Chapter 20
Paired Analysis of Variance

1 General Purpose

Paired t-tests are for assessing the effect of two treatments in a single group of patients. However, if you wish to compare three treatments, the paired t-tests can no longer be applied. Instead, paired analysis of variance (ANOVA), otherwise called repeated-measures ANOVA must be used for analysis.

2 Schematic Overview of Type of Data File

	Outcome	Outcome	Outcome
Patient no	Treatment 1	Treatment 2	Treatment 3
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.
.	.	.	.

T.J. Cleophas, A.H. Zwinderman, *Clinical Data Analysis on a Pocket Calculator*,
DOI 10.1007/978-3-319-27104-0_20

3 Primary Scientific Question

How can repeated-measures ANOVA evaluate the different effect of three different treatments.

4 Variations Expressed as the Sums of Squares

With paired ANOVA of three treatments every single patient is treated three times. The data are split:

Total variation
| |
Between-subject variation Within-subject variation
| |
Between-treatment variation Residual variation (random)

Variations is expressed as the sums of squares (SS), and can be added up to obtain the total variation in the data. We will assess, whether the between-treatment variation is large compared to the residual variation. Repeated-measure ANOVA is sometimes called two-way ANOVA (balanced, without replications), (SD = standard deviation).

Subject	Treatment 1	Treatment 2	Treatment 3	SD^2
1	–	–	–	–
2	–	–	–	–
3	–	–	–	–
4	–	–	–	–
Treatment mean	–	–	–	

Grand mean = (treatment mean 1 + 2 + 3) / 3 = ...

SS within-subject = $SD_1{}^2 + SD_2{}^2 + SD_3{}^2$
SS treatment = (treatment mean 1 − grand mean)^2 + (treatment mean 2 − grand mean)^2 + ...
SS residual = SS within-subject − SS treatment

The F-test (Fisher-test) is used for testing (dfs = degrees of freedom):

$$F = \frac{\text{SS treatment }/\text{dfs}}{\text{SS residual }/\text{ dfs}} = \frac{\text{SS treatment }/(3-1)}{\text{SS residual }/\ (3-1)(4-1)}$$

The F-table gives the P-value.

5 Real Data Example

The effect of 3 treatments on vascular resistance is assessed in four persons.

Person	Treatment 1	Treatment 2	Treatment 3	SD^2
1	22.2	5.4	10.6	147.95
2	17.0	6.3	6.2	77.05
3	14.1	8.5	9.3	18.35
4	17.0	10.7	12.3	21.45
Treatment mean	17.58	7.73	9.60	

Grand mean = 11.63

SS within-subject = 147.95 + 77.05 + ..

SS treatment = $(17.58 - 11.63)^2 + (7.73 - 11.63)^2 + ..$

SS residual = SS within-subject − SS treatment.

F = 14.31.

This value is much larger than the critical F-value producing a $p < 0.05$, because with 2 (numerator) degrees of freedom and $2 \times 3 = 6$ (denominator) degrees of freedom the critical F-value should be around 7.26. The difference between the effects of the three treatments is, thus, very significant. The table of critical F-values is given on the next page. The internet provides, however, many critical F-value calculators, that are more precise than the table given.

We should add that, in case of 2 treatments the F-value produced by the ANOVA equals the t-value squared ($F = t^2$). T-statistics is, indeed, a simple form of analysis of variance.

df of denominator	2-tailed *P*-value	1-tailed *P*-value	Degrees of freedom (*df*) of the numerator												
			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	0.025	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	0.025	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
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
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	2.61	2.38	2.22	2.11	2.02	1.95	1.89	1.84	1.68	1.52	1.13

6 Conclusion

The above examples show how repeated-measures ANOVA can be used to test the significance of difference between three treatments in a single group of patients. However, it does not tell us whether treatment 1 is better than 2, treatment 2 better than 3, or treatment 1 better than 3, or any combinations of these effects. For that purpose post hoc tests are required, comparing the treatments one by one. Paired t-tests should be appropriate for the purpose.

7 Note

More background, theoretical and mathematical information of unpaired and paired ANOVA is given Statistics applied to clinical studies 5th edition, Chap. 2, Springer Heidelberg Germany, 2012, from the same authors.