Non-parametric tests and ANOVA

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Parametric vs. non-parametric tests

- Non parametric tests:
  - No normality requirement
  - The underlying distributions being compared have the same basic shape
  - Ranks are less sensitive to outliers and to measurement error
- If the underlying distributions are approximately normal, then the parametric tests are more powerful

Non-parametric tests

	Paired data	TWO independent data
1. Set up hypothesis Determine α	H_0: median 1= median 2	
2. Decide a test statistic	The Sign test: Z_+ The Wilcoxon signed-rank test: Z_T	The Wilcoxon Rank Sum Test (the Mann-Whitney U test) : Z_W
3. Set up the decision rule	e.g. reject the null if p-value< α	
4. Compute the test statistic	$Z_+ = \frac{D-(n/2)}{\sqrt{n/4}}$ $z_T = (T - m_T)/\sigma_T$	$z_W = (W - m_W)/\sigma_W$
5. Conclusion	Reject the null / not to reject the null	

In STATA	The sign test
	`signtest var1=var2`
	The Wilcoxon signed-rank test
	`signrank var1=var2`
		`ranksum var, by(byvar)`

The Sign Test

RR

Subject	Time 1	Time 2	Difference	Sign
1	62	46	16	+
2	35	42	-7	-
3	38	40	-2	-
4	80	42	38	+
5	48	36	12	+
6	48	46	2	+
7	68	45	23	+
8	26	40	-14	-
9	48	42	6	+
10	27	40	-13	-

D: Number of +

n: Number of subjects

Z+ =0.63

of + = 6

The Wilcoxon Signed-rank Test

RR

Subject	Time 1	Time 2	Difference	Rank	Signed rank
1	62	46	16	7	
2	35	42	-7	4	-4
3	38	40	-2	1.5	-1.5
4	80	42	38	9	
5	48	36	12	5	
6	48	46	2	1.5	
7	68	45	23	8	
8	26	40	-14	6	-6
9	48	42	6	3	
10	27	40	-13	5	-5
			Sum of rank	33.5	-16.5

$z_T = (T - m_T)/\sigma_T$

T= 16.5

mT=n*(n+1)/4= 27.5

σT=sqrt(N*(n+1)*(2n+1)/24)= 9.81

zT= -1.12

The Wilcoxon Rank Sum Test

RR at Time 1 (Ns=10)	Rank	RR at Time 2 (Nl=12)	Rank
62	18	46	12.5
35	3	42	9
38	5	40	7
80	20	42	9
48	16	36	4
48	16	46	12.5
68	19	45	12
26	1	40	7
48	16	42	9
27	2	85	21
Sum of rank	116	88	22
		40	7
		Sum of rank	132

$z_W = (W - m_W) / \sigma_W$

W=116

mW=Ns(Ns+Nl+1)/2=115

σW= sqrt(Ns*Nl*(Ns+Nl+1)/12)=15.17

zW=0.07

Non-parametric tests for multiple independent samples

- The Kruskal-Wallis Test : extension of the Wilcoxon rank sum test for 2 or more independent samples. In Stata:

```
kwallis var, by(byvar)
```

- Analogous to one-way analysis of variance

ANOVA

- Testing for a difference in more than two independent means.

  H_0: all means are equal

  $\mu_1=\mu_2=\ldots=\mu_K$

  H_A: at least one mean is different from others

ANOVA

- The test statistic for testing H_0:

$$F = \frac{s_B^2}{s_W^2}$$

Between group variability

$$s_B^2 = \frac{n_1(\bar{x}_1 - \bar{X})^2 + n_2(\bar{x}_2 - \bar{X})^2 + \ldots + n_k(\bar{x}_k - \bar{X})^2}{k-1}$$

Within group variability

$$s_W^2 = \frac{(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2 + \ldots + (n_k - 1)s_k^2}{n_1 + n_2 + \ldots + n_k - k}$$

