AB Final Exercise C

```
*************************************************************************************;
*** Data originally from Box and Cox (1964) on survival times (in 10-hour units) ***;
*** of animals given one of three doses of a poison and subjected to one of      ***;
*** four different treatments.  B&C originally analysed the data using a two-    ***;
*** way ANOVA after using a reciprocal transformation on Y = survtime.  Here     ***;
*** we do the survival analysis using KM, LRT and Cox PH model too.              ***;
*** NB - no observations have been censored in this analysis.                    ***;
*************************************************************************************;

data one;
  do poison=1,2,3;
    poison2=(poison=2); poison3=(poison=3);     *** dummy vars for poisons 2 + 3 ***;
  do trt=1,2,3,4;
    trt2=(trt=2); trt3=(trt=3); trt4=(trt=4);   *** dummy vars for trts 2-4 resp ***;
    pt22=poison2*trt2; pt23=poison2*trt3; pt24=poison2*trt4; pt32=poison3*trt2;
    pt33=poison3*trt3; pt34=poison3*trt4; *** 6 interac terms ***;
  do rep=1 to 4;
    input x @@; survtime=x/100; y=1/survtime; drop rep x; output;
  end; end; end; datalines;
31 45 46 43 82 110 88  72 43 45 63 79 45  71 66 62
36 29 40 23 92  61 49 124 44 35 31 40 56 102 71 38
22 21 18 23 30  37 38  29 23 25 24 22 30  36 31 33
;
** GLM approach using the Y=1/ST (reciprocal) transformation;
proc glm;
  class poison trt;
  model y=poison trt poison*trt;
  means poison trt/snk;
run;
```

```
                                The GLM Procedure
                            Class Level Information
                          Class         Levels    Values
                          poison             3    1 2 3
                          trt                4    1 2 3 4

                        Number of Observations Read          48
                        Number of Observations Used          48

Dependent Variable: y
                                            Sum of
      Source                       DF         Squares     Mean Square    F Value    Pr > F
      Model                        11     56.93866824      5.17624257      21.42    <.0001
      Error                        36      8.69961255      0.24165590
      Corrected Total              47     65.63828079

                      R-Square     Coeff Var      Root MSE        y Mean
                      0.867461      18.75323      0.491585      2.621335

      Source                       DF       Type I SS     Mean Square    F Value    Pr > F
      poison                        2     34.95933798     17.47966899      72.33    <.0001
      trt                           3     20.38198367      6.79399456      28.11    <.0001
      poison*trt                    6      1.59734659      0.26622443       1.10    0.3804

      Source                       DF     Type III SS     Mean Square    F Value    Pr > F
      poison                        2     34.95933798     17.47966899      72.33    <.0001
      trt                           3     20.38198367      6.79399456      28.11    <.0001
      poison*trt                    6      1.59734659      0.26622443       1.10    0.3804
```

```
                          Student-Newman-Keuls Test for y
   NOTE: This test controls the Type I experimentwise error rate under the complete null
                 hypothesis but not under partial null hypotheses.

                          Alpha                        0.05
                          Error Degrees of Freedom       36
                          Error Mean Square        0.241656

                       Number of Means             2             3
                       Critical Range       0.3524891     0.4248227

              Means with the same letter are not significantly different.

                SNK Grouping          Mean      N    poison

                           A        3.7971     16    3

                           B        2.2693     16    2

                           C        1.7976     16    1


                          Student-Newman-Keuls Test for y
   NOTE: This test controls the Type I experimentwise error rate under the complete null
                 hypothesis but not under partial null hypotheses.

                          Alpha                        0.05
                          Error Degrees of Freedom       36
                          Error Mean Square        0.241656

             Number of Means              2             3             4
             Critical Range       0.4070194     0.4905431     0.5405006

              Means with the same letter are not significantly different.

                  SNK Grouping          Mean      N    trt

                             A        3.5193     12    1

                             B        2.9430     12    3

                             C        2.1610     12    4
                             C
                             C        1.8619     12    2
```

```
** Cox PH approach using original ST data;
proc phreg;
  model survtime=poison2 poison3 trt2 trt3 trt4 pt22 pt23 pt24 pt32 pt33 pt34;
run;
```

```
                              The PHREG Procedure
                                Model Information
                          Data Set                 WORK.ONE
                          Dependent Variable       survtime
                          Ties Handling            BRESLOW

                        Number of Observations Read          48
                        Number of Observations Used          48
```

