

Chapter 150

Tests for Two Correlated Proportions (McNemar Test)

Introduction

McNemar's test compares the proportions for two correlated dichotomous variables. These two variables may be two responses on a single individual or two responses from a matched pair (as in matched case-control studies).

This procedure is similar to the Matched Case-Control procedure also available in **PASS**. It differs from that procedure in three basic ways:

1. The results may be calculated exactly by binomial enumeration using an unconditional formula rather than using conditional, normal approximations to the binomial.
2. It only deals with the case of a matched pair: one case and one control (the Matched Case-Control procedure lets you match several controls with each case).
3. It is based directly on the 2-by-2 contingency table.

To fix these ideas, consider the following fictitious data concerning the relationship between smoking and lung cancer. Suppose that a sample of $N = 100$ cases of identical twins in which only one twin has lung cancer is selected for further study. The twin with lung cancer is the *case*. The other twin serves as the *control*. Each pair of twins is surveyed to determine if they smoke tobacco. The results are summarized in the following two-way table:

	<u>No Lung Cancer Twin (Control)</u>	
<u>Lung Cancer Twin (Case)</u>	<u>Smokes = Yes</u>	<u>Smokes = No</u>
Smokes = Yes	16	21
Smokes = No	4	59

There is a basic difference between this table and the more common two-way table. In the matched-paired case, the count represents the number of pairs, not the number of individuals.

The investigator wishes to compare the proportion of cases that smoke with the proportion of controls that smoke. The proportion of controls who smoke is $(16+21)/100 = 0.20$. The proportion of cases who smoke is $(16+21)/100 = 0.37$.

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Dividing each of the entries in the table by N gives the proportions:

		<u>No Lung Cancer Twin (Control)</u>		
<u>Lung Cancer Twin (Case)</u>	<u>Smokes = Yes</u>	<u>Smokes = No</u>	<u>Total</u>	
<u>Smokes = Yes</u>	0.16	0.21	0.37	
<u>Smokes = No</u>	0.04	0.59	0.63	
<u>Total</u>	0.20	0.80	0.63	

Symbolically, this table is represented as:

		<u>No Lung Cancer Twin (Control)</u>		
<u>Lung Cancer Twin (Case)</u>	<u>Smokes = Yes</u>	<u>Smokes = No</u>	<u>Total</u>	
<u>Smokes = Yes</u>	P_{11}	P_{10}	P_t	
<u>Smokes = No</u>	P_{01}	P_{00}	$1 - P_t$	
<u>Total</u>	P_s	$1 - P_s$	1	

Formally, the hypothesis of interest is that P_t equals P_s . A little algebra shows that $P_t = P_s$ is equivalent to $P_{10} = P_{01}$, since P_{11} is common to both. Thus, the null hypothesis of McNemar's test is $P_{10} = P_{01}$ and the alternative is that they are unequal. The alternative hypothesis may be one-sided (such as $P_{10} > P_{01}$) or two-sided ($P_{10} \neq P_{01}$).

The null hypothesis may also be stated in terms of the odds ratio as $OR = 1$. The odds ratio is computed differently in the matched pairs case. The formula is:

$$OR = \frac{P_{10}}{P_{01}}$$

Notice that the values of P_{11} and P_{00} are not used in these hypotheses. It turns out that their individual values are not needed, but their sum is.

For this example, the odds ratio is computed as $21/4 = 5.25$.

Technical Details

Consider the matched-pairs table again:

		<u>Controls</u>		
<u>Cases</u>	<u>Yes</u>	<u>No</u>	<u>Total</u>	
<u>Yes</u>	P_{11}	P_{10}	P_t	
<u>No</u>	P_{01}	P_{00}	$1 - P_t$	
<u>Total</u>	P_s	$1 - P_s$	1	

Pairs with the same response from cases and controls (Yes-Yes and No-No) are called *concordant* pairs. Pairs with different responses (Yes-No and No-Yes) are called *discordant* pairs. McNemar's test statistic is the estimated odds ratio:

$$Mc = \frac{P_{10}}{P_{01}}$$

The sample size problem thus reduces to a study of how many Yes-No's and No-Yes's are needed. Once this has been determined, the overall sample size is found by estimating the proportion of discordant pairs and inflating the sample size appropriately.

