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Advanced Topics in Biostatistics: Non-Parametric Methods

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Outline

- Overview test procedures
- Wilcoxon signed rank test
- Wilcoxon rank sum test = Mann-Whitney U-Test
- Kruskal-Wallis-test
- Spearman rank correlation

Test procedures for quantitative variables: Comparison of means

1 sample:

One-sample t-test

2 paired samples:

paired t-test

2 independent samples:

t-test (equal standard deviation in both groups)

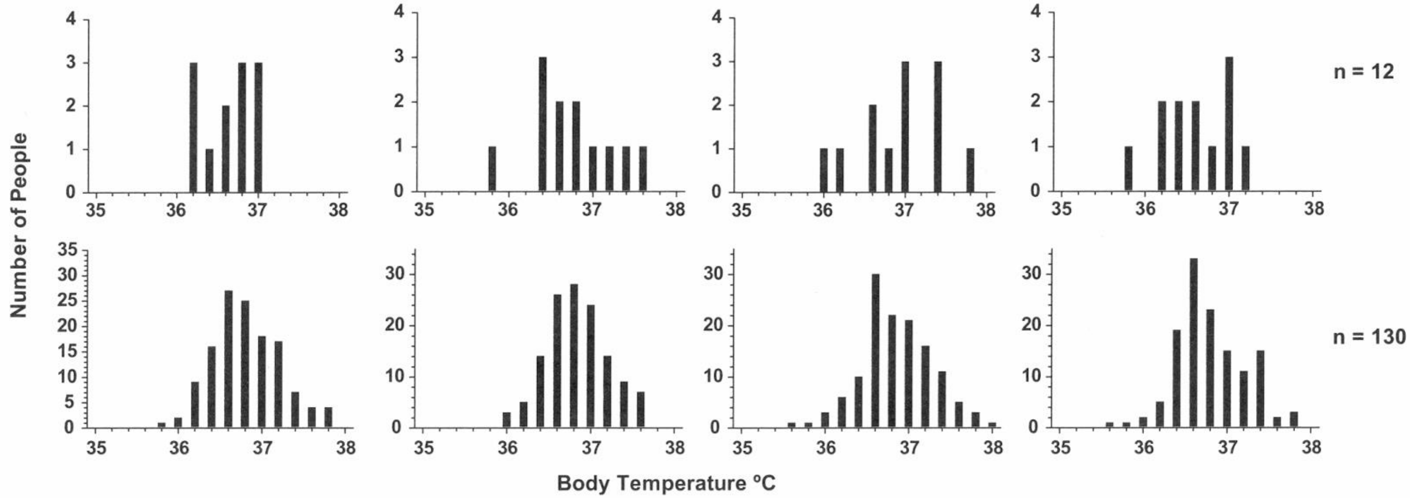
Welch-test (different standard deviation in both groups)

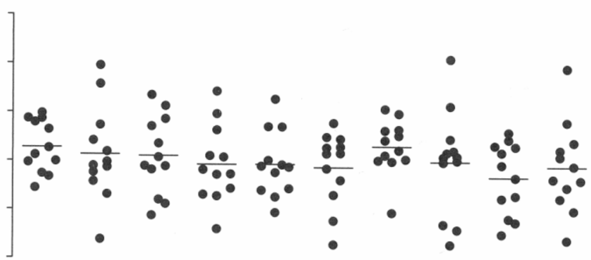
≥ 3 independent samples:

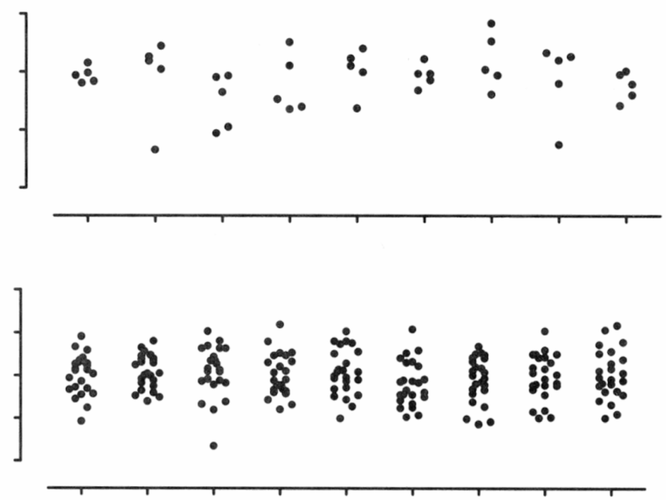
Analysis of Variance (ANOVA)

General assumption: Data come from Normal distribution

Normal distribution does not always look ‚normal‘

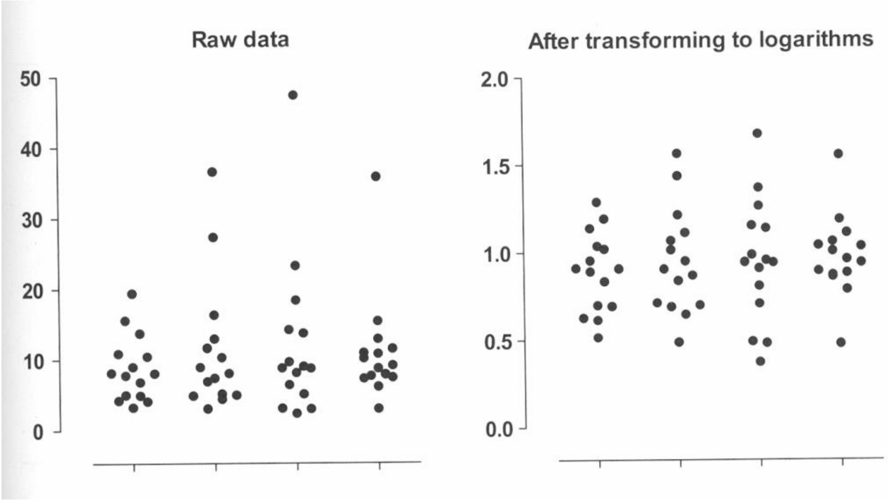






From: H. Motulsky, Intuitive Biostatistics, 2010.

Transformation to normal distribution



Raw data from a log-normal distribution seem to have outliers.

Note: most outlier tests are inappropriate when values come from a non-Gaussian distribution

From: H. Motulsky, Intuitive Biostatistics, 2010.

Non-parametric procedures based on ranks

When to use…

- Data do not come from normal distribution
- No data transformation available to transform data to normal distribution
- Transformation of data to normal distribution is hard to interpret
- Presence of outlying observations

Test Procedures for Quantitative Variables: Comparison of Means

Parametric test (assuming normal distribution)	*Non-parametric test*
<u>1 sample</u>: One-sample t-test	
<u>2 paired samples:</u> paired t-test	*Sign test, Wilcoxon signed rank test*
<u>2 independent samples:</u> t-test, Welch-test	*Wilcoxon rank sum test (= Mann-Whitney U-test)*
<u>≥ 3 independent samples:</u> Analysis of Variance (ANOVA)	*Kruskal-Wallis-test*

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<u>≥ 3 independent samples:</u> Analysis of Variance (ANOVA)	*Kruskal-Wallis-test*

Wilcoxon signed rank test: Example

A non-parametric alternative to the one-sample t-test or the paired t-test

<u>Example</u>:

Results of a placebo-controlled trial to test the effectiveness of a sleeping drug: Hours of sleep

Patient	Drug	Placebo
1	6.1	5.2
2	6.0	7.9
3	8.2	3.9
4	7.6	4.7
5	6.5	5.3
6	5.4	7.4
7	6.9	4.2
8	6.7	6.1
9	7.4	3.8
10	5.8	7.3

Wilcoxon signed rank test: Example

A non-parametric alternative to the one-sample t-test or the paired t-test

Example:

Results of a placebo-controlled trial to test the effectiveness of a sleeping drug: Hours of sleep

Patient	Drug	Placebo	Diff
1	6.1	5.2	0.9
2	6.0	7.9	-1.9
3	8.2	3.9	4.3
4	7.6	4.7	2.9
5	6.5	5.3	1.2
6	5.4	7.4	-2.0
7	6.9	4.2	2.7
8	6.7	6.1	0.6
9	7.4	3.8	3.6
10	5.8	7.3	-1.5

Wilcoxon signed rank test: Example

A non-parametric alternative to the one-sample t-test or the paired t-test

Example:

Results of a placebo-controlled trial to test the effectiveness of a sleeping drug: Hours of sleep

