

# بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ

# طراحی و تحلیل کارآزمایی های بالینی متقاطع: **Crossover Trials**

## بخش دوم : تحلیل در نرم افزار

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# نرم افزارهای تحلیل: Crossover



# چیدمان اولیه داده ها:

	id	seq	period1	period2	
1	1	1	74.675	73.675	
2	4	1	96.4	93.25	
3	5	1	101.95	102.125	
4	6	1	79.05	69.45	
5	11	1	79.05	69.025	
6	12	1	85.95	68.7	
7	15	1	69.725	59.425	
8	16	1	86.275	76.125	
9	19	1	112.675	114.875	
10	20	1	99.525	116.25	
11	23	1	89.425	64.175	
12	24	1	55.175	74.575	
13	2	2	74.825	37.35	
14	3	2	86.875	51.925	
15	7	2	81.675	72.175	
16	8	2	92.7	77.5	
17	9	2	50.45	71.875	
18	10	2	66.125	94.025	
19	2/15/2023 13	2	122.45	124.975	

# تغییر قالب داده ها جهت انجام تحلیل: Db pkshape

The screenshot shows the Stata software interface. The 'Statistics' menu is open, displaying various analysis options. The 'Epidemiology and related' sub-menu is also open, showing options like 'ROC analysis', 'Tables for epidemiologists', and 'Other'. The 'Other' sub-menu is further expanded, showing options such as 'Symmetry and marginal homogeneity test', 'Direct standardization', 'Indirect standardization', 'Interrater agreement, two unique raters', 'Define weights for the above (kap)', 'Interrater agreement, nonunique raters', 'Interrater agreement, nonunique raters with frequencies', 'Brier score decomposition', 'Pharmacokinetic measures', 'Summarize pharmacokinetic data', 'Reshape pharmacokinetic Latin-square data', 'Analyze crossover experiments', and 'Bioequivalence tests'. In the background, a table of results is visible, showing the following data:

	df	MS	F	Prob > F
Carryover variable = carry				
ID variable = id				
over study				
	2	1.33	0.19	0.8358
	3	7.00	2.62	0.1451
Multivariate time series	2	15.83	5.94	0.0378
Spatial autoregressive models	2	2.17	0.81	0.4872
Longitudinal/panel data	2	110.57	41.46	0.0003
Multilevel mixed-effects models	6	2.67		
Survival analysis	17			

pkshape id seq period1 period2, order(AB BA)

pkshape - Reshape (pharmacokinetic) Latin-square data

Identification variable: id  
Sequence variable: seq  
First period variable: period1

Remaining period variables: period2

Options

Treatments applied in this order: (example: "abc cba bac")  
AB BA

Customize names for new variables:

Outcome variable:  Treatment variable:  Carryover variable:  
 Sequence variable:  Period variable:

OK Cancel Submit

# قالب یا الگوی جدید داده بعد از تغییر

	id	sequence	outcome	treat	carry	period
1	1	AB	74.675	A	0	1
2	4	AB	96.4	A	0	1
3	5	AB	101.95	A	0	1
4	6	AB	79.05	A	0	1
5	11	AB	79.05	A	0	1
6	12	AB	85.95	A	0	1
7	15	AB	69.725	A	0	1
8	16	AB	86.275	A	0	1
9	19	AB	112.675	A	0	1
10	20	AB	99.525	A	0	1
11	23	AB	89.425	A	0	1
12	24	AB	55.175	A	0	1
13	2	BA	74.825	B	0	1
14	3	BA	86.875	B	0	1
15	7	BA	81.675	B	0	1
16	8	BA	92.7	B	0	1
17	9	BA	50.45	B	0	1
18	10	BA	66.125	B	0	1
19	13	BA	122.45	B	0	1
20	14	BA	99.075	B	0	1
21	17	BA	86.35	B	0	1
22	18	BA	49.925	B	0	1
23	21	BA	42.7	B	0	1
24	22	BA	91.725	B	0	1

2/15/2023

7 دکتر محمد حیدری : استادیار اپیدمیولوژی ، گروه اپیدمیولوژی ، دانشکده پزشکی دانشگاه علوم پزشکی ارومیه