- Decision rule for F test:

  - the level of significance level

  - two degrees of freedom: df_1=k-1, df_2=n-k

Example: Does balance performance differ by chemotherapy combination in patients with CIPN?

	ptid	ctxcombo	fabtot0
2.	1003	Only Taxan	34
3.	1004	Only Plati	38
4.	1005	Only Taxan	39
5.	1006	Only Plati	34
10.	1011	Both Plati	28
11.	1012	Only Plati	26
12.	1014	Only Taxan	40
15.	1018	Only Taxan	38
	….....		
397.	1493	Both Plati	15
398.	1497	Only Taxan	25
399.	1498	Only Plati	36

Table1. FAB scale dimensions (Danielle Hernandez et al 2009)

Static Balance	
item 2	Reach forward to retrieve object Stand
item 6	on one leg
Dynamic Balance	
item 3	Turn in a full circle
item 4	Step up and over 6 inch bench
item 5	Tandem walk
item 8	Two-footed jump
Sensory Reception and Integration	
item 1	Stand with feet together & eyes closed Stand on
item 7	foam with eyes closed
item 9	Walk with head turns
Reactive Postural Control	
item 10	Reactive postural control

H_0: $\mu_1=\mu_2=\mu_3$

H_A: at least one mean is different from others

$\alpha=0.05$

F statistic: ANOVA table

Source of variation	Sum of squares (SS)	Degree of freedom (df)	Mean squares (MS)	F
Between groups	$n_1(\bar{x}_1-\bar{x})^2+\ldots+n_{393}(\bar{x}_{393}-\bar{x})^2$ 371.11	df_1=k-1 3-1 = 2	= 371.11/2 = 185.55	=185.55/52.58 =3.53
Within group	$(n_1-1)s_1^2+\ldots+(n_{393}-1)s_{393}^2$ 11725.35	df_2=n-k 226-3 = 223	=11725.35/223 =52.58	
Total	12096.46	225		

In Stata

oneway var groupvar

```
. oneway fabtot0 ctxcombo if anypainbpi==1

                        Analysis of Variance
    Source              SS         df      MS            F     Prob > F
------------------------------------------------------------------------
Between groups      371.106612      2   185.553306      3.53     0.0310
 Within groups      11725.3536    223   52.5800608
------------------------------------------------------------------------
    Total           12096.4602    225   53.7620452

Bartlett's test for equal variances:  chi2(2) =  20.3281  Prob>chi2 =
0.000
```

reject the null hypothesis of equal means.

Bonferroni method for multiple comparisons

- The Bonferroni methods divides α by the number of possible pairs of tests

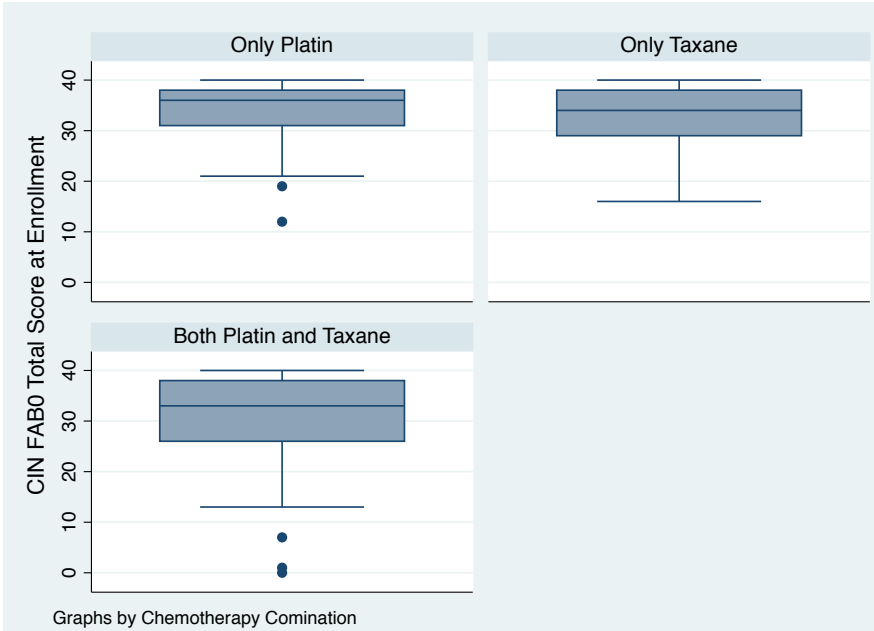
$$\alpha^* = \frac{\alpha}{\binom{k}{2}}$$