Patient	Drug	Placebo	Diff	|Diff|
1	6.1	5.2	0.9	0.9
2	6.0	7.9	-1.9	1.9
3	8.2	3.9	4.3	4.3
4	7.6	4.7	2.9	2.9
5	6.5	5.3	1.2	1.2
6	5.4	7.4	-2.0	2.0
7	6.9	4.2	2.7	2.7
8	6.7	6.1	0.6	0.6
9	7.4	3.8	3.6	3.6
10	5.8	7.3	-1.5	1.5

Wilcoxon signed rank test: Example

A non-parametric alternative to the one-sample t-test or the paired t-test

Example:

Results of a placebo-controlled trial to test the effectiveness of a sleeping drug: Hours of sleep

Patient	Drug	Placebo	Diff	|Diff|	Rank
1	6.1	5.2	0.9	0.9	
2	6.0	7.9	-1.9	1.9	
3	8.2	3.9	4.3	4.3	
4	7.6	4.7	2.9	2.9	
5	6.5	5.3	1.2	1.2	
6	5.4	7.4	-2.0	2.0	
7	6.9	4.2	2.7	2.7	
8	6.7	6.1	0.6	0.6	
9	7.4	3.8	3.6	3.6	
10	5.8	7.3	-1.5	1.5	

Wilcoxon signed rank test: Example

A non-parametric alternative to the one-sample t-test or the paired t-test

Example:

Results of a placebo-controlled trial to test the effectiveness of a sleeping drug: Hours of sleep

Patient	Drug	Placebo	Diff	|Diff|	Rank
1	6.1	5.2	0.9	0.9	2
2	6.0	7.9	-1.9	1.9	5
3	8.2	3.9	4.3	4.3	10
4	7.6	4.7	2.9	2.9	8
5	6.5	5.3	1.2	1.2	3
6	5.4	7.4	-2.0	2.0	6
7	6.9	4.2	2.7	2.7	7
8	6.7	6.1	0.6	0.6	1
9	7.4	3.8	3.6	3.6	9
10	5.8	7.3	-1.5	1.5	4

Sum of ranks of positive differences: $T_+ = 40$

Sum of ranks of negative differences: $T_- = 15$

Wilcoxon signed rank test: Procedure

A non-parametric alternative to the one-sample t-test or the paired t-test

Situation:

Two paired samples

No assumption about distribution of differences

Hypotheses:

H_0 : Median($F_{drug\text{-}placebo}$) = 0

H_1 : Median($F_{drug\text{-}placebo}$) ≠ 0

Test statistic:

Follow algorithm:

1. Exclude differences = 0, N=#nonzero differences
2. Rank absolute differences
3. T_+ = rank sum of positive differences
   T_- = rank sum of negative differences
   $T = \min\{T_+ , T_- \}$

Test decision for small sample size:

If T < critical value from Table $\rightarrow$ reject H_0

A non-parametric alternative to the one-sample t-test or the paired t-test

Table A7 Critical values for the Wilcoxon matched pairs signed rank test.

Reproduced from Table 21 of White *et al*. (1979) with permission of the authors and publishers.

N = number of non-zero differences; T = smaller of T_+ and T_-; Significant if $T <$ critical value.

	One-sided P-value			
	0.05	0.025	0.01	0.005
	Two-sided P-value			
N	0.1	0.05	0.02	0.01
5	1			
6	2	1		
7	4	2	0	
8	6	4	2	0
9	8	6	3	2
10	11	8	5	3
11	14	11	7	5
12	17	14	10	7
13	21	17	13	10
14	26	21	16	13
15	30	25	20	16
16	36	30	24	19
17	41	35	28	23
18	47	40	33	28
19	54	46	38	32
20	60	52	43	37
21	68	59	49	43
22	75	66	56	49
23	83	73	62	55
24	92	81	69	61
25	101	90	77	68
26	110	98	85	76
27	120	107	93	84
28	130	117	102	92
29	141	127	111	100

	One-sided P-value			
	0.05	0.025	0.01	0.005
	Two-sided P-value			
N	0.1	0.05	0.02	0.01
30	152	137	120	109
31	163	148	130	118
32	175	159	141	128
33	188	171	151	138
34	201	183	162	149
35	214	195	174	160
36	228	208	186	171
37	242	222	198	183
38	256	235	211	195
39	271	250	224	208
40	287	264	238	221
41	303	279	252	234
42	319	295	267	248
43	336	311	281	262
44	353	327	297	277
45	371	344	313	292
46	389	361	329	307
47	408	397	345	323
48	427	397	362	339
49	446	415	380	356
50	466	434	398	373

A non-parametric alternative to the one-sample t-test or the paired t-test

Table A7 Critical values for the Wilcoxon matched pairs signed rank test.

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N = number of non-zero differences; T = smaller of T_+ and T_-; Significant if $T <$ critical value.

	One-sided P-value 0.05	0.025	0.01	0.005
N	Two-sided P-value 0.1	0.05	0.02	0.01
5	1			
6	2	1		
7	4	2	0	
8	6	4	2	0
9	8	6	3	2
10	11	8	5	3
11	14	11	7	5
12	17	14	10	7
13	21	17	13	10
14	26	21	16	13
15	30	25	20	16
16	36	30	24	19
17	41	35	28	23
18	47	40	33	28
19	54	46	38	32
20	60	52	43	37
21	68	59	49	43
22	75	66	56	49
23	83	73	62	55
24	92	81	69	61
25	101	90	77	68
26	110	98	85	76
27	120	107	93	84
28	130	117	102	92
29	141	127	111	100
30	152	137	120	109
31	163	148	130	118
32	175	159	141	128
33	188	171	151	138
34	201	183	162	149
35	214	195	174	160
36	228	208	186	171
37	242	222	198	183
38	256	235	211	195
39	271	250	224	208
40	287	264	238	221
41	303	279	252	234
42	319	295	267	248
43	336	311	281	262
44	353	327	297	277
45	371	344	313	292
46	389	361	329	307
47	408	397	345	323
48	427	397	362	339
49	446	415	380	356
50	466	434	398	373

Example:

$N = 10$

$T_+ = 40$

$T_- = 15$

$\rightarrow T = \min\{T_+, T_-\} = 15$

$15 > 8$

$\rightarrow$ do not reject H_0 at 5% level

Wilcoxon signed rank test: Procedure (2)

A non-parametric alternative to the one-sample t-test or the paired t-test

Test decision for large sample size:

$$z = \frac{T - \frac{1}{4}N(N+1)}{\sqrt{\frac{N(N+1)(2N+1)}{24}}} = -1.274$$

T = min{T_+ , T_- }, N: #non-zero differences

z has Standard Normal Distribution $\rightarrow$ compare with quantile $z_{1-\alpha/2}$ from SND

If |z| > 1.96 $\rightarrow$ reject H_0 at 5% level

Remark:
Confidence interval for median of differences can be calculated by tedious method.

Wilcoxon signed rank test: What is a large sample size?