# مسیر انجام تحلیل اصلی : Db pkcross

Original outcomes  
Categorical outcomes  
Count outcomes  
Fractional outcomes  
Generalized linear models  
Choice models  
Time series  
Multivariate time series  
Spatial autoregressive models  
Longitudinal/panel data  
Multilevel mixed-effects models  
Survival analysis  
Epidemiology and related  
Endogenous covariates  
Sample-selection models  
Treatment effects  
SEM (structural equation modeling)  
LCA (latent class analysis)  
FMM (finite mixture models)  
IRT (item response theory)  
Multivariate analysis  
Survey data analysis  
Lasso  
Meta-analysis  
Multiple imputation  
Nonparametric analysis  
Exact statistics

AB BA)

Sequence variable = sequence  
Period variable = period  
Treatment variable = treat  
Carryover variable = carry  
ID variable = id

Crossover study

	df	MS	F	Prob > F
1		62.79	0.38	0.5468
1		35.97	0.22	0.0005
22		167.25		

47

treatment and carryover = 29.28

ROC analysis  
Tables for epidemiologists  
Other

Symmetry and marginal homogeneity test  
Symmetry and marginal homogeneity test calculator  
Direct standardization  
Indirect standardization  
Interrater agreement, two unique raters  
Define weights for the above (kap)  
Interrater agreement, nonunique raters  
Interrater agreement, nonunique raters with frequencies  
Brier score decomposition  
Pharmacokinetic measures  
Summarize pharmacokinetic data  
Reshape pharmacokinetic Latin-square data  
Analyze crossover experiments  
Bioequivalence tests



# تعیین پارامترهای مختلف تحلیل:

pkcross - Analyze crossover experiments

Model if/in Parameterization

Outcome variable:  
outcome

Options

Sequence variable: sequence Treatment variable: treat

Period variable: period ID variable: id

Carryover variable:  
 carry  None

Specify the model to fit: (default is "sequence period treat carry")

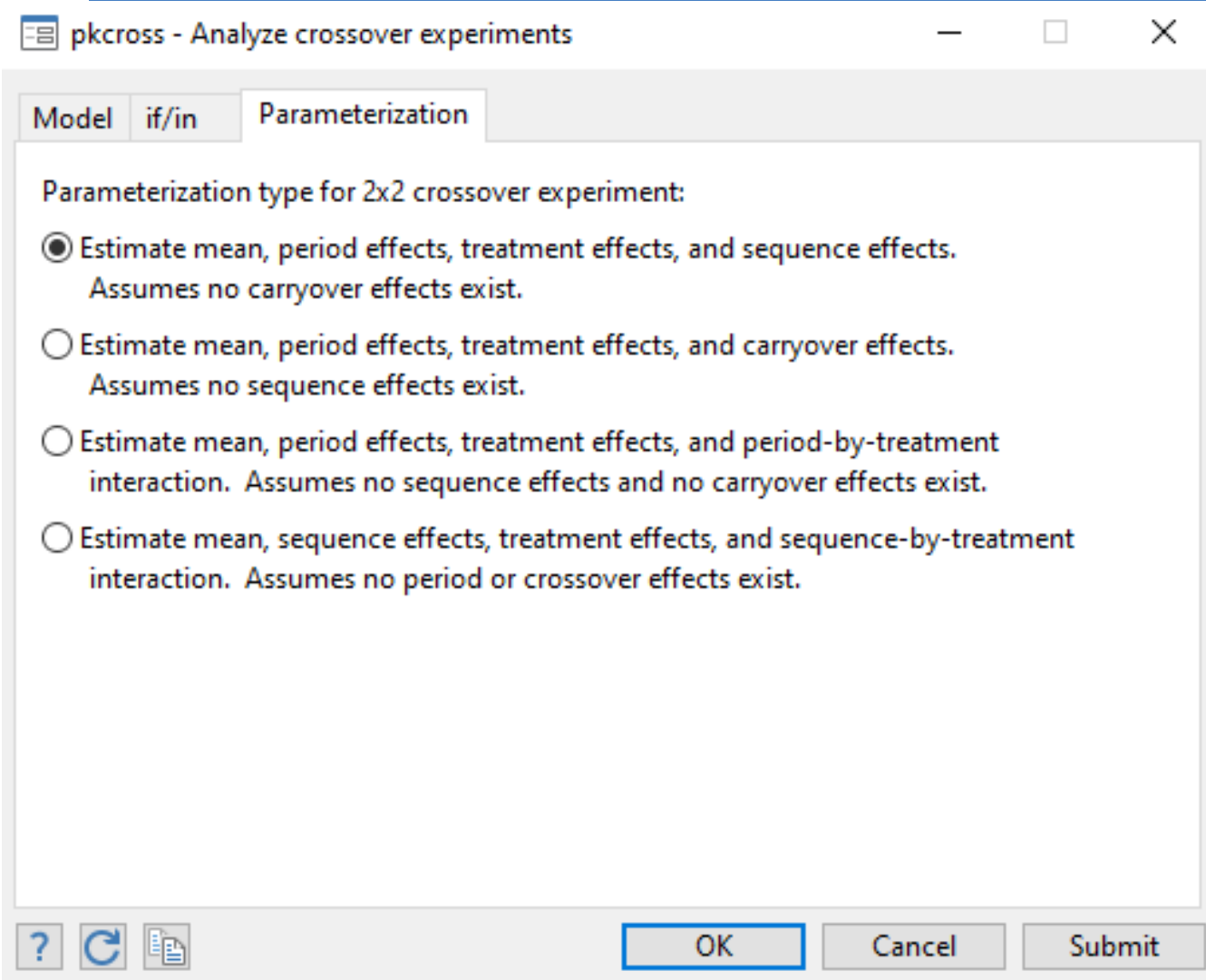
Estimate sequential instead of partial sums of squares

