

## Biostatistics 140.623 Third Term, 2017-2018

### Laboratory Exercise 3

The times to “drug failure” (as determined by a treating psychiatrist) for 25 patients in a study comparing a new treatment for schizophrenia to a standard treatment as used in Self-Evaluation Problems Class 5 are:

Trt group	Times (weeks)
Standard	3, 5+, 6, 8, 8, 9, 13, 15+, 16, 16, 17, 18
New	4, 6, 9, 9, 10+, 11, 12, 13+, 14+, 16, 17, 18, 20

+ denotes a censored observation

The corresponding dataset can be found in the Stata file `trt.dta`

1. Check the listing below to confirm that the data set has been set up appropriately:

```
. list
      trt      weeks  failure      id
  1.      0         3         1        1
  2.      0         5         0        2
  3.      0         6         1        3
  4.      0         8         1        4
  5.      0         8         1        5
  6.      0         9         1        6
  7.      0        13         1        7
  8.      0        15         0        8
  9.      0        16         1        9
 10.      0        16         1       10
 11.      1        14         0       11
 12.      0        17         1       12
 13.      0        18         1       13
 14.      1         4         1       14
 15.      1         6         1       15
 16.      1         9         1       16
 17.      1         9         1       17
 18.      1        10         0       18
 19.      1        11         1       19
 20.      1        12         1       20
 21.      1        13         0       21
 22.      1        16         1       22
 23.      1        17         1       23
 24.      1        18         1       24
 25.      1        20         1       25
```

2. The next step is to define the data as “survival time data” using the “**stset**” command. Here the event is defined as drug failure.

```
. stset weeks, failure(failure==1) id(id)
```

```

      id: id
      failure event: failure == 1
obs. time interval: (weeks[_n-1], weeks]
exit on or before: failure

```

```

-----
      25 total obs.
      0 exclusions
-----
      25 obs. remaining, representing
      25 subjects
      20 failures in single failure-per-subject data
      293 total analysis time at risk, at risk from t =          0
              earliest observed entry t =          0
              last observed exit t =          20

```

3. The **drug failure incidence rates** can be obtained in the new and standard treatment groups:

```
. stir trt
```

```

      failure _d: failure == 1
analysis time _t: weeks
      id: id

```

note: Exposed <-> trt==1 and Unexposed <-> trt==0

	trt		
	Exposed	Unexposed	Total
Failure	10	10	20
Time	159	134	293
Incidence rate	.0628931	.0746269	.0682594
	Point estimate		[95% Conf. Interval]
Inc. rate diff.	-.0117338		-.0722224 .0487549
Inc. rate ratio	.8427673		.3148131 2.256122 (exact)
Prev. frac. ex.	.1572327		-1.256122 .6851869 (exact)
Prev. frac. pop	.0853242		
	(midp) Pr(k<=10) =		0.3529 (exact)
	(midp) 2*Pr(k<=10) =		0.7058 (exact)

4. Next, we can obtain the **Kaplan-Meier estimates** of the survivor “drug-failure free” function for each treatment group:

```
sts list if trt==0
```

```
      failure _d: failure == 1
analysis time _t: weeks
      id: id
```

Time	Beg. Total	Fail	Net Lost	Survivor Function	Std. Error	[95% Conf. Int.]	
3	12	1	0	0.9167	0.0798	0.5390	0.9878
5	11	0	1	0.9167	0.0798	0.5390	0.9878
6	10	1	0	0.8250	0.1128	0.4609	0.9533
8	9	2	0	0.6417	0.1441	0.3022	0.8483
9	7	1	0	0.5500	0.1499	0.2321	0.7829
13	6	1	0	0.4583	0.1503	0.1689	0.7102
15	5	0	1	0.4583	0.1503	0.1689	0.7102
16	4	2	0	0.2292	0.1370	0.0382	0.5143
17	2	1	0	0.1146	0.1061	0.0067	0.3917
18	1	1	0	0.0000	.	.	.