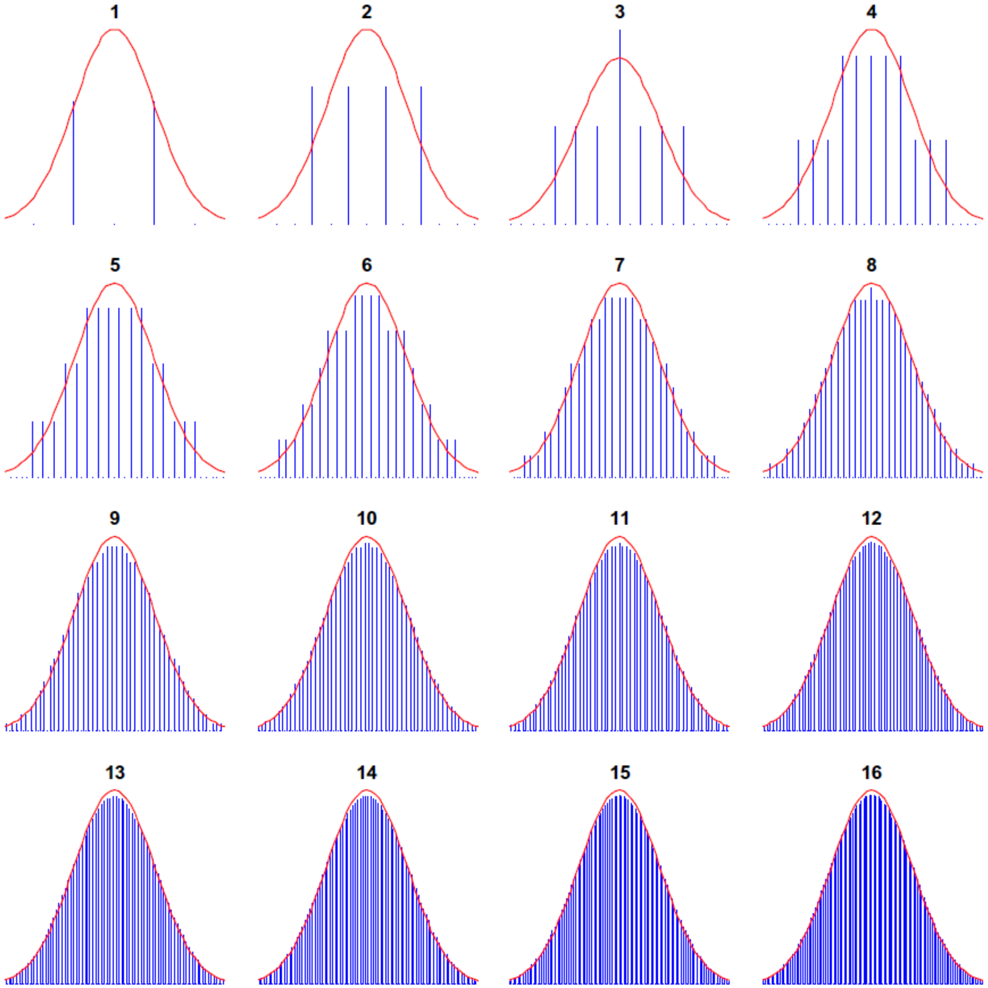
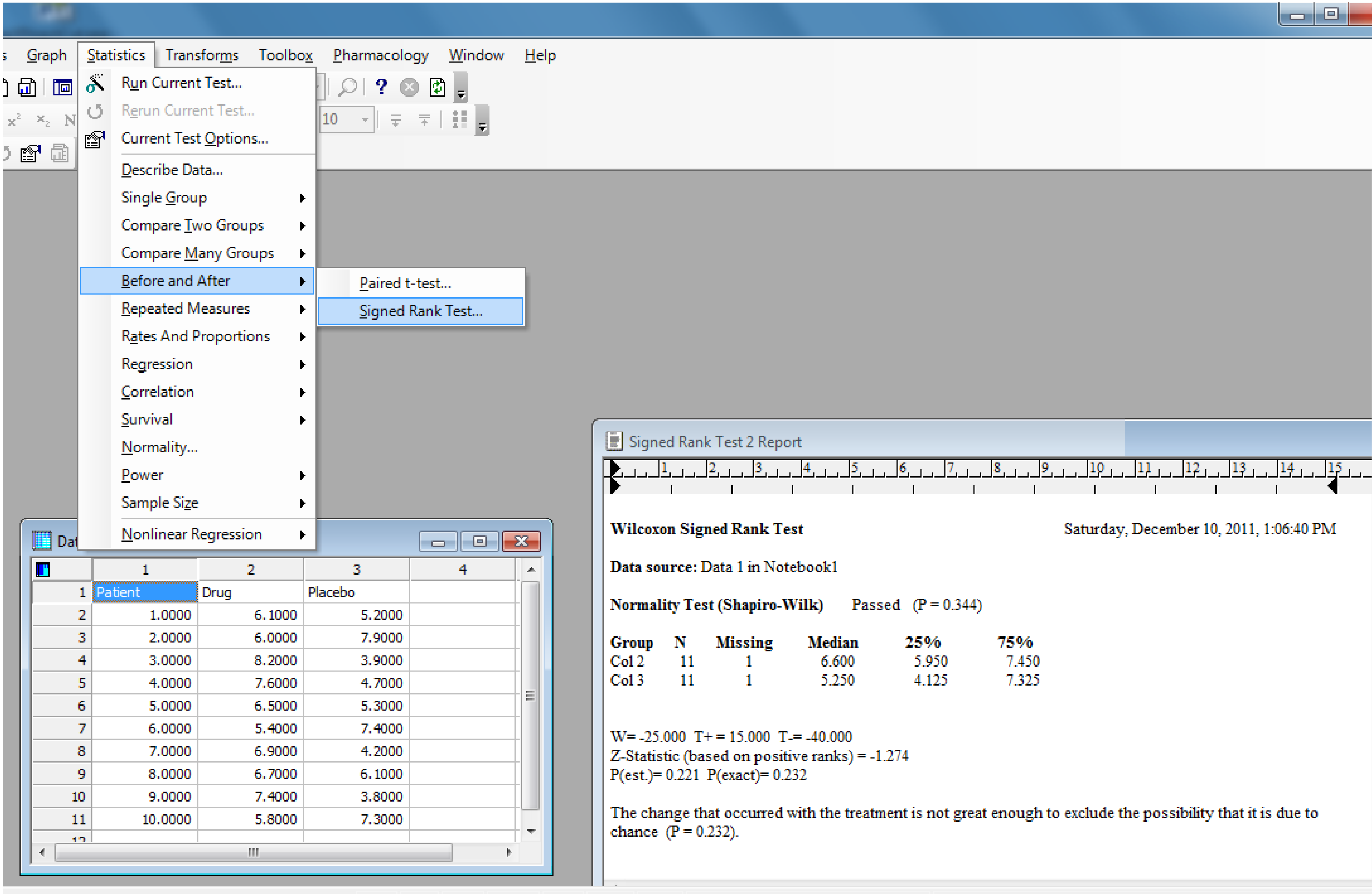


Figure 2. Exact distribution of the Wilcoxon signed-rank statistic for sample of sizes ($1 \leq n \leq 16$), and curve of the normal distribution with mean $n(n+1)/4$ and variance $n(n+1)(2n+1)/24$.

From: Bellera et al, J Stat Edu 2010.

Wilcoxon signed rank test in SigmaPlot



Wilcoxon signed rank test in Web tool

Treatment 1	Treatment 2	*Sign*	*Abs*	*R*	*Sign R*
6.1	5.2	1	0.9	2	2
6.0	7.9	-1	1.9	5	-5
8.2	3.9	1	4.3	10	10
7.6	4.7	1	2.9	8	8
6.5	5.3	1	1.2	3	3
5.4	7.4	-1	2	6	-6
6.9	4.2	1	2.7	7	7
6.7	6.1	1	0.6	1	1
7.4	3.8	1	3.6	9	9
5.8	7.3	-1	1.5	4	-4

Significance Level:

- ○ .01
- ◉ .05

1 or 2-tailed hypothesis?:

- ○ One-tailed
- ◉ Two-tailed

Result Details

W-value: 15
Mean Difference: -1.24
Sum of pos. ranks: 40
Sum of neg. ranks: 15

Z-value: -1.2741
Mean (*W*): 27.5
Standard Deviation (*W*): 9.81

Sample Size (*N*): 10

https://www.socscistatistics.com/tests/signedranks/default2.aspx

Result 1 - Z-value

The value of *z* is-1.2741. The *p*-value is .20408.

The result is *not* significant at $p < .05$.

Result 2 - W-value

The value of *W* is 15. The critical value for *W* at $N = 10$ ($p < .05$) is 8.

The result is *not* significant at $p < .05$.