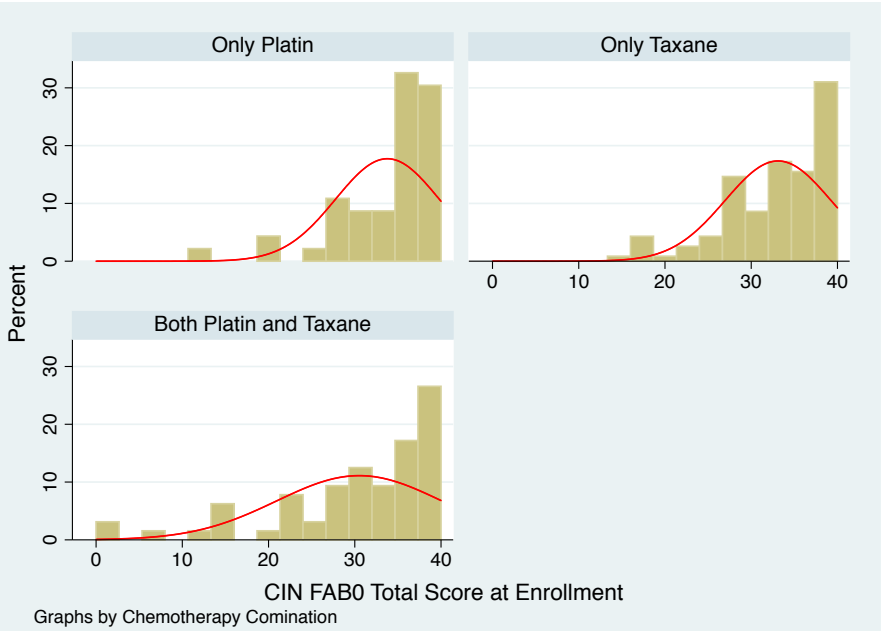
In Stata: `oneway var groupvar, bonferroni`