? ↻ 📄 OK Cancel Submit

# STATA: Parametrization : The default is param(3)

- **param(3)**: estimate mean and the period, treatment, and sequence effects;  
assume no carryover effects exist; the default
- **param(1)**: estimate mean and the period, treatment, and carryover effects;  
assume no sequence effects exist
- **param(2)**: estimate mean, period and treatment effects, and period-by-treatment interaction; assume no sequence or carryover effects exist
- **param(4)** : estimate mean, sequence and treatment effects, and sequence-by-treatment interaction; assume no period or carryover effects exist.

# پنجره تعیین نوع مدل تحلیل:



# خروجی مدل پارامتر 3: Pkcross outcome

. pkcross outcome

```
Sequence variable = sequence  
Period variable = period  
Treatment variable = treat  
Carryover variable = carry  
ID variable = id
```

Analysis of variance (ANOVA) for a 2x2 crossover study

Source of variation	Partial SS	df	MS	F	Prob > F
<b>Intersubjects</b>					
Sequence effect	276.00	1	276.00	0.37	0.5468
Residuals	16211.49	22	736.89	4.41	0.0005
<b>Intrasubjects</b>					
Treatment effect	62.79	1	62.79	0.38	0.5463
Period effect	35.97	1	35.97	0.22	0.6474
Residuals	3679.43	22	167.25		
Total	20265.68	47			

Omnibus measure of separability of treatment and carryover = 29.2893%

# خروجی مدل پارامتر 2: Pkcross outcome

```
. pkcross outcome, param(2)
```

```
Sequence variable = sequence  
Period variable = period  
Treatment variable = treat  
Carryover variable = carry  
ID variable = id
```

```
Analysis of variance (ANOVA) for a 2x2 crossover study
```

Source of variation	Partial SS	df	MS	F	Prob > F
Treatment effect	62.79	1	62.79	0.14	0.7112
Period effect	35.97	1	35.97	0.08	0.7792
Treatment * Period	276.00	1	276.00	0.61	0.4388
Residuals	19890.92	44	452.07		
Total	20265.68	47			

```
Omnibus measure of separability of treatment and carryover = 29.2893%
```

# خروجی مدل پارامتر 1: Pkcross outcome

pkcross outcome, param(1)

Sequence variable = sequence  
Period variable = period  
Treatment variable = treat  
Carryover variable = carry  
ID variable = id

Analysis of variance (ANOVA) for a 2x2 crossover study

Source of variation	Partial SS	df	MS	F	Prob > F
Treatment effect	301.04	1	301.04	0.67	0.4189
Period effect	255.62	1	255.62	0.57	0.4561
Carryover effect	276.00	1	276.00	0.61	0.4388
Residuals	19890.92	44	452.07		
Total	20265.68	47			