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
48	48	0	0.00

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	282.651	199.535
AIC	282.651	221.535
SBC	282.651	242.119

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	83.1158	11	<.0001
Score	105.6660	11	<.0001
Wald	43.9503	11	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
poison2	1	1.95814	0.85310	5.2686	0.0217	7.086
poison3	1	6.47928	1.44197	20.1903	<.0001	651.499
trt2	1	-2.96859	0.91105	10.6173	0.0011	0.051
trt3	1	-1.52833	0.82338	3.4453	0.0634	0.217
trt4	1	-1.58934	0.81723	3.7822	0.0518	0.204
pt22	1	-2.05031	1.15014	3.1779	0.0746	0.129
pt23	1	0.66958	1.10496	0.3672	0.5445	1.953
pt24	1	-2.61030	1.14863	5.1645	0.0231	0.074
pt32	1	-1.48972	1.60837	0.8579	0.3543	0.225
pt33	1	0.36281	1.14538	0.1003	0.7514	1.437
pt34	1	-2.57641	1.54770	2.7711	0.0960	0.076

```
proc phreg;
  model survtime=poison2 poison3 trt2 trt3 trt4;
run;
```

The PHREG Procedure

Model Information

Data Set	WORK.ONE
Dependent Variable	survtime
Ties Handling	BRESLOW

Number of Observations Read	48
Number of Observations Used	48

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
48	48	0	0.00

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	282.651	211.557
AIC	282.651	221.557
SBC	282.651	230.913

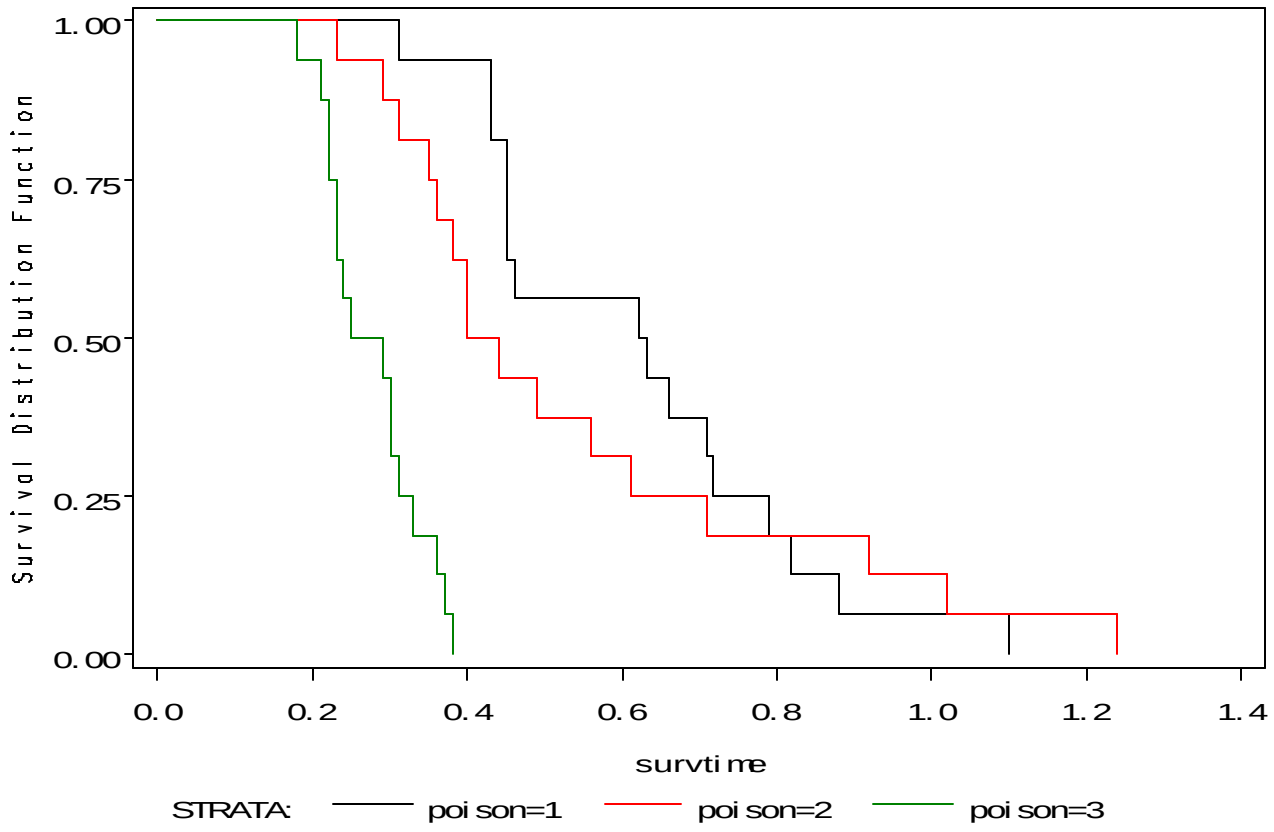
Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	71.0941	5	<.0001
Score	71.6342	5	<.0001
Wald	46.9573	5	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
poison2	1	0.89422	0.43128	4.2990	0.0381	2.445
poison3	1	4.61559	0.74904	37.9704	<.0001	101.048
trt2	1	-3.39131	0.60326	31.6031	<.0001	0.034
trt3	1	-1.08710	0.45138	5.8002	0.0160	0.337
trt4	1	-2.79199	0.58431	22.8317	<.0001	0.061

```
** KM estimates and Logrank tests on original ST data;
proc lifetest plot=(s);
  time survtime;
  strata poison;
run;
```



The LIFETEST Procedure

Stratum 1: poison = 1

Product-Limit Survival Estimates

survtime	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.00000	1.0000	0	0	0	16
0.31000	0.9375	0.0625	0.0605	1	15
0.43000	.	.	.	2	14
0.43000	0.8125	0.1875	0.0976	3	13
0.45000	.	.	.	4	12
0.45000	.	.	.	5	11
0.45000	0.6250	0.3750	0.1210	6	10
0.46000	0.5625	0.4375	0.1240	7	9
0.62000	0.5000	0.5000	0.1250	8	8
0.63000	0.4375	0.5625	0.1240	9	7
0.66000	0.3750	0.6250	0.1210	10	6
0.71000	0.3125	0.6875	0.1159	11	5
0.72000	0.2500	0.7500	0.1083	12	4
0.79000	0.1875	0.8125	0.0976	13	3
0.82000	0.1250	0.8750	0.0827	14	2
0.88000	0.0625	0.9375	0.0605	15	1
1.10000	0	1.0000	0	16	0

Summary Statistics for Time Variable survtime

Quartile Estimates

Percent	Point Estimate	95% Confidence Interval [Lower	Upper)
75	0.75500	0.63000	0.88000
50	0.62500	0.45000	0.72000
25	0.45000	0.43000	0.62000

Mean	Standard Error
0.61938	0.05273

Stratum 2: poison = 2

Product-Limit Survival Estimates

survtime	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.00000	1.0000	0	0	0	16
0.23000	0.9375	0.0625	0.0605	1	15
0.29000	0.8750	0.1250	0.0827	2	14
0.31000	0.8125	0.1875	0.0976	3	13
0.35000	0.7500	0.2500	0.1083	4	12
0.36000	0.6875	0.3125	0.1159	5	11
0.38000	0.6250	0.3750	0.1210	6	10
0.40000	.	.	.	7	9
0.40000	0.5000	0.5000	0.1250	8	8
0.44000	0.4375	0.5625	0.1240	9	7
0.49000	0.3750	0.6250	0.1210	10	6
0.56000	0.3125	0.6875	0.1159	11	5
0.61000	0.2500	0.7500	0.1083	12	4
0.71000	0.1875	0.8125	0.0976	13	3
0.92000	0.1250	0.8750	0.0827	14	2
1.02000	0.0625	0.9375	0.0605	15	1
1.24000	0	1.0000	0	16	0

Summary Statistics for Time Variable survtime

Quartile Estimates

Percent	Point Estimate	95% Confidence Interval [Lower	Upper)
75	0.66000	0.44000	1.02000
50	0.42000	0.36000	0.61000
25	0.35500	0.29000	0.40000

Mean	Standard Error
0.54438	0.07234

Stratum 3: poison = 3

Product-Limit Survival Estimates

survtime	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.00000	1.0000	0	0	0	16
0.18000	0.9375	0.0625	0.0605	1	15
0.21000	0.8750	0.1250	0.0827	2	14
0.22000	.	.	.	3	13
0.22000	0.7500	0.2500	0.1083	4	12
0.23000	.	.	.	5	11
0.23000	0.6250	0.3750	0.1210	6	10
0.24000	0.5625	0.4375	0.1240	7	9
0.25000	0.5000	0.5000	0.1250	8	8
0.29000	0.4375	0.5625	0.1240	9	7
0.30000	.	.	.	10	6
0.30000	0.3125	0.6875	0.1159	11	5
0.31000	0.2500	0.7500	0.1083	12	4
0.33000	0.1875	0.8125	0.0976	13	3
0.36000	0.1250	0.8750	0.0827	14	2
0.37000	0.0625	0.9375	0.0605	15	1
0.38000	0	1.0000	0	16	0

Summary Statistics for Time Variable survtime

Quartile Estimates

Percent	Point Estimate	95% Confidence Interval [Lower	Upper)
75	0.32000	0.29000	0.37000
50	0.27000	0.23000	0.31000
25	0.22500	0.21000	0.25000

Mean	Standard Error
0.27625	0.01557

Summary of the Number of Censored and Uncensored Values

Stratum	poison	Total	Failed	Censored	Percent Censored
1	1	16	16	0	0.00
2	2	16	16	0	0.00
3	3	16	16	0	0.00
Total		48	48	0	0.00

Testing Homogeneity of Survival Curves for survtime over Strata

Rank Statistics

poison	Log-Rank	Wilcoxon
1	-7.749	-331.00
2	-3.918	-114.00
3	11.667	445.00

Covariance Matrix for the Log-Rank Statistics

poison	1	2	3
1	10.8042	-9.1214	-1.6828
2	-9.1214	10.6853	-1.5639
3	-1.6828	-1.5639	3.2467

