect of CV_M on sample size. Suppose that a cluster randomized study is to be conducted in which the control proportion is assumed to be $P_1 = 0.70$, and the treatment proportion is $P_2 = 0.58$. Each cluster is assumed to have about 70 individuals. A range of values between 0.05 and 0.5 for CV_M will be examined. The desired power and alpha are 0.9 and 0.05, respectively. The test will be a two-sided test.

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Tests for the Matched-Pair Difference of Two Proportions in a Cluster-Randomized Design** procedure window. You may then make the appropriate entries as listed below, or open **Example 1** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	K (Number of Cluster Pairs)
Alternative Hypothesis	Two-Sided
Power	0.90
Alpha	0.05
M (Cluster Size)	80
P1 (Proportion for Group 1)	0.80
Enter P2, Diff, or Ratio for Group 2	P2 (Proportion for Group 2)
P2 (Proportion for Group 2)	0.58
CVM (Within-Pair Coefficient of Variation)	0.05 to 0.50 by 0.05

Annotated Output

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

Numeric Results

Numeric Results for a Two-Sided Test of Matched-Pair Proportion Difference in a Cluster-Randomized Design

Group 1 = Control. Group 2 = Treatment.

Power	Number of Pairs K	Total Number of Clusters 2K	Cluster Size M	Total Size N = 2KM	Prop. Gr 1 P1	Prop. Gr 2 P2	Prop. Diff. P2 - P1	Prop. Ratio P2 / P1	Coefficient of Variation CVM	Two-Sided Alpha
0.9491	4	8	80	640	0.8000	0.5800	-0.2200	0.73	0.050	0.050
0.9511	6	12	80	960	0.8000	0.5800	-0.2200	0.73	0.100	0.050
0.9064	8	16	80	1280	0.8000	0.5800	-0.2200	0.73	0.150	0.050
0.9119	12	24	80	1920	0.8000	0.5800	-0.2200	0.73	0.200	0.050
0.9123	17	34	80	2720	0.8000	0.5800	-0.2200	0.73	0.250	0.050
0.9111	23	46	80	3680	0.8000	0.5800	-0.2200	0.73	0.300	0.050
0.9094	30	60	80	4800	0.8000	0.5800	-0.2200	0.73	0.350	0.050
0.9078	38	76	80	6080	0.8000	0.5800	-0.2200	0.73	0.400	0.050
0.9062	47	94	80	7520	0.8000	0.5800	-0.2200	0.73	0.450	0.050
0.9047	57	114	80	9120	0.8000	0.5800	-0.2200	0.73	0.500	0.050

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References

- Hayes, R.J. and Bennett, S. 1999. 'Simple sample size calculation for cluster-randomized trials'. International Journal of Epidemiology. Vol 28, pages 319-326.
- Hayes, R.J. and Moulton, L.H. 2009. Cluster Randomised Trials. CRC Press. New York.
- Campbell, M.J. and Walters, S.J. 2014. How to Design, Analyse and Report Cluster Randomised Trials in Medicine and Health Related Research. Wiley. New York.

Report Definitions

Power is the probability of rejecting a false null hypothesis. It should be close to one.

K represents the number of cluster pairs needed in the design.

2K is the total number of clusters in the design, 2 clusters per pair.

M is the average number of individuals or items in each cluster.

N is the total number of individuals or items in the design. $N = 2KM$.

P1 is the proportion for the control group. This is the baseline proportion.

P2 is the proportion for the treatment group.

$P2 - P1$ is the difference between the treatment proportion and the control proportion.

$P2 / P1$ is the ratio of the treatment proportion to the control proportion.