Omnibus measure of separability of treatment and carryover = 29.2893%

# خروجی مدل پارامتر 4: Pkcross outcome

pkcross outcome, param(4)

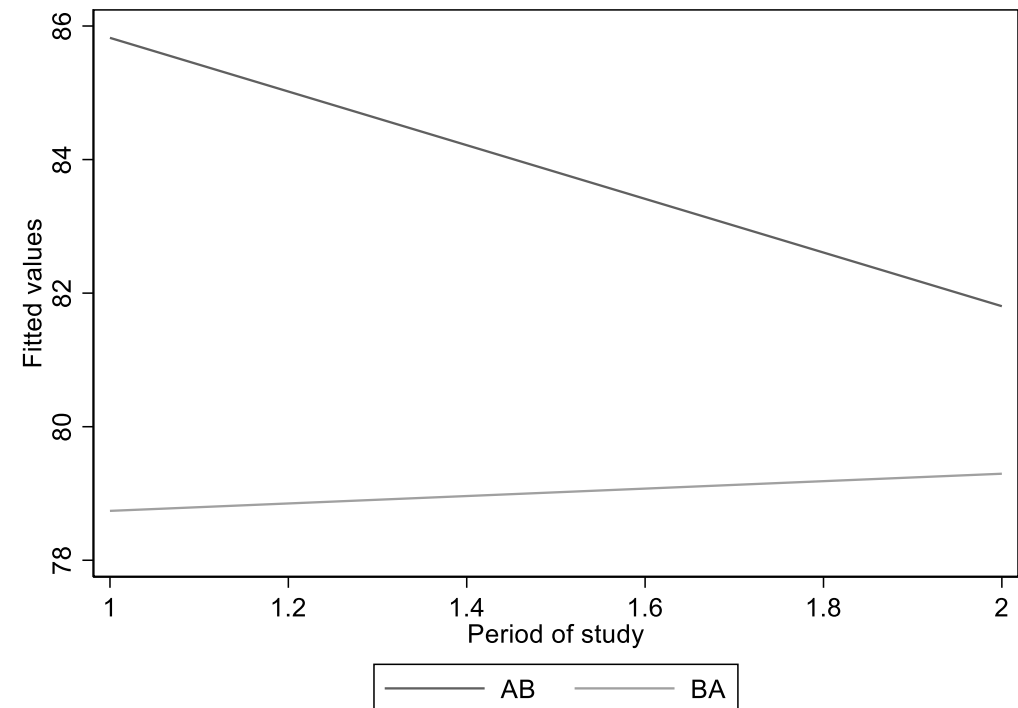
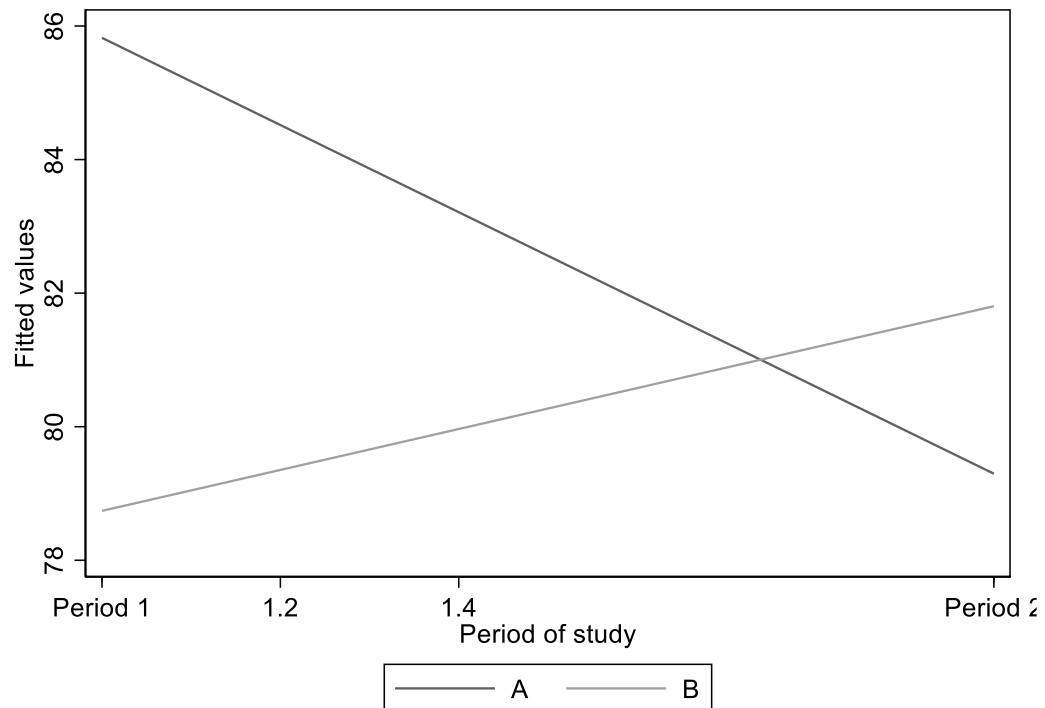
Sequence variable = **sequence**  
Period variable = **period**  
Treatment variable = **treat**  
Carryover variable = **carry**  
ID variable = **id**

