Essential statistics for the pharmaceutical sciences

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Additional topics as supplements to the book:

McNemar's test

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Introduction

Just as the two sample t-test has its close relative the paired t-test, the contingency chi-square test has its paired equivalent – McNemar's test. A typical use is where each subject generates two classifications and we want to know whether there is a systematic difference between these. An example follows.

An 'azole' antifungal is available for treating skin infections as both cream and spray formulations. There is a suspicion that the spray formulation is more likely to cause skin irritation. A group of volunteers have two small areas of skin on their backs treated – one with the spray and the other with the cream. After a period of treatment, the relevant areas are simply classified as 'Irritated' or 'Not irritated'

The results are then collected into a special form of contingency table as below (Table 1):

Table 1. Skin irritation after application of antifungal

		Cream form	
		Not irritated	Irritated
Spray form	Not irritated	165	3
	Irritated	12	18

The interpretation of this table is as follows:

- 165 subjects suffered no irritation with either form.
- 18 subjects suffered irritation with both forms.
- 3 subjects suffered irritation with the cream form but not the spray
- 12 subjects suffered irritation with the spray form but not the cream

Note the pairing

The structure of the trial is paired because each subject receives both treatments. It would have been possible to set up an unpaired trial by treating one group of subjects with the spray and another separate group with the cream. Such a trial would (in principle) have been able to answer the same question. However, just as the paired t-test can be a lot more powerful than the two sample t-test, paired trials such as that shown in Table 1 are more powerful than an unpaired approach.

How the test works

Those who suffered no irritation with either form are not considered as providing any useful information to allow us to differentiate between the formulations as their response to both was the same. Similarly those who were irritated by both provide no contrast.

Consequently, the test only takes account of those individuals who reacted differently to the two forms. It will therefore take note of the 3 who reacted to the cream and not the spray and the 12 showing the opposite pattern. The test is then essentially a consideration of whether one of these numbers is convincingly greater than the other. It does look as if the spray is causing more problems than the cream, but the test will provide an objective assessment of the question.

Calculating the test manually.

Some packages (including Minitab) do not offer McNemar's test, so you may need to calculate it manually. It's very simple:

Call the numbers of individuals who showed differing responses n1 and n2. It doesn't matter which number is allocated to which symbol. I will use n1 = 3 and n2 = 12.

The calculation uses a so-called 'Absolute' value. What this means is that we perform a subtraction, but if we obtain a negative value, we drop the minus sign. It is therefore the difference between two numbers without regard to which is greater.

A chi-square value is calculated as:

$$\text{Chi-square} = \frac{(\text{Abs}(n1 - n2) - 1)^2}{n1 + n2}$$

$$= \frac{(\text{Abs}(3 - 12) - 1)^2}{3 + 12}$$

$$= \frac{(\text{Abs}(-9) - 1)^2}{15}$$

(In this case, the subtraction does produce a negative result, so we drop the minus sign.)

$$= \frac{(9 - 1)^2}{15}$$

$$= \frac{8^2}{15}$$

$$= \frac{64}{15}$$

Chi-square = 4.27

Then judge the significance of the result against Table 2

Table 2. Critical chi-square values

P-value	Critical chi-square
0.05	3.841
0.025	5.024
0.01	6.635
0.005	7.879
0.001	10.828

For the most basic claim of statistical significance (P < 0.05), the achieved chi-square value must equal or exceed 3.841(Top line of Table 2). Our value of 4.27 achieves that. If our chi-square value had also exceeded any of the other values shown then we could have claimed an appropriately low P value For example a chi-square value of 9.10 would allow us to claim P<0.005, but not to claim P<0.001. In our case, we can just make the basic claim of statistical significance (P<0.05), but no stronger claim is justified.

Using SPSS to perform the test

Set up two string variables (1 character) to take the results and call them 'Cream' and 'Spray'. Results will be coded as y or n (y = Yes, was irritated; n = No, was not irritated)

For the first 165 individuals, enter 'n' in both the Cream and Spray columns, then 3 should be entered as 'y' in the Cream column and 'n' in the Spray column and so on.

Follow the menus *Analyze / Descriptive Statistics / Crosstabs …*

Move 'Cream' into the 'Row(s)' box.

Move 'Spray' into the 'Column(s)' box.

Click the 'Statistics…' button and check the box for McNemar.

Click Continue and OK.

The output will include:

cream * spray Crosstabulation

Count

		spray		Total
		n	y	
cream	n	165	12	177
	y	3	18	21
Total		168	30	198

Chi-Square Tests

	Value	Exact Sig. (2-sided)
McNemar Test		.035(a)
N of Valid Cases	198	

a. Binomial distribution used.

The first table (Yellow) is a contingency table equivalent to the one we started with (Table 1). The second provides a P-value of 0.035 (Green). This is consistent with the manual calculation that P<0.05 but >0.025.