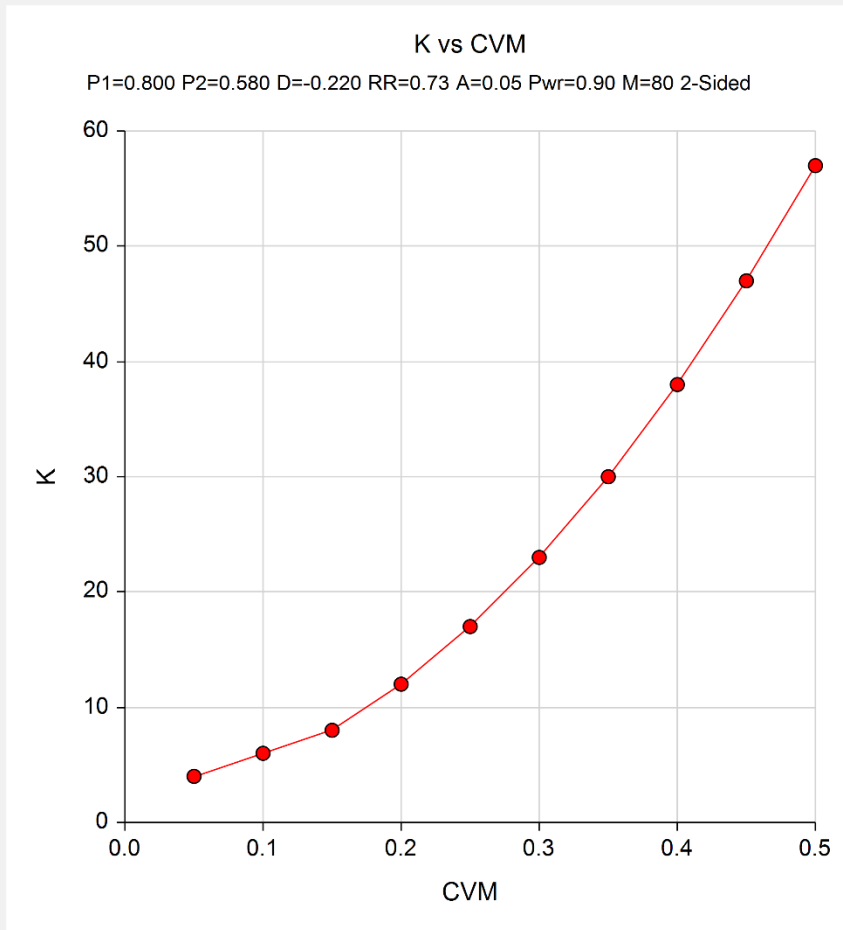
CVM is the within-pair coefficient of variation between clusters in the absence of intervention. See the documentation or references for suggestions for estimating CVM.

Alpha is the probability of rejecting a true null hypothesis, that is, rejecting H_0 when the proportions are actually equal.

Summary Statements

A sample of 4 cluster pairs (8 clusters) with 80 individuals per cluster achieves 95% power to detect a difference of -0.2200 between the treatment proportion 0.5800 and the control proportion 0.8000. The within-pair coefficient of variation between clusters is 0.050. A two-sided paired test of the proportion difference is assumed, with a significance level of 0.050.

Chart Section



This report shows the needed number of cluster pairs for each of the coefficient of variation values.

Example 2 – Validation using Hayes and Moulton (2009)

Hayes and Bennett (1999) and Hayes and Moulton (2009) give an example of calculating the required number of cluster pairs for a two-sided matched-pair difference of proportions in a cluster-randomized design. The group 1 proportion was 0.02 and the group 2 proportion was 0.01. The cluster size was 1,000 adults per cluster. A CV_M value of 0.25 was used. The power and alpha were 80% and 0.05, respectively.

The calculated number of cluster pairs needed is 6.8 (or 7 with proper rounding).

Setup

This section presents the values of each of the parameters needed to run this example. First, from the PASS Home window, load the **Tests for the Matched-Pair Difference of Two Proportions in a Cluster-Randomized Design** procedure window. You may then make the appropriate entries as listed below, or open **Example 2** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	K (Number of Cluster Pairs)
Alternative Hypothesis	Two-Sided
Power	0.80
Alpha	0.05
M (Cluster Size)	1000
P1 (Proportion for Group 1)	0.02
Enter P2, Diff, or Ratio for Group 2	P2 (Proportion for Group 2)
P2 (Proportion for Group 2)	0.01
CVM (Within-Pair Coefficient of Variation)	0.25

Output

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

Numeric Results

Numeric Results for a Two-Sided Test of Matched-Pair Proportion Difference in a Cluster-Randomized Design

Group 1 = Control. Group 2 = Treatment.

	Number of Cluster Pairs	Total Number of Clusters	Cluster Size M	Total Size N = 2KM	Prop. Gr 1 P1	Prop. Gr 2 P2	Prop. Diff. P2 - P1	Prop. Ratio P2 / P1	Coeffi- cient of Variation CVM	Two- Sided Alpha
Power	K	2K	M	N = 2KM	P1	P2	P2 - P1	P2 / P1	CVM	Two-Sided Alpha
0.8183	7	14	1000	14000	0.0200	0.0100	-0.0100	0.50	0.250	0.050

PASS calculates the number of cluster pairs needed to be 7, which matches the rounded-up calculation value of Hayes and Moulton (2009).