lysis of variance (ANOVA) for a 2x2 crossover study

Source of variation	Partial SS	df	MS	F	Prob > F
Treatment effect	62.79	1	62.79	0.38	0.5463
Sequence effect	276.00	1	276.00	0.37	0.5468
Id Sequence	16211.49	22	736.89	4.41	0.0005
Treatment * Sequence	35.97	1	35.97	0.22	0.6474
Residuals	3679.43	22	167.25		
Total	20265.68	47			

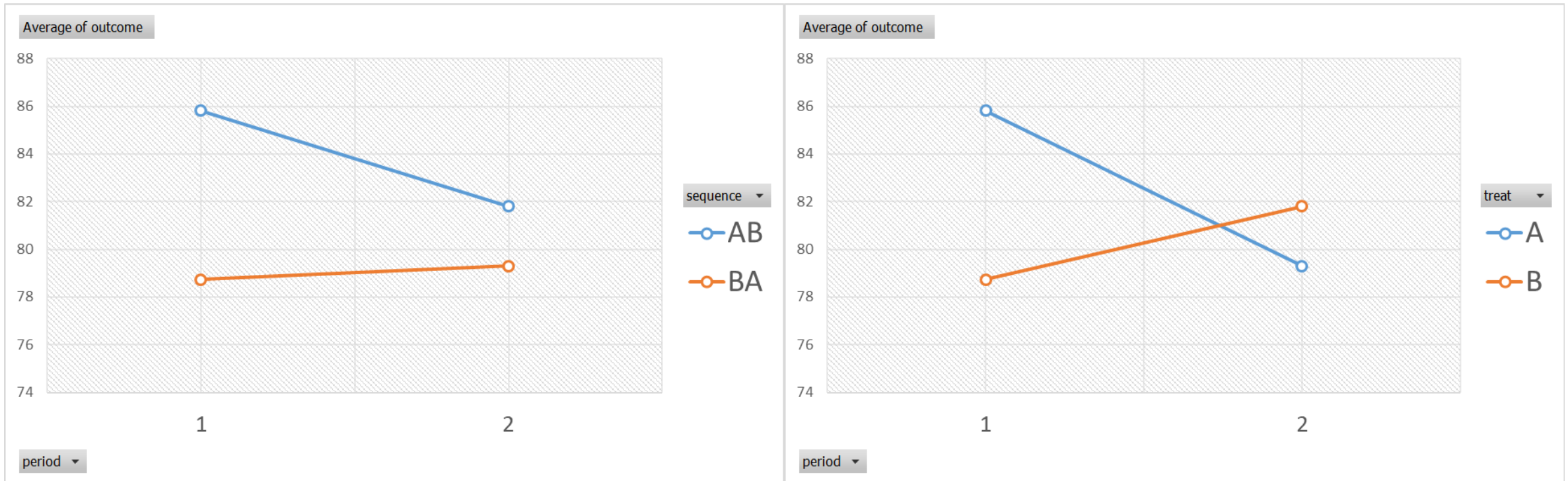
Omnibus measure of separability of treatment and carryover = 29.2893%