Test Procedures for Quantitative Variables: Comparison of Means

Parametric test (assuming normal distribution)	*Non-parametric test*
1 sample: One-sample t-test	
2 paired samples: paired t-test	*Sign test,* *Wilcoxon signed rank test*
2 independent samples: t-test Welch-test	*Wilcoxon rank sum test* *(= Mann-Whitney U-test)*
≥ 3 independent samples: Analysis of Variance (ANOVA)	*Kruskal-Wallis-test*

Wilcoxon rank sum test: Example

A non-parametric alternative to the two-sample t-test

Example:

Comparison of birth weights (in kg) of children born to 14 heavy smoking mothers with those of children born to 15 non-smoking mothers

Heavy smokers (group 1) weight	Non-smokers (group 0) weight
2.34	2.71
2.38	3.31
2.74	3.36
2.86	3.41
2.90	3.51
3.18	3.54
3.23	3.60
3.27	3.61
3.42	3.70
3.53	3.73
3.60	3.83
3.65	3.89
3.65	3.99
3.69	4.08
	4.13

Wilcoxon rank sum test: Example

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Heavy smokers (group 1) weight	rank	Non-smokers (group 0) weight	rank
2.34	1	2.71	3
2.38	2	3.31	10
2.74	4	3.36	11
2.86	5	3.41	12
2.90	6	3.51	14
3.18	7	3.54	16
3.23	8	3.60	
3.27	9	3.61	
3.42	13	3.70	
3.53	15	3.73	
3.60		3.83	
3.65		3.89	
3.65		3.99	
3.69		4.08	
		4.13	

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<u>Example</u>:

Comparison of birth weights (in kg) of children born to 14 heavy smoking mothers with those of children born to 15 non-smoking mothers

Heavy smokers (group 1)		Non-smokers (group 0)	
weight	rank	weight	rank
2.34	1	2.71	3
2.38	2	3.31	10
2.74	4	3.36	11
2.86	5	3.41	12
2.90	6	3.51	14
3.18	7	3.54	16
3.23	8	3.60	17.5
3.27	9	3.61	
3.42	13	3.70	
3.53	15	3.73	
3.60	17.5	3.83	
3.65		3.89	
3.65		3.99	
3.69		4.08	
		4.13	

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3.18	7	3.54	16
3.23	8	3.60	17.5
3.27	9	3.61	19
3.42	13	3.70	23
3.53	15	3.73	24
3.60	17.5	3.83	25
3.65	20.5	3.89	26
3.65	20.5	3.99	27
3.69	22	4.08	28
		4.13	29

Wilcoxon rank sum test: Example

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2.90	6	3.51	14
3.18	7	3.54	16
3.23	8	3.60	17.5
3.27	9	3.61	19
3.42	13	3.70	23
3.53	15	3.73	24
3.60	17.5	3.83	25
3.65	20.5	3.89	26
3.65	20.5	3.99	27
3.69	22	4.08	28
Rank sum: $R_1 = 150.5$		4.13	29

Rank sum: $R_0 = 284.5$

Wilcoxon rank sum test: Procedure

A non-parametric alternative to the two-sample t-test

Situation:

Two independent samples

No assumptions about distribution

Hypotheses:

$H_0 : F_{smokers} = F_{non\text{-}smokers}$

$H_1 : F_{smokers} \neq F_{non\text{-}smokers}$

Test statistic:

Follow algorithm:

1. Rank values from both groups together
2. T = rank sum in group with smaller sample size

Test decision for small sample size:

Use Table for critical values

If $T \leq W_{\alpha/2}$ or $T \geq W_{1-\alpha/2} \rightarrow$ reject H_0 at level α

Quantiles for Wilcoxon rank sum test

$W_{\alpha/2}$, $W_{1-\alpha/2}$

n_0, n_1	α=0.05	α=0.01	α=0.001
2, 8	3, 19		
2, 9	3, 21		
2, 10	3, 23		
2, 11	4, 24		
2, 12	4, 26		
2, 13	4, 28		
2, 14	4, 30		
2, 15	4, 32		
2, 16	4, 34		
2, 17	5, 35		
2, 18	5, 37		
2, 19	5, 39	3, 41	
2, 20	5, 41	3, 43	
2, 21	6, 42	3, 45	
2, 22	6, 44	3, 47	
2, 23	6, 46	3, 49	
2, 24	6, 48	3, 51	
2, 25	6, 50	3, 53	
3, 5	6, 21		
3, 6	7, 23		
3, 7	7, 26		
3, 8	8, 28		
3, 9	8, 31	6, 33	
3, 10	9, 33	6, 36	
3, 11	9, 36	6, 39	
3, 12	10, 38	7, 41	
3, 13	10, 41	7, 44	
3, 14	11, 43	7, 47	
3, 15	11, 46	8, 49	
3, 16	12, 48	8, 52	
3, 17	12, 51	8, 55	
3, 18	13, 53	8, 58	
3, 19	13, 56	9, 60	
3, 20	14, 58	9, 63	
3, 21	14, 61	9, 66	6, 69
3, 22	15, 63	10, 68	6, 72
3, 23	15, 66	10, 71	6, 75
3, 24	16, 68	10, 74	6, 78
3, 25	19, 71	11, 76	6, 81
4, 4	10, 26		
4, 5	11, 29		
4, 6	12, 32	10, 34	
4, 7	13, 35	10, 38	
4, 8	14, 38	11, 41	
4, 9	15, 41	11, 45	
4, 10	15, 45	12, 48	
4, 11	16, 48	12, 52	
4, 12	17, 51	13, 55	

n_0, n_1	α=0.05	α=0.01	α=0.001
4, 13	18, 54	14, 58	10, 62
4, 14	19, 57	14, 62	10, 66
4, 15	20, 60	15, 65	10, 70
4, 16	21, 63	15, 69	11, 73
4, 17	21, 67	16, 72	11, 77
4, 18	22, 70	16, 76	11, 81
4, 19	23, 73	17, 79	12, 84
4, 20	24, 76	18, 82	12, 88
4, 21	25, 79	18, 86	12, 92
4, 22	26, 82	19, 89	13, 95
4, 23	27, 85	19, 93	13, 99
4, 24	28, 88	20, 96	13, 103
4, 25	28, 92	20, 100	14, 106
5, 5	17, 38	15, 40	
5, 6	18, 42	16, 44	
5, 7	20, 45	17, 48	
5, 8	21, 49	17, 53	
5, 9	22, 53	18, 57	15, 60
5, 10	23, 57	19, 61	15, 65
5, 11	24, 61	20, 65	16, 69
5, 12	26, 64	21, 69	16, 74
5, 13	27, 68	22, 73	17, 78
5, 14	28, 72	22, 78	17, 83
5, 15	29, 76	23, 82	18, 87
5, 16	31, 79	24, 86	18, 92
5, 17	32, 83	25, 90	19, 96
5, 18	33, 87	26, 94	19, 101
5, 19	34, 91	27, 98	20, 105
5, 20	35, 95	28, 102	20, 110
5, 21	37, 98	29, 106	21, 114
5, 22	38, 102	29, 111	21, 119
5, 23	39, 106	30, 115	22, 123
5, 24	40, 110	31, 119	23, 127
5, 25	42, 113	32, 123	23, 132
6, 6	26, 52	23, 55	
6, 7	27, 57	24, 60	
6, 8	29, 61	25, 65	21, 69
6, 9	31, 65	26, 70	22, 74
6, 10	32, 70	27, 75	23, 79
6, 11	34, 74	28, 80	23, 85
6, 12	35, 79	30, 84	24, 90
6, 13	37, 83	31, 89	25, 95
6, 14	38, 88	32, 94	26, 100
6, 15	40, 92	33, 99	26, 106
6, 16	42, 96	34, 104	27, 111
6, 17	43, 101	36, 108	28, 116
6, 18	45, 105	37, 113	29, 121

Quantiles for Wilcoxon rank sum test

$W_{\alpha/2}$, $W_{1-\alpha/2}$

n_0, n_1	α=0.05	α=0.01	α=0.001
6, 19	46, 110	38, 118	29, 127
6, 20	48, 114	39, 123	30, 132
6, 21	50, 118	40, 128	31, 137
6, 22	51, 123	42, 132	32, 142
6, 23	53, 127	43, 137	33, 147
6, 24	55, 131	44, 142	34, 152
7, 7	36, 69	32, 73	28, 77
7, 8	38, 74	34, 78	29, 83
7, 9	40, 79	35, 84	30, 89
7, 10	42, 84	37, 89	31, 95
7, 11	44, 89	38, 95	32, 101
7, 12	46, 94	40, 100	33, 107
7, 13	48, 99	41, 106	34, 113
7, 14	50, 104	43, 111	35, 119
7, 15	52, 109	44, 117	36, 125
7, 16	54, 114	46, 122	37, 131
7, 17	56, 119	47, 128	38, 137
7, 18	58, 124	49, 133	39, 143
7, 19	60, 129	50, 139	41, 148
7, 20	62, 134	52, 144	42, 154
7, 21	64, 139	53, 150	43, 160
7, 22	66, 144	55, 155	44, 166
7, 23	68, 149	57, 160	45, 172
8, 8	49, 87	43, 93	38, 98
8, 9	51, 93	45, 99	40, 104
8, 10	53, 99	47, 105	41, 111
8, 11	55, 105	49, 111	42, 118
8, 12	58, 110	51, 117	43, 125
8, 13	60, 116	53, 123	45, 131
8, 14	63, 121	54, 130	46, 138
8, 15	65, 127	56, 136	47, 145
8, 16	67, 133	58, 142	49, 151
8, 17	70, 138	60, 148	50, 158
8, 18	72, 144	62, 154	51, 165
8, 19	74, 150	64, 160	53, 171
8, 20	77, 155	66, 166	54, 178
8, 21	79, 161	68, 172	56, 184
8, 22	82, 166	70, 178	57, 191
9, 9	63, 108	56, 115	50, 121
9, 10	65, 115	58, 122	52, 128
9, 11	68, 121	61, 128	53, 136
9, 12	71, 127	63, 135	55, 143
9, 13	73, 134	65, 142	56, 151
9, 14	76, 140	67, 149	58, 158

n_0, n_1	α=0.05	α=0.01	α=0.001
9, 15	79, 146	70, 155	60, 165
9, 16	82, 152	72, 162	61, 173
9, 17	84, 159	74, 169	63, 180
9, 18	87, 165	76, 176	65, 187
9, 19	90, 171	78, 183	66, 195
9, 20	93, 177	81, 189	68, 202
9, 21	95, 184	83, 196	70, 209
10, 10	78, 132	71, 139	63, 147
10, 11	81, 139	74, 146	65, 155
10, 12	85, 145	76, 154	67, 163
10, 13	88, 152	79, 161	69, 171
10, 14	91, 159	81, 169	71, 179
10, 15	94, 166	84, 176	73, 187
10, 16	97, 173	86, 184	75, 195
10, 17	100, 180	89, 191	77, 203
10, 18	103, 187	92, 198	79, 211
10, 19	107, 193	94, 206	81, 219
10, 20	110, 200	97, 213	83, 227
11, 11	96, 157	87, 166	78, 175
11, 12	99, 165	90, 174	81, 183
11, 13	103, 172	93, 182	83, 192
11, 14	106, 180	96, 190	85, 201
11, 15	110, 187	99, 198	87, 210
11, 16	114, 194	102, 206	90, 218
11, 17	117, 202	105, 214	92, 227
11, 18	121, 209	108, 222	94, 236
11, 19	124, 217	111, 230	97, 244
12, 12	115, 185	106, 194	95, 205
12, 13	119, 193	109, 203	98, 214
12, 14	123, 201	112, 212	100, 224
12, 15	127, 209	115, 221	103, 233
12, 16	131, 217	119, 229	105, 243
12, 17	135, 225	122, 238	108, 252
12, 18	139, 233	125, 247	111, 261
13, 13	137, 214	125, 226	114, 237
13, 14	141, 223	129, 235	116, 248
13, 15	145, 232	133, 244	119, 258
13, 16	150, 240	137, 253	122, 268
13, 17	154, 249	140, 263	125, 278
14, 14	160, 246	147, 259	134, 272
14, 15	164, 256	151, 269	137, 283
14, 16	169, 265	155, 279	140, 294
15, 15	185, 280	171, 294	156, 309

Wilcoxon rank sum test: Procedure

A non-parametric alternative to the two-sample t-test

Situation:

Two independent samples
No assumptions about distribution

Hypotheses:

$H_0 : F_{smokers} = F_{non\text{-}smokers}$
$H_1 : F_{smokers} \neq F_{non\text{-}smokers}$

Test statistic:

Follow algorithm:
1. Rank values from both groups together
2. T = rank sum in group with smaller sample size

→ Example: T = 150.5

Test decision for small sample size:

150.5 < 164 $\rightarrow$ reject H_0 at 5% level

n_0, n_1	α=0.05	α=0.01	α=0.001
14, 14	160, 246	147, 259	134, 272
14, 15	164, 256	151, 269	137, 283
14, 16	169, 265	155, 279	140, 294
15, 15	185, 280	171, 294	156, 309

Wilcoxon rank sum test: Procedure (2)

A non-parametric alternative to the two-sample t-test

Test decision for large sample size:

$$z = \frac{R_1 - \frac{n_1(n_0+n_1+1)}{2}}{\sqrt{\frac{n_1 n_0 (n_0+n_1+1)}{12}}} = -2.597$$

z has Standard Normal Distribution $\rightarrow$ compare with quantile $z_{1-\alpha/2}$ from SND

If $|z| > 1.96 \rightarrow$ reject H_0 at 5% level

It makes no difference which group is chosen for evaluation of rank sum:

$$\frac{R_1 - \frac{n_1(n_0+n_1+1)}{2}}{\sqrt{\frac{n_1 n_0 (n_0+n_1+1)}{12}}} = -\frac{R_0 - \frac{n_0(n_0+n_1+1)}{2}}{\sqrt{\frac{n_1 n_0 (n_0+n_1+1)}{12}}}$$

Wilcoxon rank sum test
What is a large sample size?

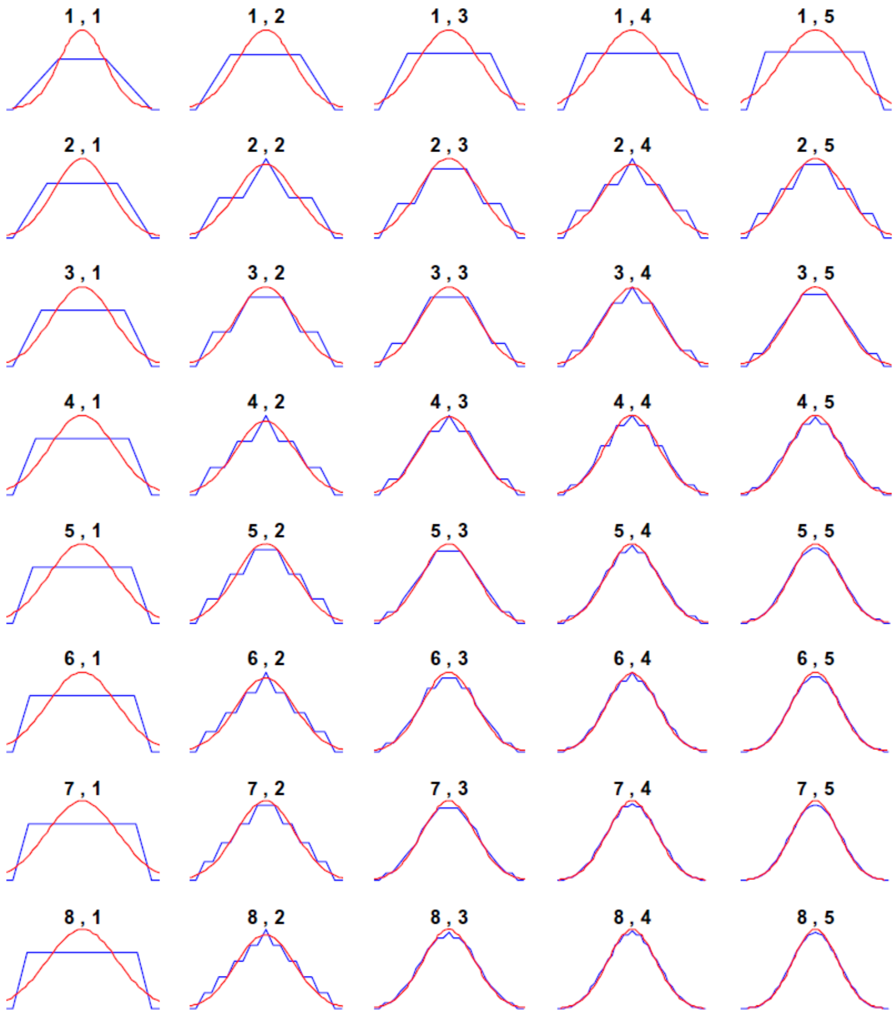


Figure 4. Exact distribution of the Wilcoxon rank-sum statistic for samples of sizes $n_1 = 1$ to 5 and $n_2 = 1$ to 8, and curve of the normal distribution with mean $(n_1 + n_2 + 1)/2$ and variance $n_1 n_2 (n_1 + n_2 + 1)/12$.

From: Bellera et al, J Stat Edu 2010.

dkfz.

Wilcoxon rank sum test: Remarks

Wilcoxon rank sum test = Mann-Whitney U-test

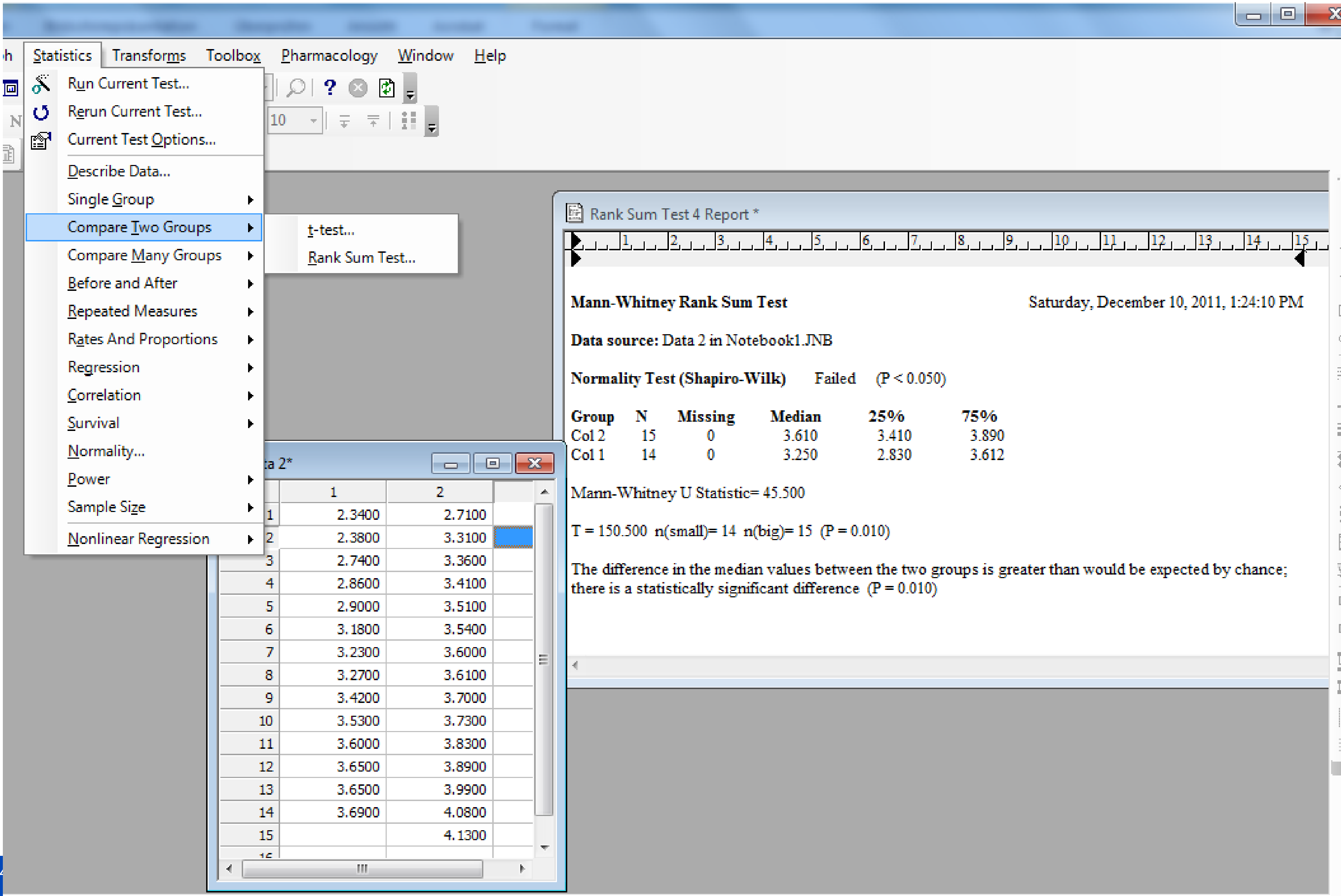
$$U = R_1 - \frac{n_1(n_1+1)}{2} = 150.5 - 105 = 45.5$$

U: test statistic for Mann-Whitney U-test

- If distribution in the two groups differ only by shift in location, the Wilcoxon rank sum test tests for the difference of two medians.
- In this situation confidence interval for difference of medians:
  Hodges-Lehmann estimate.
- If number of ties is large, then use correction for ties.

Wilcoxon rank sum test in SigmaPlot

A non-parametric alternative to the two-sample t-test



Wilcoxon rank sum test in Web tool

Mann-Whitney U Test Calculator

The value of U is 45.5.

You'll notice below that we have calculated a critical value for U based on alpha level and whether your hypothesis is one or two tailed. We have also calculated a value for *Z* and its associated *p*-value. Results in blue reach significance. Results in red do not.

Sample 1	Sample 2
2.34	2.71
2.38	3.31
2.74	3.36
2.86	3.41
2.90	3.51
3.18	3.54
3.23	3.60
3.27	3.61
3.42	3.70
3.53	3.73
3.60	3.83
3.65	3.89
3.65	3.99
3.69	4.08
	4.13

https://www.socscistatistics.com/tests/mannwhitney/default2.aspx

Significance Level:

- ○ .01
- ◉ .05

1 or 2-tailed hypothesis?:

- ○ One-tailed
- ◉ Two-tailed

The *U*-value is 45.5. The critical value of *U* at $p < .05$ is 59. Therefore, the result is significant at $p < .05$.

The *z*-score is 2.57497. The *p*-value is .01016. The result is significant at $p < .05$.

Wilcoxon rank sum test in Web tool

Sample 1	Sample 2	*S1 Values*	*S1 Ranks*	*S2 Values*	*S2 Ranks*
2.34	2.71	2.34	1	2.71	3
2.38	3.31	2.38	2	3.31	10
2.74	3.36	2.74	4	3.36	11
2.86	3.41	2.86	5	3.41	12
2.90	3.51	2.9	6	3.51	14
3.18	3.54	3.18	7	3.54	16
3.23	3.60	3.23	8	3.6	17.5
3.27	3.61	3.27	9	3.61	19
3.42	3.70	3.42	13	3.7	23
3.53	3.73	3.53	15	3.73	24
3.60	3.83	3.6	17.5	3.83	25
3.65	3.89	3.65	20.5	3.89	26
3.65	3.99	3.65	20.5	3.99	27
3.69	4.08	3.69	22	4.08	28
	4.13			4.13	29

Significance Level:

- ○ 0.01
- ◉ 0.05

1 or 2-tailed hypothesis?:

- ○ One-tailed
- ◉ Two-tailed

Result Details

Sample 1
Sum of ranks: 150.5
Mean of ranks: 10.75
Expected sum of ranks: 210
Expected mean of ranks: 15
U-value: 164.5
Expected *U*-value: 105

Sample 2
Sum of ranks: 284.5
Mean of ranks: 18.97
Expected sum of ranks: 225
Expected mean of ranks: 15
U-value: 45.5
Expected *U*-value: 105

Sample 1 & 2 Combined
Sum of ranks: 435
Mean of ranks: 15
Standard Deviation: 22.9129

Result 1 - U-value

The *U*-value is 45.5. The critical value of *U* at *p* < .05 is 59. Therefore, the result is significant at *p* < .05.

Result 2 - Z-ratio

The *Z*-Score is 2.57497. The *p*-value is .01016. The result is significant at *p* < .05.

Test Procedures for Quantitative Variables: Comparison of Means

Parametric test (assuming normal distribution)	*Non-parametric test*
1 sample: One-sample t-test	
2 paired samples: paired t-test	*Sign test, Wilcoxon signed rank test*
2 independent samples: t-test, Welch-test	*Wilcoxon rank sum test (= Mann-Whitney U-test)*
≥ 3 independent samples: Analysis of Variance (ANOVA)	*Kruskal-Wallis-test*

Kruskal-Wallis test: Example

Effect of gene knock down on tumor volume (cf. ANOVA lecture, 10 Oct 2018):

Wild	knock.A	knock.B
26	50	20
46	75	50
63	60	6
20	72	48
61	120	72
56	80	60

Kruskal-Wallis test: Example

A non-parametric alternative to ANOVA

Effect of gene knock down on tumor volume:

Wild	rank	knock.A	rank	knock.B	rank
26	4	50	7.5	20	2.5
46	5	75	16	50	7.5
63	13	60	10.5	6	1
20	2.5	72	14.5	48	6
61	12	120	18	72	14.5
56	9	80	17	60	10.5

Kruskal-Wallis test: Example

A non-parametric alternative to ANOVA

Effect of gene knock down on tumor volume:

Wild	rank	knock.A	rank	knock.B	rank
26	4	50	7.5	20	2.5
46	5	75	16	50	7.5
63	13	60	10.5	6	1
20	2.5	72	14.5	48	6
61	12	120	18	72	14.5
56	9	80	17	60	10.5

Rank sum $R_1 = 45.5$
$n_1 = 6$
$\bar{R}_1 = R_1 / n_1 = 7.583$

Rank sum $R_2 = 83.5$
$n_2 = 6$
$\bar{R}_2 = R_2 / n_2 = 13.912$

Rank sum $R_3 = 42$
$n_3 = 6$
$\bar{R}_3 = R_3 / n_3 = 7.0$

Kruskal-Wallis test: Procedure

A non-parametric alternative to ANOVA

Situation:

Three or more independent samples

No assumptions about distribution, but distributions have same shape

Hypotheses:

$H_0 : F_1 = F_2 = \ldots = F_k$

H_1 : not all distributions are equal

Test statistic:

Follow algorithm:

1. Rank values from all groups together
2. Calculate in each group rank sum R_i and mean rank $\bar{R}_i$
3. Calculate test statistic

$$H = \frac{12}{N(N+1)} \sum_{i=1}^{k} n_i \left(\bar{R}_i - \frac{N+1}{2} \right)^2 = \frac{12}{N(N+1)} \sum_{i=1}^{k} \frac{R_i^2}{n_i} - 3(N+1)$$

If number of ties large, then use correction for ties.