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Some power analysis programs follow an approximate procedure. Since the McNemar statistic follows the binomial probability distribution for a fixed number of discordant pairs, they use formulas that use the normal approximation to the binomial and then adjust the sample size depending on the proportion of discordant pairs, $PD=P10+P01$. This is called the conditional procedure.

One such approximate formula is given by Machin, Campbell, Fayers, and Pinol (1997).

$$N_{pairs} = \frac{\left\{ z_{1-\alpha/s}(OR+1) + z_{1-\beta} \sqrt{(OR+1)^2 - (OR-1)^2 PD} \right\}^2}{(OR-1)^2 PD}$$

where s is the number of sides to the test (one or two), $OR = \frac{P10}{P01}$, $PD = P10 + P01$, and alpha and beta are the usual error rate probabilities.

However, Schork and Williams (1980) published a formula which provides the exact results for the unconditional case using binomial enumeration of all possible outcomes. This formulation is also available in **PASS**.

$$Power = \sum_{R=r}^N \sum_{n_{12}=0}^{IR} \frac{N!}{(N-R)!n_{12}!(R-n_{12})!} (1-PD)^{N-R} \left(\frac{D+PD}{2} \right)^{n_{12}} \left(\frac{PD-D}{2} \right)^{R-n_{12}}$$

where

$$PD = P10+P01$$

$$D = P10-P01$$

N is total of all four cells ($N11+N12+N21+N22$)

r is the smallest integer for which $\left(\frac{1}{2}\right)^r \leq \alpha$

IR is the largest integer such that $\sum_{j=0}^{IR} \binom{R}{j} \left(\frac{1}{2}\right)^R \leq \alpha$

Difference or Odds Ratio

The formula given above is parameterized in terms of the difference. This formula is also used when odds ratios are specified. The program simply converts the OR value into its corresponding D value.

Discussion

The binomial enumeration (exact) algorithm works for $N < 2000$. Above 2000, computing time goes up and the algorithm has numerical problems. **PASS** lets you select either the binomial enumeration (exact), or the approximate, solutions. We have found that the approximate solution tends to use a sample size that is about 10% less than the exact solution.

Because of the lengthy computer time necessary to compute the exact answer when $N > 1500$, we suggest that you use the approximate formula to begin with and then revert to the exact formula when you are ready for your final results.

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 the parameters associated with this test such as the proportions, sample sizes, alpha, and beta. This chapter covers two procedures, which have different options. This section documents options that are common to both procedures. Later, unique options for each procedure will be documented.

Solve For

Solve For

This option specifies the parameter to be solved for from the other parameters. The parameters that may be selected are *Odds Ratio*, *Difference*, *Sample Size*, *Alpha*, and *Power*. Under most situations, you will select either *Power* or *Sample Size*.

The program is set up to evaluate power directly. For the other parameters, a search is made using an iterative procedure until an appropriate value is found. Two solutions can often be found when searching for the *Odds Ratio* or the *Difference*. You may specify the region in which you want the solution to be searched for. For example, you may search for an odds ratio either above or below one. Also note that the parameter selected must match the procedure you are using. For example, if you are searching for the odds ratio, you must be in the odds ratio window.

Note that the value selected here always appears as the vertical axis on the charts.

Power Calculation

Power Calculation Method

Select the method to be used to calculate power.

The choices are

- **Binomial Enumeration**

Power is computed using binomial enumeration of all possible outcomes when $N \leq \text{Max } N$ for Binomial Enumeration (otherwise, the normal approximation is used). Binomial enumeration of all outcomes is possible because of the discrete nature of the data.

- **Normal Approximation**

Approximate power is computed using the normal approximation to the binomial distribution.

The binomial enumeration formulas require lengthy calculations for large values of N and may be very time consuming. They should not be used for $N > 2000$.

The approximate formulas tend to underestimate the N necessary to achieve a certain power value by about 10%, so they should only be used when the calculation time gets very prohibitive or when $N > 2000$.