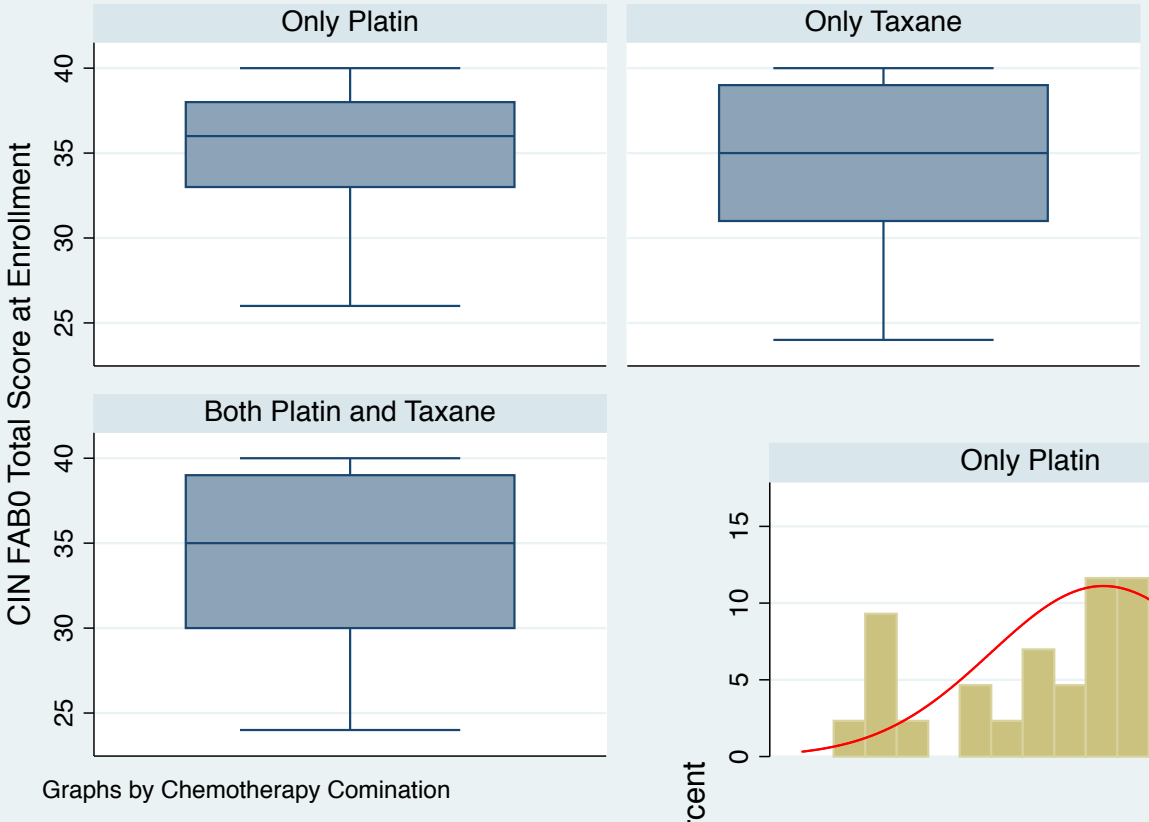
ANOVA

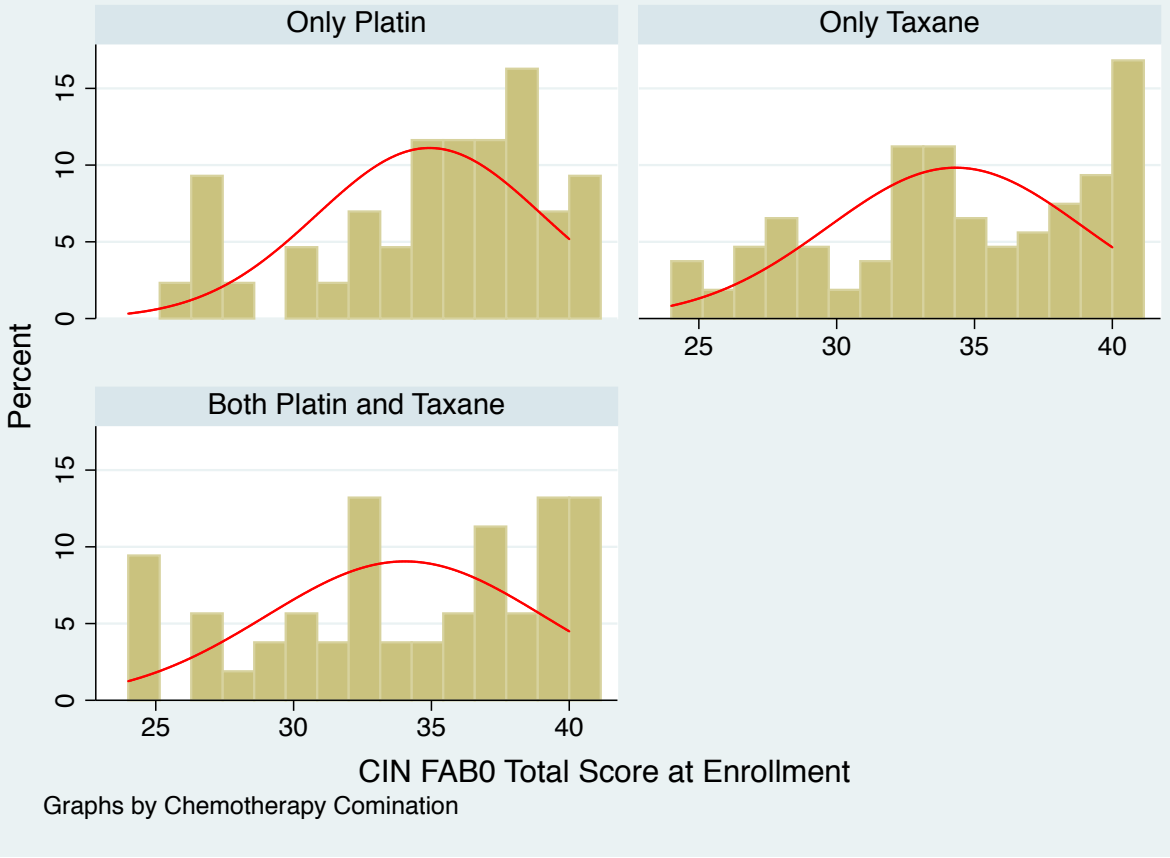
- Assumptions:
  - normal distribution
  - independent observations
  - homoscedasticity

```
. tabstat fabtot0 if anypainbpi==1, by(ctxcombo) s(n mean sd p25 median p75)

Summary for variables: fabtot0
     by categories of: ctxcombo (Chemotherapy Comination)

        ctxcombo |         N      mean        sd       p25       p50       p75
-----------------+--------------------------------------------------------------
     Only Platin |        46  33.78261  5.999678        31        36        38
     Only Taxane |       116  33.11207  6.134396        29        34        38
Both Platin and  |        64  30.51563  9.576745        26        33        38
-----------------+--------------------------------------------------------------
           Total |       226  32.51327  7.332261        29        34        38
-------------------------------------------------------------------------------
```






Only Platin
Only Taxane
Both Platin and Taxane
CIN FAB0 Total Score at Enrollment
25
30
35
40
Graphs by Chemotherapy Comination


Only Platin
Only Taxane
Both Platin and Taxane
Percent
0
5
10
15
25
30
35
40
CIN FAB0 Total Score at Enrollment
Graphs by Chemotherapy Comination

```
. oneway fabtot0 ctxcombo if anypainbpi==1 &fabtot0>23

                        Analysis of Variance
    Source              SS         df      MS             F     Prob > F
------------------------------------------------------------------------
Between groups      19.6353104      2   9.81765519      0.46     0.6346
 Within groups      4307.91149    200   21.5395574
------------------------------------------------------------------------
    Total            4327.5468    202    21.423499

Bartlett's test for equal variances:  chi2(2) =   1.9062  Prob>chi2 = 0.386
```

Fail to reject the null, mean FAB scores in CIPN patients receiving three kinds of chemotherapy regimens are identical.

Alternatives to F-test in ANOVA to deal with Heterogeneity

- Use non-parametric tests (the Kruskal-Wallis test)
- Transform original outcome using square roots, log-/ arcsine transformations
- Use robust methods, e.g. two-sample Welch-test (Rasch et al 2009).
- Select a new critical value of F at a more stringent significance level, not appropriate (Moder 2010).

The Kruskal-Wallis Test

```
Kruskal-Wallis equality-of-populations rank test

  +-----------------------------+
  |   ctxcombo | Obs | Rank Sum |
  |------------+-----+----------|
  | Only Plati |  46 |  5618.00 |
  | Only Taxan | 116 | 13456.00 |
  | Both Plati |  64 |  6577.00 |
  +-----------------------------+

chi-squared =     2.696 with 2 d.f.
probability =     0.2598

chi-squared with ties =     2.710 with 2 d.f.
probability =     0.2580
```