Test decision:

H has χ^2_{k-1}-distribution: If H > $\chi^2_{k-1,1-\alpha}$ $\rightarrow$ reject H_0 at level α

Kruskal-Wallis test: Example calculation

A non-parametric alternative to ANOVA

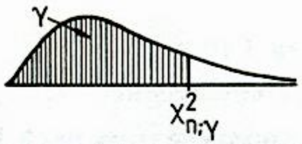
Test statistic:

$$H=\frac{12}{N(N+1)}\sum_{i=1}^{k}n_i\left(\bar{R}_i-\frac{N+1}{2}\right)^2=\frac{12}{N(N+1)}\sum_{i=1}^{k}\frac{R_i^{\,2}}{n_i}-3(N+1)$$

$$=\frac{12}{18(18+1)}\,\frac{45.5^2+83.5^2+42^2}{6}-3\cdot(18+1)=6.196$$

Test decision:

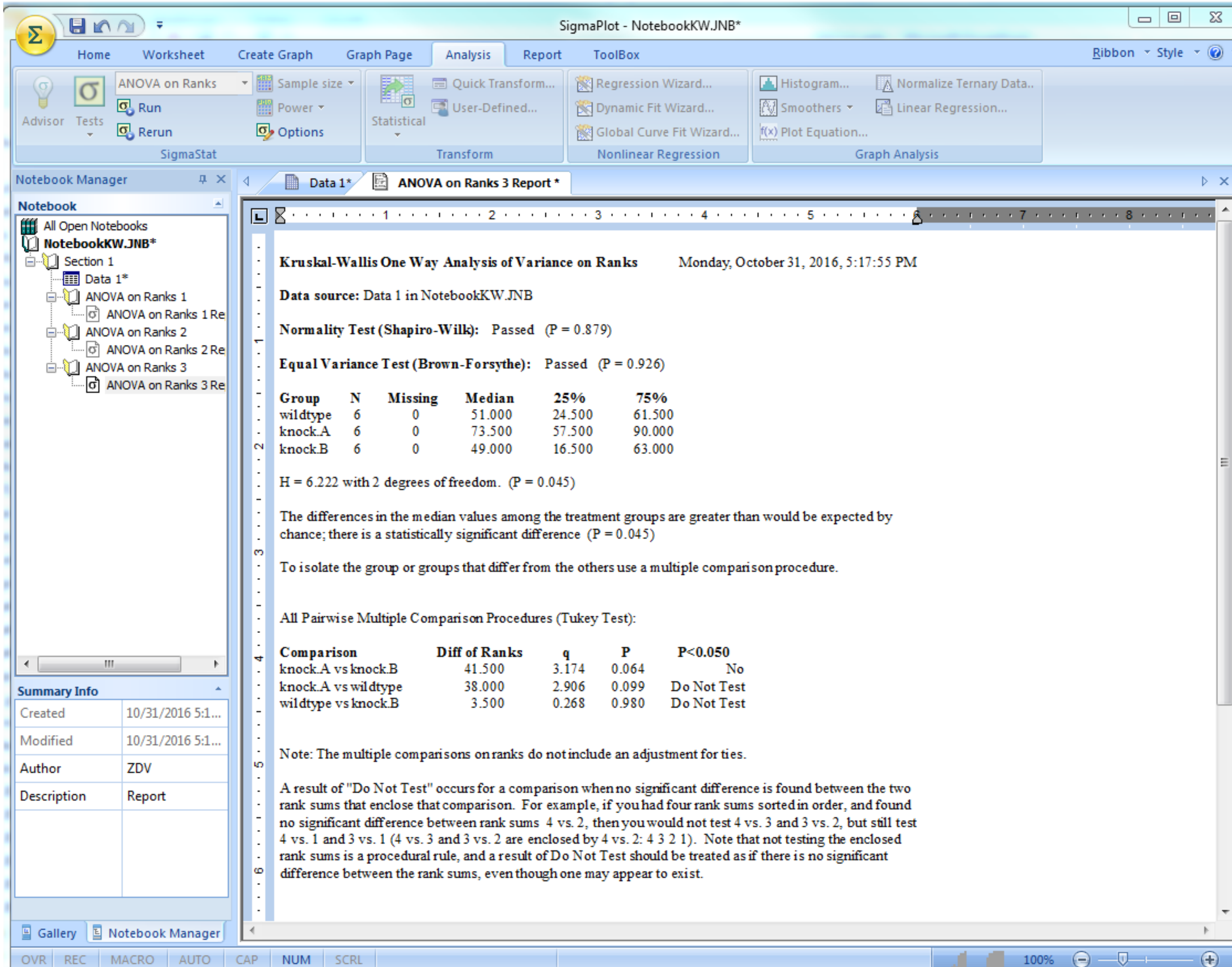
H has $\chi^2_{3-1}=\chi^2_2$-distribution: 6.196 > 5.991 → reject H_0 at 5% level



Tab. 4: Quantile $\chi^2_{n;\gamma}$ der χ^2-Verteilung

n \ γ	0,995	0,990	0,975	0,950	0,900	0,750	0,500	0,250	0,100	0,050	0,025	0,010	0,005
1	7,879	6,635	5,024	3,841	2,706	1,323	0,455	0,102	$^{-2}$1,58	$^{-3}$3,93	$^{-4}$9,82	$^{-4}$1,57	$^{-5}$3,93
2	10,60	9,210	7,378	5,991	4,605	2,773	1,386	0,575	0,211	0,103	$^{-2}$5,06	$^{-2}$2,01	$^{-2}$1,00
3	12,84	11,34	9,348	7,815	6,251	4,108	2,366	1,213	0,584	0,352	0,216	0,115	$^{-2}$7,17
4	14,86	13,28	11,14	9,488	7,779	5,385	3,357	1,923	1,064	0,711	0,484	0,297	0,207
5	16,75	15,09	12,83	11,07	9,236	6,626	4,351	2,675	1,610	1,145	0,831	0,554	0,412

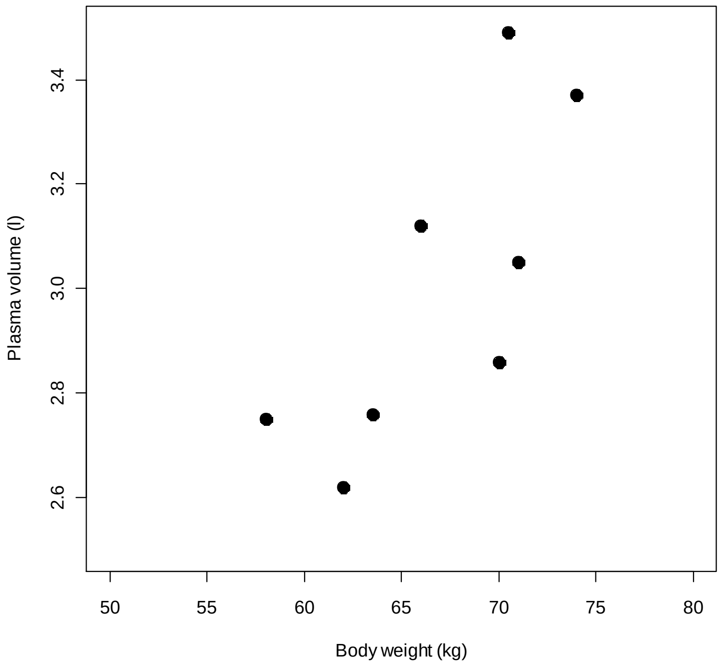
Kruskal-Wallis test in SigmaPlot



Bivariate Analysis:
Investigating the association between two variables

A non-parametric alternative to Pearson correlation:

Spearman rank correlation

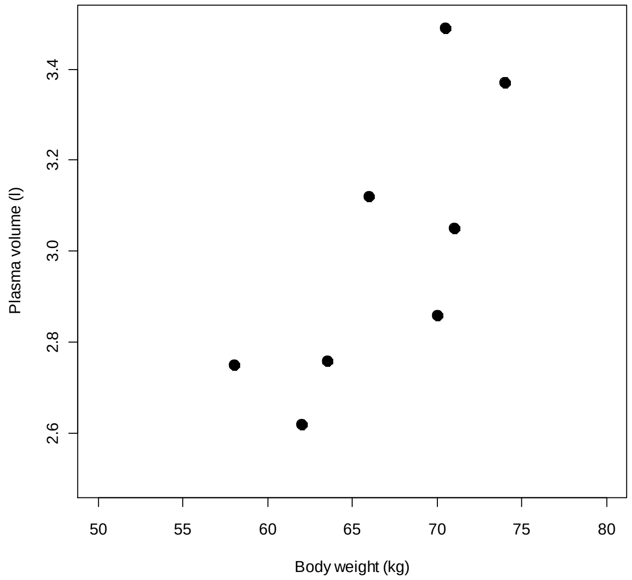


Spearman rank correlation: Example

A non-parametric alternative to Pearson correlation

Example: Plasma volume and body weight in eight healthy men:

Subject	Body weight (kg) value	Plasma volume (l) value
1	58.0	2.75
2	70.0	2.86
3	74.0	3.37
4	63.5	2.76
5	62.0	2.62
6	70.5	3.49
7	71.0	3.05
8	66.0	3.12



Spearman rank correlation

A non-parametric alternative to Pearson correlation

- Independently rank the values of X and Y
- Calculate Pearson's correlation for the ranks

Subject	Body weight (kg) value	Body weight (kg) rank	Plasma volume (l) value	Plasma volume (l) rank
1	58.0	1	2.75	2
2	70.0	5	2.86	4
3	74.0	8	3.37	7
4	63.5	3	2.76	3
5	62.0	2	2.62	1
6	70.5	6	3.49	8
7	71.0	7	3.05	5
8	66.0	4	3.12	6

Spearman rank correlation: test

A non-parametric alternative to Pearson correlation

Significance test for Spearman rank correlation coefficient r_S:
Use test for Pearson correlation coefficient if $n \geq 10$, i.e.

$$t = r_S \sqrt{\frac{n-2}{1-{r_S}^2}}$$

and compare with t distribution, n-2 d.f.

$r_S = 0.81$

$t = 3.378$

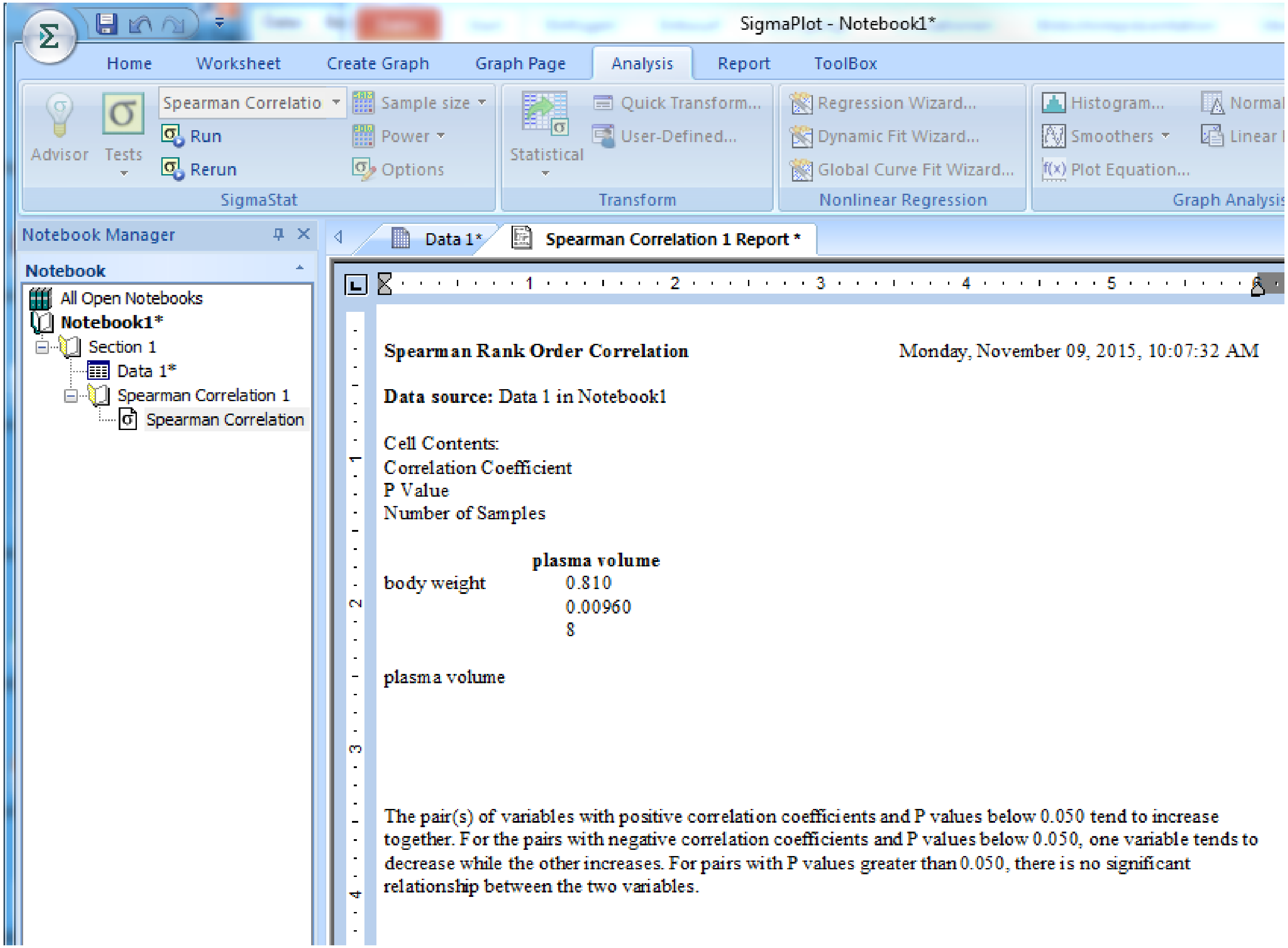
$t = 3.378 > 2.447 = t_{6,0.975}$
→ reject H_0 at 5% significance level

Quantiles $t_{n,\gamma}$ of t-distribution

n \ γ	0,990	0,975	0,950	0,900
1	31,821	12,706	6,314	3,078
2	6,965	4,303	2,920	1,886
3	4,541	3,182	2,353	1,638
4	3,747	2,776	2,132	1,533
5	3,365	2,571	2,015	1,476
6	3,143	$\boxed{2,447}$	1,943	1,440
7	2,998	2,365	1,895	1.415

Spearman rank correlation in SigmaPlot

A non-parametric alternative to Pearson correlation



Non-parametric methods

Advantages …

- Don‘t require the assumption that data come from a Normal distribution.
- Robust to outliers.
- Robust against misspecification of distribution assumption.
- For large sample size almost as powerful as parametric methods.
- (Easy to calculate manually)

Disadvantages …

- Less power than parametric tests when data come from Normal distribution.
- May have power 0 for small samples: e.g. two-sided Wilcoxon rank sum test for 3 vs. 3 samples at 5% level.
- Difficult to obtain confidence intervals.
- Not easily extended to regression models.

When to use non-parametric methods

- If no data transformation is available to transform data to normal distribution.

- In the presence of outliers.

- From formal perspective:
  Automatic choice between parametric and non-parametric test, e.g. by Shapiro-Wilks test for normality, is not advised.
  But from practical perspective: preliminary testing for normality does not seem to cause much harm (see Rochon et al. BMC Medical Research Methodology 2012, 12:81).

- Similar data should be evaluated with the same test.

- **Do not** run both parametric and non-parametric test and choose p-value you like!

- For large samples non-parametric nearly as powerful as parametric tests.

Next lexture

11 November

Diagnostic tests

Dr. Diana Tichy