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Max N for Binomial Enumeration

Only shown when Power Calculation Method = "Binomial Enumeration"

Below this value of N, power calculation formulas using binomial enumeration are used. Above this value of N, approximate formulas based on the normal approximation to the binomial are used.

The binomial enumeration formulas require lengthy calculations for large values of N and may be very time consuming. They should not be used for $N > 2000$.

The approximate formulas tend to underestimate the N necessary to achieve a certain power value by about 10%, so they should only be used when the calculation time gets very prohibitive or when $N > 2000$.

Test

Alternative Hypothesis

Specify whether the test is one-sided or two-sided. A one-sided hypothesis uses an inequality as in $P10 > P01$ or Odds Ratio > 1 . A two-sided hypothesis states that the proportions are not equal without specifying which is greater. If you do not have any special reason to do otherwise, you should use the two-sided option.

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 also commonly used.

If your only interest is in determining the appropriate sample size for a confidence interval, set power to 0.5.

Alpha

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

Sample Size

N (Number of Pairs)

Enter a value (or range of values) for the sample size, N , the number of pairs in the study.

You may enter a range of values such as *100,200,300* or *200 to 400 by 50*.

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Effect Size

Input Type

Indicate what type of values to enter to specify the effect size. Regardless of the entry type chosen, the calculations are the same. This option is simply given for convenience in specifying the effect size.

Difference (P10-P01)

Only shown when Input Type = "Differences"

The difference, $P10-P01$, is a popular parameter to specify because it comes directly from the alternative hypothesis that Pt not equal Ps . If Pt and Ps are not equal, the obvious question is, by how much? The answer is, by $P10-P01$ since $Pt-Ps = (P11+P10)-(P11+P01) = P10-P01$. Hence, this is a value that may easily be set.

The range of values is between -1 and 1. You may enter a list of value list $0.1, 0.15, 0.2$ or 0.05 to 0.20 by 0.05 .

Odds Ratio (P10/P01)

Only shown when Input Type = "Odds Ratios"

The odds ratio is a popular parameter to specify because of its simple interpretability and close relationship to the relative risk. An odds ratio of 2.0 means that the odds of the numerator variable is twice the odds of the denominator variable. Note that several values of $P10$ and $P01$ can yield the same odds ratio. For example, $0.2/0.1$ and $0.4/0.2$ both have an odds ratio of 2.0, but are based on very different values of $P10$ and $P01$. Under the null hypothesis, the odds ratio is one. Only positive values are allowed.

You may enter a list of values like $1.5, 2.0, 3.0$ or 1.2 to 2.4 by 0.2 .

Proportion Discordant (P10+P01)

This is the proportion of discordant pairs ($P10 + P01$). This value will be difficult to specify unless you have previous studies that give you some idea of what to expect. When you have no idea, Machin, Campbell, Fayers, and Pinol (1997) suggest the following strategy. Estimate values of Pt and Ps . Calculate the proportion of discordant pairs using the approximation

$$PD = Pt(1 - Ps) + Ps(1 - Pt)$$

This approximation assumes that the two responses are independent in each subject, which will usually not be true. However, it may be the only way of determining a ball park value for this parameter.

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Example 1 – Calculating Power using Odds Ratios

This example will show how to calculate the power of a retrospective study for several sample sizes and odds ratio values. Suppose that a matched case-control study is to be run in which the odds ratios might be 1.5, 2.5, or 3.5; PD is 0.3, $N = 50$ to 300 by 50; alpha is 0.05; and power is to be calculated.

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 Two Correlated Proportions (McNemar Test)** procedure window by expanding **Proportions**, then **Two Correlated Proportions**, then clicking on **Test (Inequality)**, and then clicking on **Tests for Two Correlated Proportions (McNemar Test)**. You may 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	Power
Power Calculation Method.....	Binomial Enumeration
Max N for Binomial Enumeration.....	1500
Alternative Hypothesis.....	Two-Sided
Alpha.....	0.05
N (Number of Pairs).....	50 to 200 by 50
Input Type.....	Odds Ratios
Odds Ratio (P10/P01).....	1.5 2.0 2.5
Proportion Discordant (P10+P01)	0.3