# رسم نمودارها در STATA :

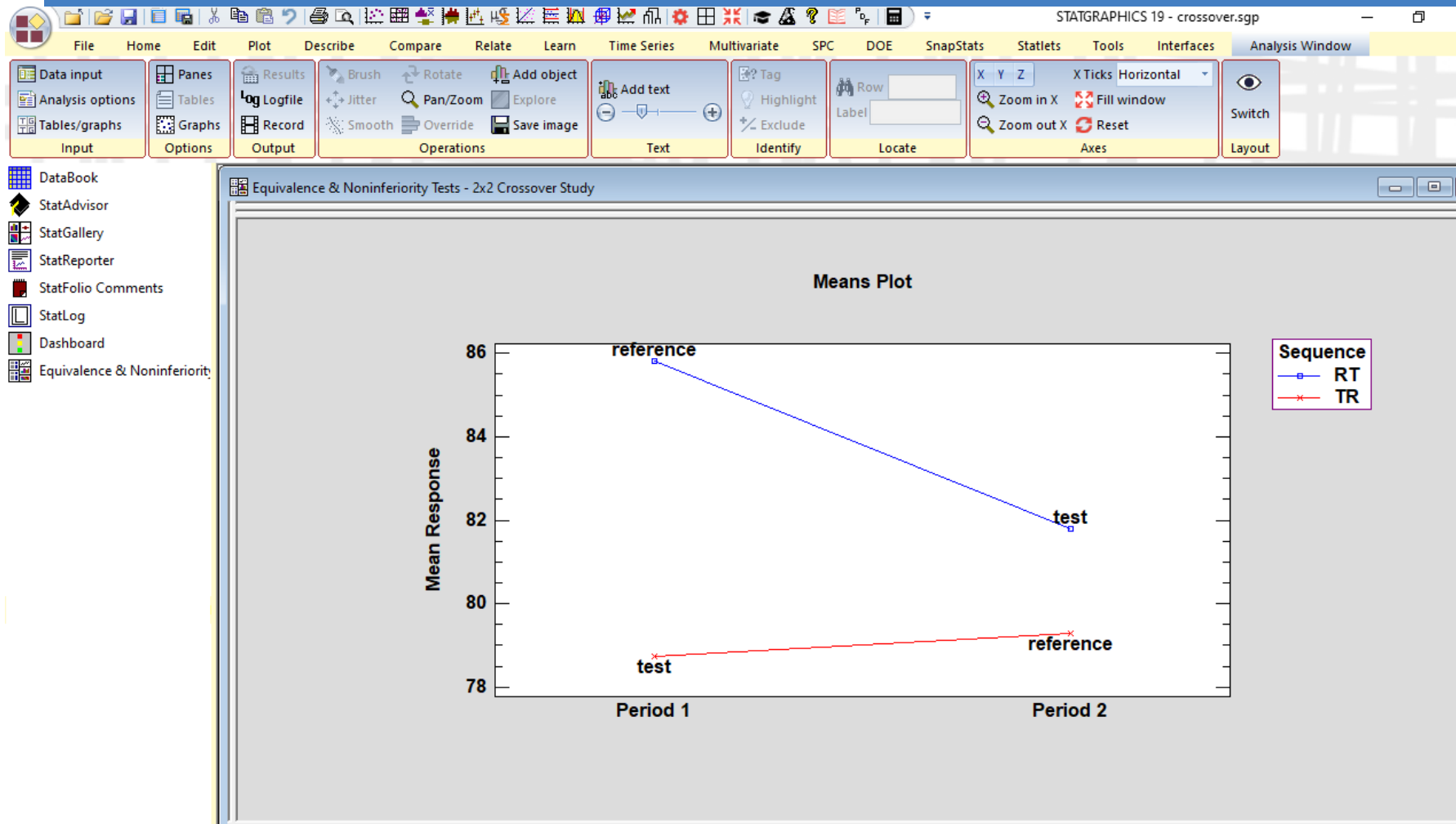




# رسم نمودارها در اکسل:



# انجام تحلیل در Statgraphics



# کار عملی و رفع پاسخ به سوالات: