Biostatistics 140.623
Third Term, 2002-2003

Laboratory Exercise 5
Answer Key

Below find times to "drug failure" (as determined by a treating psychiatrist) for 15 patients in a study comparing a new treatment for schizophrenia to a standard treatment (modification of SEP #11).

Trt group	Times (wks)
Standard	3, 5+, 6+, 9, 13+, 15+, 16+
New	4, 6, 9, 9, 10+, 11+, 13+, 14+

1. Construct the Kaplan-Meier survival curves by treatment. Compare to the `Stata` log on the next page:

Standard Treatment					New Treatment				
Event-Time (t_i)	Number at Risk (n_i)	Events (y_i)	$\frac{(n_i - y_i)}{n_i}$	$\hat{S}(t_i)$	Event-Time (t_i)	Number at Risk (n_i)	Events (y_i)	$\frac{(n_i - y_i)}{n_i}$	$\hat{S}(t_i)$
0	-	-	-	1.000	0	-	-	-	1.000
3	7	1	(7-1)/7= 0.857	0.857	4	8	1	(8-1)/8= 0.875	0.875
9	4	1	(4-1)/4= 0.750	0.643	6	7	1	(7-1)/7= 0.857	0.750
					9	6	2	(6-2)/6= 0.667	0.500

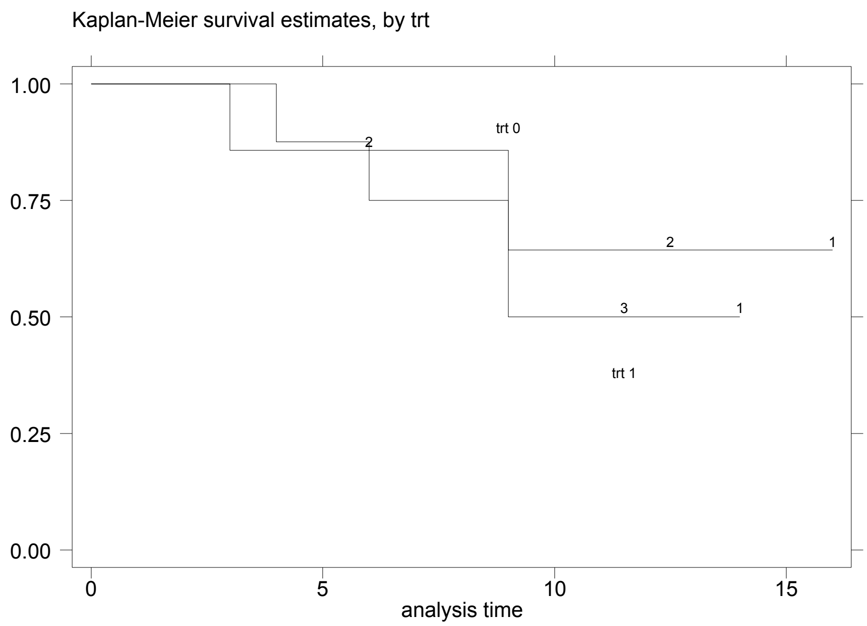
```
. list

        weeks       trt        id   failure
  1.        3         0         1         1
  2.        5         0         2         0
  3.        6         0         3         0
```



```
  4.        9         0         4         1
  5.       13         0         5         0
  6.       15         0         6         0
  7.       16         0         7         0
  8.        4         1         8         1
  9.        6         1         9         1
 10.        9         1        10         1
 11.        9         1        11         1
 12.       10         1        12         0
 13.       11         1        13         0
 14.       13         1        14         0
 15.       14         1        15         0


. 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

------------------------------------------------------------------------------
       15  total obs.
        0  exclusions
------------------------------------------------------------------------------
       15  obs. remaining, representing
       15  subjects
        6  failures in single failure-per-subject data
      143  total analysis time at risk, at risk from t =         0
                             earliest observed entry t =         0
                                  last observed exit t =        16


. sts list if trt==0

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

           Beg.          Net            Survivor      Std.
  Time    Total   Fail   Lost           Function     Error     [95% Conf. Int.]
-------------------------------------------------------------------------------
     3        7      1      0             0.8571    0.1323     0.3341    0.9786
     5        6      0      1             0.8571    0.1323     0.3341    0.9786
     6        5      0      1             0.8571    0.1323     0.3341    0.9786
     9        4      1      0             0.6429    0.2104     0.1515    0.9017
    13        3      0      1             0.6429    0.2104     0.1515    0.9017
    15        2      0      1             0.6429    0.2104     0.1515    0.9017
    16        1      0      1             0.6429    0.2104     0.1515    0.9017
-------------------------------------------------------------------------------
. sts list if trt==1

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

           Beg.          Net            Survivor      Std.
```


Time	Total	Fail	Lost	Function	Error	[95% Conf. Int.]	
4	8	1	0	0.8750	0.1169	0.3870	0.9814
6	7	1	0	0.7500	0.1531	0.3148	0.9309
9	6	2	0	0.5000	0.1768	0.1520	0.7749
10	4	0	1	0.5000	0.1768	0.1520	0.7749
11	3	0	1	0.5000	0.1768	0.1520	0.7749
13	2	0	1	0.5000	0.1768	0.1520	0.7749
14	1	0	1	0.5000	0.1768	0.1520	0.7749

2. Based upon the plot of the Kaplan-Meier curves for each treatment group, which treatment, if any, should be preferred?



There is much overlap between the two curves and the sample sizes are very small. The curves do not appear to be distinguishable from each other.

3. Calculate the log-rank statistic to test whether overall drug failure differs between the two treatments. Compute by hand the log-rank test statistic from the 2x2 tables based on each event time.

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

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

Event Times:

Time=3 weeks:

	Event	No Event	Total
Standard Trt	1	6	7
New Trt	0	8	8
Total	1	14	15

a_j =1 E(a_j)= (1)(7)/15 a_j-E(a_j) = 8/15 Var(a_j)=(1)(14)(7)(8)/[15^2(14)] = 0.2489

Time=4 weeks:

	Event	No Event	Total
Standard Trt	0	6	6
New Trt	1	7	8
Total	1	13	14

a_j =0 E(a_j)= (1)(6)/14 a_j-E(a_j) = -6/14 Var(a_j)=(1)(13)(6)(8)/[14^2(13)] = 0.2449

Time=6 weeks:

	Event	No Event	Total
Standard Trt	0	5	5
New Trt	1	6	7
Total	1	11	12

a_j =0 E(a_j)= (1)(5)/12 a_j-E(a_j) = -5/12 Var(a_j)=(1)(11)(5)(7)/[12^2(11)] = 0.2431

Time=9 weeks:

	Event	No Event	Total
Standard Trt	1	3	4
New Trt	2	4	6
Total	3	7	10

a_j =1 E(a_j)= (3)(4)/10 a_j-E(a_j) = -2/10 Var(a_j)=(3)(7)(4)(6)/[10^2(9)] = 0.56

$$\chi^2_{\text{LR}} = \frac{\left[\sum_j (\mathrm{a}_j - E(\mathrm{a}_j))\right]^2}{\sum_j V\hat{a}r(\mathrm{a}_j)} = \frac{(-0.5119)^2}{1.2969} = 0.2021$$ **where p > 0.05 and we would fail to refect the null hypothesis of equal survival in both groups.**

Compare your calculation to that obtained by `Stata` below.

```
Log-rank test for equality of survivor functions

      |   Events         Events
trt   |  observed       expected
------+-------------------------
0     |         2           2.51
1     |         4           3.49
------+-------------------------
Total |         6           6.00

            chi2(1) =       0.20
            Pr>chi2 =     0.6531
```