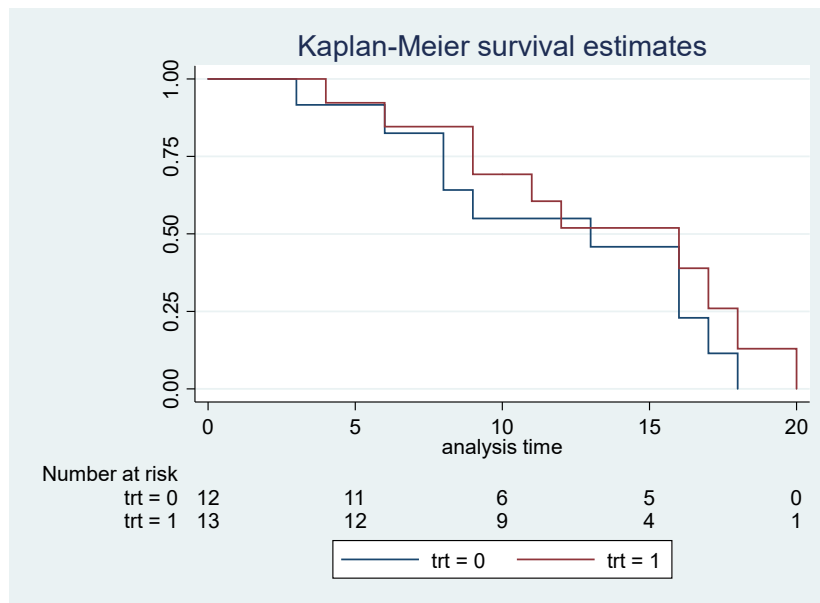
```
. sts list if trt==1
```

```
      failure _d: failure == 1
analysis time _t: weeks
      id: id
```

Time	Beg. Total	Fail	Net Lost	Survivor Function	Std. Error	[95% Conf. Int.]	
4	13	1	0	0.9231	0.0739	0.5664	0.9888
6	12	1	0	0.8462	0.1001	0.5122	0.9591
9	11	2	0	0.6923	0.1280	0.3734	0.8718
10	9	0	1	0.6923	0.1280	0.3734	0.8718
11	8	1	0	0.6058	0.1382	0.2943	0.8143
12	7	1	0	0.5192	0.1430	0.2246	0.7500
13	6	0	1	0.5192	0.1430	0.2246	0.7500
14	5	0	1	0.5192	0.1430	0.2246	0.7500
16	4	1	0	0.3894	0.1554	0.1152	0.6626
17	3	1	0	0.2596	0.1482	0.0454	0.5553
18	2	1	0	0.1298	0.1180	0.0076	0.4260
20	1	1	0	0.0000	.	.	.

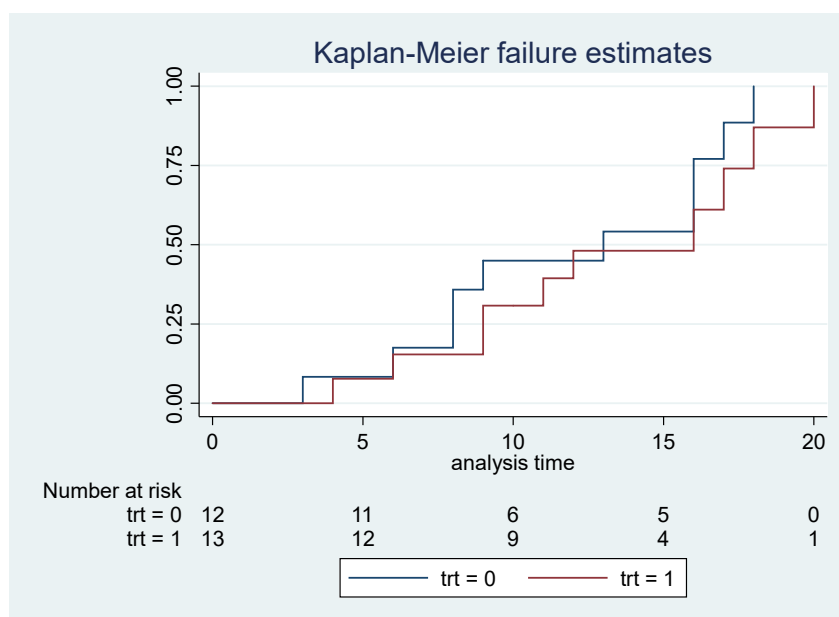
5. The “survival curves” by treatment group can be plotted along with a risk table:  
Based upon the plot of the Kaplan-Meier curves for each treatment group, which treatment, if any, should be preferred?

```
.sts graph, by(trt) risktable
```



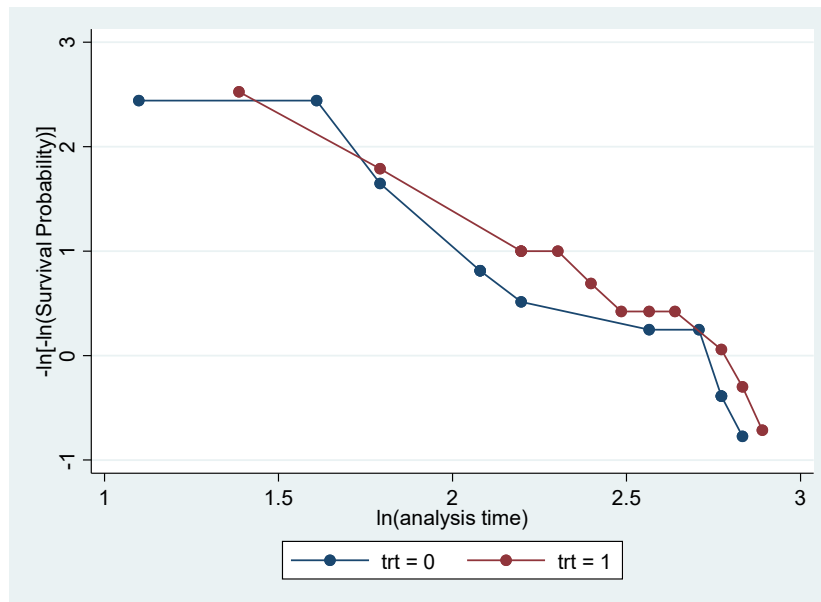
6. The cumulative hazard of drug failure by treatment group can be plotted using the “failure” option:

```
.sts graph, by(trt) failure risktable
```



7. What do you observe in the **complementary log log (CLL) plot** below?

```
.stphplot, by(trt)
```



8. The **log-rank statistic** can be calculated to test the null hypothesis of no difference in overall survival by treatment.

```
.sts test trt
```

```
      failure _d:  failure == 1
analysis time _t:  weeks
           id:  id
```

Log-rank test for equality of survivor functions

trt	Events observed	Events expected
0	10	8.27
1	10	11.73
Total	20	20.00

chi2(1) =	0.76
Pr>chi2 =	0.3831

9. Set up the log-rank statistic to test whether overall drug failure differs between the two treatments. **The log-rank test statistic can be computed by hand from the 2x2 tables based on each event time.**

$$\chi^2_{LR} = \frac{\left[ \sum_j (a_j - E(a_j)) \right]^2}{\sum_j \text{Var}(a_j)} \text{ where } E(a_j) = d_j \cdot \frac{n_{ja}}{n_j} \text{ and } \text{Var}(a_j) = \frac{d_j(n_j - d_j)n_{ja}n_{jb}}{n_j^2(n_j - 1)}$$

	Event	No Event	Total
Standard Trt	$a_j$		$n_{ja}$
New Trt	$c_j$		$n_{jb}$
Total	$d_j$		$n_j$

**Observed Event Times:**

**Time=j =3 weeks:**

	Event	No Event	Total
Standard Trt	1	11	12
New Trt	0	13	13
Total	1	24	25

$$a_j=1 \quad E(a_j) = (1)(12)/25 \quad a_j - E(a_j) = 13/25 \quad \text{Var}(a_j) = (1)(24)(12)(13)/[25^2(24)] = 0.2496$$

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

	Event	No Event	Total
Standard Trt			
New Trt			
Total			

Compare your calculation to that obtained by `Stata` above in step 8.