Chapter 44
Trend Tests Will Be Statistically Significant if Traditional Tests Are Not (30 and 106 Patients)

General Purpose

Incremental dosages of medicines usually cause incremental treatment efficacies. This chapter is to assess whether trend tests are more sensitive than traditional ANOVAs for continuous outcome data (analyses of variance) and chi-square tests for binary outcome data to demonstrate the incremental efficacies.

Specific Scientific Questions

In patients with hypertension do incremental treatment dosages cause incremental beneficial effect on blood pressure? We will use the examples previously used in the Chaps. 9 and 12 of SPSS for starters part one, pp 33–34, and 43–46, entitled "Trend test for continuous data" and "trend tests for binary data", Springer Heidelberg Germany, 2010, from the same authors.

Example 1

In a parallel group study of 30 patients with hypertension 3 incremental antihypertensive treatment dosages are assessed. The first 13 patients of the data file is given underneath. The entire data file is in extras.springer.com, and is entitled "trend.sav".

Variable	
1	2
1,00	113,00
1,00	131,00

(continued)

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Variable	
1,00	112,00
1,00	132,00
1,00	114,00
1,00	130,00
1,00	115,00
1,00	129,00
1,00	122,00
2,00	118,00
2,00	109,00
2,00	127,00
2,00	110,00

Var 1 = treatment dosage (Var = variable)
Var 2 = treatment response (mean blood pressure after treatment)

We will first perform a one-way ANOVA (see also Chap. 8, SPSS for starters part one, entitled "One way ANOVA, Kruskall-Wallis", pp 29–31, Springer Heidelberg Germany, 2012, from the same authors) to see, if there are any significant differences in the data. If not, we will perform a trend test using simple linear regression.

Command:

Analyze....Compare Means....One-way ANOVA....dependent list: mean blood pressure after treatment - factor: treatment dosage....OK

ANOVA					
VAR00002					
	Sum of squares	df	Mean square	F	Sig.
Between groups	246,667	2	123,333	2,035	,150
Within groups	1636,000	27	60,593		
Total	1882,667	29			

The output table shows that there is no significant difference in efficacy between the treatment dosages, and so, sadly, this is a negative study. However, a trend test having just 1 degree of freedom has more sensitivity than a usual one-way ANOVA, and it could, therefore, be statistically significant even so.

Command:

Analyze....regression....linear....dependent = mean blood pressure after treatment.... independent = treatment dosage....OK

ANOVA[b]					
Model	Sum of squares	df	Mean square	F	Sig.
1 Regression	245,000	1	245,000	4,189	,050[a]
Residual	1637,667	28	58,488		
Total	1882,667	29			

[a]Predictors: (Constant), VAR00001
[b]Dependent Variable: VAR00002

The above output table shows that treatment dosage is a significant predictor of treatment response wit a p-value of 0.050. There is, thus, a significantly incremental response with incremental dosages.

Example 2

In a parallel group study of 106 patients with hypertension 3 incremental antihypertensive treatment dosages are assessed. The first 13 patients of the data file is given underneath. The entire data file is in extras.springer.com, and is entitled "trend.sav".

responder (1 = yes, 0 = no)	Treatment (1 = low, 2 = medium, 3 = high dosage)
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	1,00
1,00	2,00
1,00	2,00
1,00	2,00

Command:

Analyze....Descriptive Statistics....Crosstabs....Row(s): enter responders.... Column(s): enter treatment....click Cell(s)....Counts: mark Observed..... Percentage: mark Columns....click continue....click OK

The underneath contingency table shows that with incremental dosages the % of responders incrementally rises from 40 % to 51.3 % and then to 64.3 %.

			Treatment			
			1,00	2,00	3,00	Total
Responder	,00	Count	15	19	15	49
		% within treatment	60,0 %	48,7 %	35,7 %	46,2 %
	1,00	Count	10	20	27	57
		% within treatment	40,0 %	51,3 %	64,3 %	53,8 %
Total		Count	25	39	42	106
		% within treatment	100,0 %	100,0 %	100,0 %	100,0 %

Subsequently, a chi-square test will be performed to assess whether the cells are significantly different from one another.

Command:

Analyze....Descriptive Statistics....Crosstabs.... Row(s): enter responders.... Column(s): enter treatment....click Statistics....Chi-square....OK

Chi-square tests			
	Value	df	Asy mp. Sig. (2-sided)
Pearson chi-square	3,872[a]	2	,144
Likelihood ratio	3,905	2	,142
Linear-by-linear association	3,829	1	,050
N of valid cases	106		

[a]0 cells (,0 %) have expected court less than 5. The minimum expected count is 11,56

The output table shows that the Pearson chi-square value for multiple groups testing is not significant with a value of 3.872 and a p-value of 0.144, and we need to conclude that there is no significant difference between the cells. Subsequently, a chi-square test for trends is required for that purpose. Actually, the "linear-by-linear association" from the same table is appropriate. It has approximately the same chi-square value, but it has only 1 degree of freedom, and, therefore it reaches statistical significance with a p-value of 0.050. There is, thus, a significant incremental trend of responding with incremental dosages. As an alternative the trend in this example can also be tested using logistic regression with responding as outcome variable and treatment as independent variable.

Command:

Analyze....Regression....Binary Logistic Regression....Dependent: enter responder.... Covariates: enter treatment....click OK

Variables in the equation							
		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	Treatment	,500	,257	3,783	1	,052	1,649
	Constant	-,925	,587	2,489	1	,115	,396

[a]Variable(s) entered on step 1: treatment.

The output sheet shows that the p-value of the logistic model is virtually identical to the p-value of chi-square test for trends, 0.052 and 0.050.

Conclusion

The examples in this chapter show that both with continuous and binary outcome variables trend tests are more sensitive to demonstrate significant effects in dose response studies than traditional statistical tests.

Note

More background, theoretical and mathematical information of trend tests are given in the Chap. 27, Trend-testing, pp 313–318, in: Statistics applied to clinical studies 5th edition, Springer Heidelberg Germany, 2012, from the same authors.