Chapter 21
Variability Analysis for One or Two Samples

1 General Purpose

In some clinical studies, the spread of the data may be more relevant than the average of the data. E.g., when we assess how a drug reaches various organs, variability of drug concentrations is important, as in some cases too little and in other cases dangerously high levels get through. Also, variabilities in drug response may be important. For example, the spread of glucose levels of a slow-release-insulin is important. This chapter assesses how to estimate the spread of one and two data-samples.

2 Schematic Overview of Type of Data File

Outcome
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T.J. Cleophas, A.H. Zwinderman, *Clinical Data Analysis on a Pocket Calculator*,
DOI 10.1007/978-3-319-27104-0_21

3 Primary Scientific Question

Is the spread in a data set larger than required, is the difference in variabilities between two data samples statistically significant.

4 One Sample Variability Analysis

For testing whether the standard deviation (or variance) of a sample is significantly different from the standard deviation (or variance) to be expected, the chi-square test with multiple degrees of freedom is adequate. The test statistic (the chi-square-value = χ^2 –value) is calculated according to

$$\chi^2 = \frac{(n-1)s^2}{\sigma^2} \text{ for n} - 1 \text{ degrees of freedom}$$

n = sample size, s = standard deviation, s^2 = variance sample, σ = expected standard deviation, σ^2 = expected variance).

For example, the aminoglycoside compound gentamicin has a small therapeutic index. The standard deviation of 50 measurements is used as a criterion for variability. Adequate variability will be accepted, if the standard deviation is less than 7 μg/l. In our sample a standard deviation of 9 μg/l is observed. The test procedure is given.

$$\chi^2 = (50-1)\,9^2/7^2 = 81$$

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. It shows that, for 50–1 = 49 degrees of freedom (close to 50 df row), we will find that a chi-square value 76.154 will produce a p-value < 0.01. This sample's standard deviation is significantly larger than that required. This means that the variability in plasma gentamicin concentrations is larger than acceptable.

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

(continued)

	Two-tailed *P*-value			
df	0.10	0.05	0.01	0.001
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
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

5 Two Sample Variability Test

F-tests can be applied to test if the variabilities of two samples are significantly different from one another. The division sum of the samples' variances (larger variance / smaller variance) is used for the analysis. For example, two formulas of gentamicin produce the following standard deviations of plasma concentrations.

	Patients (n)	Standard deviation (SD) (μg/l)
formula-A	10	3.0
formula-B	15	2.0

$$
\begin{aligned}
\text{F-value} &= SD_A^2/SD_B^2 \\
&= 3.0^2/2.0^2 \\
&= 9/4 = 2.25
\end{aligned}
$$

with degrees of freedom (dfs) for

$$
\begin{aligned}
\text{formula-A of } 10 - 1 &= 9 \\
\text{formula-B of } 15 - 1 &= 14
\end{aligned}
$$

The table of critical F-values producing a $p < 0.05$ is on the next page. It shows that with 9 and 14 degrees of freedom respectively in the numerator and denominator an F-value around 3.12 or more is required in order to reject the null – hypothesis. Our F-value is only 2.25, and, so, the p-value is > 0.05, and the null-hypothesis cannot be rejected. No significant difference between the two formulas can be demonstrated.

d*f* of denominator	2-tailed	L-tailed	Degrees of freedom (*df*) of the numerator												
	P-value	*P*-value	1	2	3	4	5	6	7	8	9	10	15	25	500
1	0.05	0.025	647.8	799.5	864.2	899.6	921.8	937.1	948.2	956.6	963.3	968.6	984.9	998.1	1017.0
1	0.10	0.05	161.4	199.5	215.7	224.6	230.2	234.0	236.8	238.9	240.5	241.9	245.9	249.3	254.1
2	0.05	0.025	38.51	39.00	39.17	39.25	39.30	39.33	39.36	39.37	39.39	39.40	39.43	39.46	39.50
2	0.10	0.05	18.51	19.00	19.16	19.25	19.30	19.33	19.35	19.37	19.38	19.40	19.43	19.46	19.49
3	0.05	0.025	17.44	16.04	15.44	15.10	14.88	14.73	14.62	14.54	14.47	14.42	14.25	14.12	13.91
3	0.10	0.05	10.13	9.55	9.28	9.12	9.01	8.94	8.89	8.85	8.81	8.79	8.70	8.63	8.53
4	0.05	0.025	12.22	10.65	9.98	9.60	9.36	9.20	9.07	8.98	8.90	8.84	8.66	8.50	8.27
4	0.10	0.05	7.71	6.94	6.59	6.39	6.26	6.16	6.09	6.04	6.00	5.96	5.86	5.77	5.64
5	0.05	0.025	10.01	8.43	7.76	7.39	7.15	6.98	6.85	6.76	6.68	6.62	6.43	6.27	6.03
5	0.10	0.05	6.61	5.79	5.41	5.19	5.05	4.95	4.88	4.82	4.77	4.74	4.62	4.52	4.37
6	0.05	0.25	8.81	7.26	6.60	6.23	5.99	5.82	5.70	5.60	5.52	5.46	5.27	5.11	4.86
6	0.10	0.05	5.99	5.14	4.76	4.53	4.39	4.28	4.21	4.15	4.10	4.06	3.94	3.83	3.68
7	0.05	0.025	8.07	6.54	5.89	5.52	5.29	5.12	4.99	4.90	4.82	4.76	4.57	4.40	4.16
7	0.10	0.05	5.59	4.74	4.35	4.12	3.97	3.87	3.79	3.73	3.68	3.64	3.51	3.40	3.24
8	0.05	0.25	7.57	6.06	5.42	5.05	4.82	4.65	4.53	4.43	4.36	4.30	4.10	3.94	3.68
8	0.10	0.05	5.32	4.46	4.07	3.84	3.69	3.58	3.50	3.44	3.39	3.35	3.22	3.11	2.94
9	0.05	0.025	7.21	5.71	5.08	4.72	4.48	4.32	4.20	4.10	4.03	3.96	3.77	3.60	3.35
9	0.10	0.05	5.12	4.26	3.86	3.63	3.48	3.37	3.29	3.23	3.18	3.14	3.01	2.89	2.72
10	0.05	0.025	6.94	5.46	4.83	4.47	4.24	4.07	3.95	3.85	3.78	3.72	3.52	3.35	3.09
10	0.10	0.05	4.96	4.10	3.71	3.48	3.33	3.22	3.14	3.07	3.02	2.98	2.85	2.73	2.55
15	0.05	0.025	6.20	4.77	4.15	3.80	3.58	3.41	3.29	3.20	3.12	3.06	2.86	2.69	2.41
15	0.10	0.05	4.54	3.68	3.29	3.06	2.90	2.79	2.71	2.64	2.59	2.54	2.40	2.28	2.08
20	0.05	0.025	5.87	4.46	3.86	3.51	3.29	3.13	3.01	2.91	2.84	2.77	2.57	2.40	2.10
20	0.10	0.05	4.35	3.49	3.10	2.87	2.71	2.60	2.51	2.45	2.39	2.35	2.20	2.07	1.86
30	0.05	0.025	5.57	4.18	3.59	3.25	3.03	2.87	2.75	2.65	2.57	2.51	2.31	2.12	1.81

(continued)

d*f* of denominator	2-tailed	L-tailed	Degrees of freedom (*df*) of the numerator												
	P-value	*P*-value	1	2	3	4	5	6	7	8	9	10	15	25	500
30	0.10	0.05	4.17	3.32	2.92	2.69	2.53	2.42	2.33	2.27	2.21	2.16	2.01	1.88	1.64
50	0.05	0.025	5.34	3.97	3.39	3.05	2.83	2.67	2.55	2.46	2.38	2.32	2.11	1.92	1.57
50	0.10	0.05	4.03	3.18	2.79	2.56	2.40	2.29	2.20	2.13	2.07	2.03	1.87	1.73	1.46
100	0.05	0.025	5.18	3.83	3.25	2.92	2.70	2.54	2.42	2.32	2.24	2.18	1.97	1.77	1.38
100	0.10	0.05	3.94	3.09	2.70	2.46	2.31	2.19	2.10	2.03	1.97	1.93	1.77	1.62	1.31
100	0.10	0.05	3.94	3.09	2.70	2.46	2.31	2.19	2.10	1.03	1.97	1.93	1.77	1.62	1.31
1000	0.05	0.025	5.04	3.70	3.13	2.80	2.58	2.42	2.30	2.20	2.13	2.06	1.85	1.64	1.16
1000	0.10	0.05	3.85	3.00	2.16	2.38	2.22	2.11	2.02	1.95	1.89	1.84	1.68	1.52	1.13

6 Conclusion

In some clinical studies, the spread of the data may be more relevant than the average of the data. For example, the spread of glucose levels of a slow-release-insulin is important. This chapter assesses how the spread of one and two data-samples can be estimated. In the Chap. 22 statistical tests for variability assessments with three or more samples will be given.

7 Note

More background, theoretical and mathematical information of variability assessments is given in Statistics applied to clinical studies 5th edition, Chap. 44, Springer Heidelberg Germany, 2012, from the same authors.