Annotated Output

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

Numeric Results**Numeric Results for a Two-Sided McNemar Test**

Power*	Pairs		P10	P01	Difference P10-P01	Odds Ratio P10/P01	Proportion Discordant P10+P01	Alpha
	N							
0.07467	50		0.180	0.120	0.060	1.500	0.300	0.050
0.14214	100		0.180	0.120	0.060	1.500	0.300	0.050
0.22451	150		0.180	0.120	0.060	1.500	0.300	0.050
0.29790	200		0.180	0.120	0.060	1.500	0.300	0.050
0.17849	50		0.200	0.100	0.100	2.000	0.300	0.050
0.37305	100		0.200	0.100	0.100	2.000	0.300	0.050
0.56457	150		0.200	0.100	0.100	2.000	0.300	0.050
0.70340	200		0.200	0.100	0.100	2.000	0.300	0.050
0.29601	50		0.214	0.086	0.129	2.500	0.300	0.050
0.59122	100		0.214	0.086	0.129	2.500	0.300	0.050
0.80105	150		0.214	0.086	0.129	2.500	0.300	0.050
0.90751	200		0.214	0.086	0.129	2.500	0.300	0.050

* Power was computed using binomial enumeration of all possible outcomes.

References

- Schork, M. and Williams, G. 1980. 'Number of Observations Required for the Comparison of Two Correlated Proportions.' Communications in Statistics-Simula. Computa., B9(4), 349-357.
- Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd Edition. Blackwell Science. Malden, MA.

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Report Definitions

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

N is the number of pairs in the sample.

P10 is the proportion of pairs in cell 1,2 of the 2x2 table.

P01 is the proportion of pairs in cell 2,1 of the 2x2 table.

Difference is the difference between proportions parameter under the alternative hypothesis.

Odds Ratio is the value of this parameter under the alternative hypothesis.

Proportion Discordant is the total of P10 and P01.

Alpha is the probability of rejecting a true null hypothesis. It should be small.

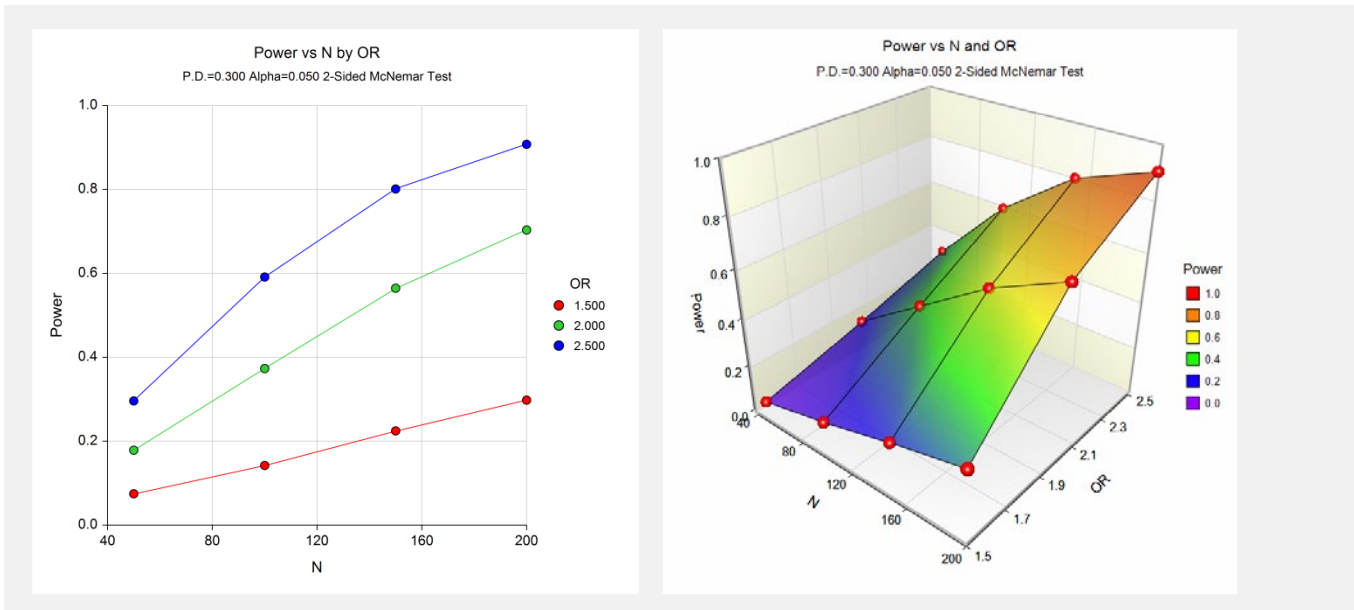
Beta is the probability of accepting a false null hypothesis. It should be small.

Summary Statements

A sample size of 50 pairs achieves 7.467% power to detect an odds ratio of 1.500 using a two-sided McNemar test with a significance level of 0.050. The odds ratio is equivalent to a difference between two paired proportions of 0.060 which occurs when the proportion in cell 1,2 is 0.180 and the proportion in cell 2,1 is 0.120. The proportion of discordant pairs is 0.300.

This report shows the power for each of the scenarios.

Plot Section



These plots show the power versus the sample size for the three odds ratios.

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Example 2 – Validation using Schork and Williams (1980)

Schork and Williams (1980) page 354 present a table of sample sizes for various combinations of the other parameters. When the difference is 0.2, the proportion discordant is 0.7, the power is 80%, and the one-sided significance level is 0.025, the sample size is 144.

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 Two Correlated Proportions (McNemar Test)** procedure window by expanding **Proportions**, then **Two Correlated Proportions**, then clicking on **Test (Inequality)**, and then clicking on **Tests for Two Correlated Proportions (McNemar Test)**. You may 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	Power
Power Calculation Method.....	Binomial Enumeration
Max N for Binomial Enumeration.....	1500
Alternative Hypothesis.....	One-Sided
Alpha.....	0.025
N (Number of Pairs).....	144
Input Type.....	Differences
Difference (P10-P01).....	0.2
Proportion Discordant (P10+P01)	0.7

Output

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

Numeric Results

Numeric Results for a Two-Sided McNemar Test							
Power*	Pairs N	P10	P01	Difference P10-P01	Odds Ratio P10/P01	Proportion Discordant P10+P01	Alpha
0.80092	144	0.450	0.250	0.200	1.800	0.700	0.025

* Power was computed using binomial enumeration of all possible outcomes.

PASS also finds the power to be about 80%.

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Example 3 – Computing Sample Size for a 2x2 Cross-Over Design

Julious (2010) indicates on page 167 that a 2x2 cross-over trial can be analyzed using McNemar's test if the period effect is ignored. This example will show you how to estimate the sample size for a 2x2 cross-over trial based on McNemar's test calculations. In example 10.1 on page 170, Julious (2010) calculates a required sample size of 190 to detect an odds ratio of 2 with 90% power at a significance level of 0.05 when the proportion discordant is 0.48. Note that Julious (2010) uses a slightly different asymptotic sample size formula (see page 169) from that used by this procedure.

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 Two Correlated Proportions (McNemar Test)** procedure window by expanding **Proportions**, then **Two Correlated Proportions**, then clicking on **Test (Inequality)**, and then clicking on **Tests for Two Correlated Proportions (McNemar Test)**. You may make the appropriate entries as listed below or open **Example 3** by going to the **File** menu and choosing **Open Example Template**.

<u>Option</u>	<u>Value</u>
Design Tab	
Solve For	Sample Size
Power Calculation Method.....	Normal Approximation
Alternative Hypothesis	Two-Sided
Power.....	0.90
Alpha.....	0.05
Input Type.....	Odds Ratios
Odds Ratio (P10/P01).....	2
Proportion Discordant (P10+P01)	0.48

Output

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

Numeric Results

Numeric Results for a Two-Sided McNemar Test							
Power*	Pairs N	P10	P01	Difference P10-P01	Odds Ratio P10/P01	Proportion Discordant P10+P01	Alpha
0.90000	193	0.320	0.160	0.160	2.000	0.480	0.050

* Power was computed using the normal approximation method.

PASS finds the sample size to be 193. It's not surprising that the sample size is slightly different from Julious (2010) because the calculation formulas are not exactly the same.