Chapter 42
Chi-Square Tests for Large Cross-Tabs

1 General Purpose

Chi-square tests are adequate for testing 2 × 2 interaction cross-tabs of two treatment modalities and two numbers of responders to treatment (Chap. 38). These tests can, however, equally well, be applied for testing larger tables.

2 Schematic Overview of Type of Data File

Predictor (1–3...)	outcome (binary)
.	.
.	.
.	.
.	.
.	.
.	.
.	.

T.J. Cleophas, A.H. Zwinderman, *Clinical Data Analysis on a Pocket Calculator*,
DOI 10.1007/978-3-319-27104-0_42

3 Primary Scientific Question

In a 3×2 interaction cross-tab, is there a significant difference between three treatment modalities in numbers of responders to treatment?

4 Data Example One: 3×2 Cross-Tab

In three different treatment groups of hypertensive patients the numbers of responders (normotensive after treatment) is assessed.

	Responders		
	yes	no	total
Treatment 1	60	40	100
Treatment 2	100	120	220
Treatment 3	80	60	140
total	240	220	460

The best estimate of expectation is calculated from the above data under the null-hypothesis, that the results are not significantly different between the groups. E.g., estimate expected number of responders in treatment group 1 by dividing all responders (240) by all observations (460), and multiply by observations in treatment group 1 (100). Then, this estimate (the expected numbers E) is compared with the actually observed numbers of responders (observed numbers O). The procedure is illustrated below for responders and, also, non-responders in the treatment 1 group.

	Expected (E)		O−E	$(O-E)^2/E$
	Responders			
	yes	no		
Treatment 1	$(240/460) \times 100$	$(220/460) \times 100$	...	...
Treatment 2	...	...	...	...
Treatment 3	...	...	...	...

The add-up sum of the above three $(O - E)^2/E$ terms equal the chi-square value. The p-value can be read from the chi-square table for $3 - 1 = 2$ degrees of freedom.

The above procedure is laborious, and a *fast* method producing the same result is given underneath.

$240^2/460 =$ 125.22

Subtract the above value from the add-up sum of the underneath values.

$60^2/100 =$ 36.00
$100^2/220 =$ 45.45
$80^2/140 =$ 45.71

The result equals 1.9. . .

The chi-square value =

$$1.9\ldots/[(240/460) \times (220/460)] = 7.19\ldots$$

The underneath chi-square table has an upper row with areas under the curve, a left-end column with degrees of freedom, and a whole lot of chi-square values. The chi-square table shows that with 3 – 1 = 2 degrees of freedom (second row) 7.19. . . is between 5.991 and 9.210, and, thus, that the corresponding p-value (in the top-row) is between 0.05 and 0.01.

Chi-squared distribution

	Two-tailed *P*-value			
df	0.10	0.05	0.01	0.001
1	2.706	3.841	6.635	10.827
2	4.605	5.991	9.210	13.815
3	6.251	7.851	11.345	16.266
4	7.779	9.488	13.277	18.466
5	9.236	11.070	15.086	20.515
6	10.645	12.592	16.812	22.457
7	12.017	14.067	18.475	24.321
8	13.362	15.507	20.090	26.124
9	14.684	16.919	21.666	27.877
10	15.987	18.307	23.209	29.588
11	17.275	19.675	24.725	31.264
12	18.549	21.026	26.217	32.909
13	19.812	22.362	27.688	34.527
14	21.064	23.685	29.141	36.124
15	22.307	24.996	30.578	37.698
16	23.542	26.296	32.000	39.252
17	24.769	27.587	33.409	40.791
18	25.989	28.869	34.805	42.312
19	27.204	30.144	36.191	43.819
20	28.412	31.410	37.566	45.314
21	29.615	32.671	38.932	46.796
22	30.813	33.924	40.289	48.268
23	32.007	35.172	41.638	49.728
24	33.196	36.415	42.980	51.179
25	34.382	37.652	44.314	52.619
26	35.536	38.885	45.642	54.051
27	36.741	40.113	46.963	55.475
28	37.916	41.337	48.278	56.892
29	39.087	42.557	49.588	58.301
30	40.256	43.773	50.892	59.702

(continued)

	Two-tailed *P*-value			
df	0.10	0.05	0.01	0.001
40	51.805	55.758	63.691	73.403
50	63.167	67.505	76.154	86.660
60	74.397	79.082	88.379	99.608
70	85.527	90.531	100.43	112.32
80	96.578	101.88	112.33	124.84
90	107.57	113.15	124.12	137.21
100	118.50	124.34	135.81	149.45

Obviously, the three treatment modalities are significantly different from one another. In order to find out, whether the significant effect is between the treatments 1 and 2, 2 and 3, or 1 and 3, subsequent post hoc tests must be performed using 2 × 2 chi-square tests (Chap. 38). Bonferroni adjustments are to be recommended (Chap. 18).

5 Data Example Two: Theoretical Distribution

A random sample of 200 subjects was assessed for sleepiness during the day. We have been given demographic information (theoretical distribution) about the prevalence of sleepiness in the population from which the sample was taken. We wish to know whether the sample's distribution is not different from that of the population.

	Expected (theoretically)	Observed	O – E
1.sleepy	0.24	64	$64-(0.24\times200)=16$
2.sleepy rarely	0.60	124	$124-(0.6\times200)=4$
3.sleepy never	0.16	12	$12-(0.16\times200)=-20$

	$(O-E)^2/E$		
1.sleepy	$16^2/(0.24\times200)$	=	5.33
2.sleepy rarely	$4^2/(0.60\times200)$	=	0.05
3.sleepy never	$(-20^2)/(0.16\times200)$	=	12.50
total			17.88

According to the chi-square value of 17.88 with $3-1=2$ degrees of freedom, which is larger than 13.815, the p-value should <0.001 (see chi-square table in the above Sect. 42.4). Many more sleepy people were in the observed population than expected from the theoretical distribution. And, so, they must have had some reason for being so sleepy, that should be searched for properly.

6 Conclusion

Chi-square tests are adequate for testing 2×2 interaction cross-tabs of two treatment modalities and two numbers of responders to treatment. They can, however, equally well be applied for testing larger tables. In clinical research 2×2 tables are far more commonly used than large tables, because clinicians are mostly interested to find a single best treatment rather than a significant difference somewhere in multiple treatments. After an overall assessment of a larger table, multiple Bonferroni -adjusted subsequent 2×2 tests are required to find out this single best treatment. You may consider to skip the overall assessment and start with 2×2 tests from the very beginning.

7 Note

More background, theoretical and mathematical information of large chi-square tables are given in Statistics applied to clinical studies 5th edition, Chap. 3, Springer Heidelberg Germany, from the same authors.