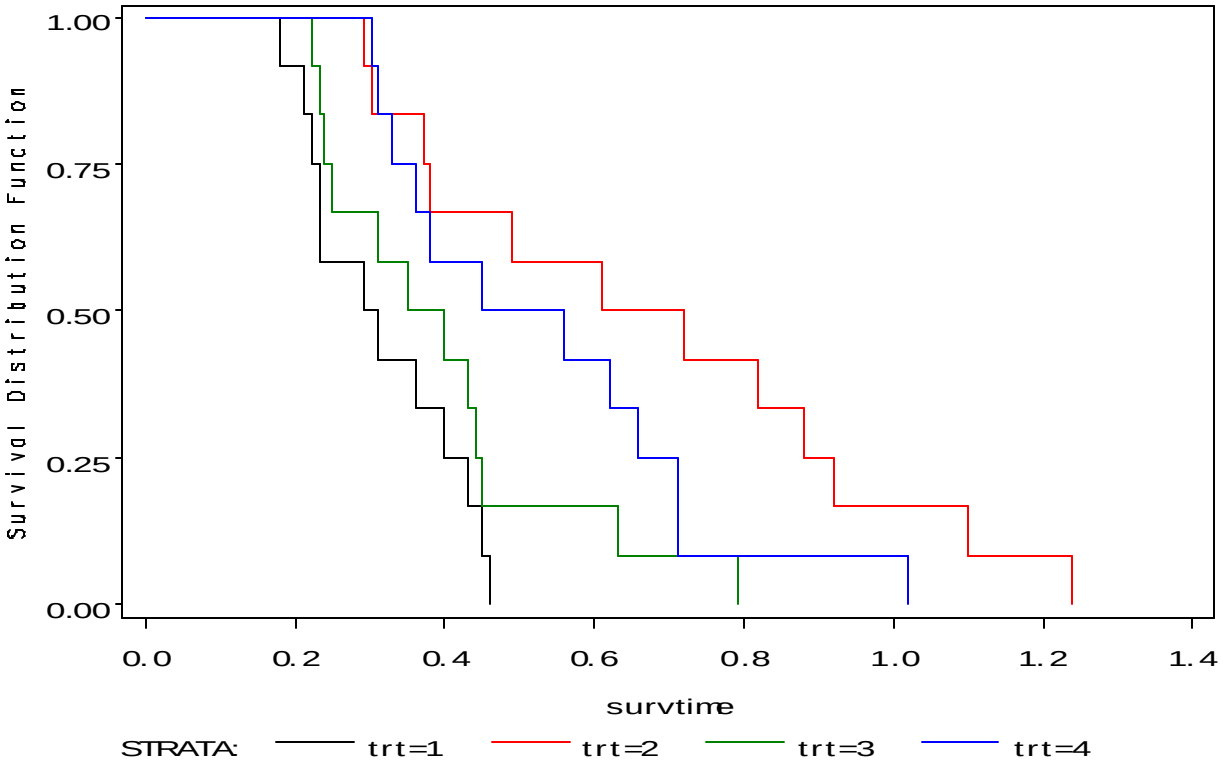
Covariance Matrix for the Wilcoxon Statistics

poison	1	2	3
1	8994.63	-6263.71	-2730.92
2	-6263.71	8857.52	-2593.81
3	-2730.92	-2593.81	5324.73

Test of Equality over Strata

Test	Chi-Square	DF	Pr > Chi-Square
Log-Rank	42.2184	2	<.0001
Wilcoxon	38.5805	2	<.0001
-2Log(LR)	5.4945	2	0.0641

```
proc lifetest plot=(s);
  time survtime;
  strata trt;
run;
```



The LIFETEST Procedure

Stratum 1: trt = 1

Product-Limit Survival Estimates

survtime	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.00000	1.0000	0	0	0	12
0.18000	0.9167	0.0833	0.0798	1	11
0.21000	0.8333	0.1667	0.1076	2	10
0.22000	0.7500	0.2500	0.1250	3	9
0.23000	.	.	.	4	8
0.23000	0.5833	0.4167	0.1423	5	7
0.29000	0.5000	0.5000	0.1443	6	6
0.31000	0.4167	0.5833	0.1423	7	5
0.36000	0.3333	0.6667	0.1361	8	4
0.40000	0.2500	0.7500	0.1250	9	3
0.43000	0.1667	0.8333	0.1076	10	2
0.45000	0.0833	0.9167	0.0798	11	1
0.46000	0	1.0000	0	12	0

Summary Statistics for Time Variable survtime

Quartile Estimates

Percent	Point Estimate	95% Confidence Interval [Lower	Upper)
75	0.41500	0.29000	0.45000
50	0.30000	0.23000	0.40000
25	0.22500	0.21000	0.31000

Mean	Standard Error
0.31417	0.02953

Stratum 2: trt = 2

Product-Limit Survival Estimates

survtime	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.00000	1.0000	0	0	0	12
0.29000	0.9167	0.0833	0.0798	1	11
0.30000	0.8333	0.1667	0.1076	2	10
0.37000	0.7500	0.2500	0.1250	3	9
0.38000	0.6667	0.3333	0.1361	4	8
0.49000	0.5833	0.4167	0.1423	5	7
0.61000	0.5000	0.5000	0.1443	6	6
0.72000	0.4167	0.5833	0.1423	7	5
0.82000	0.3333	0.6667	0.1361	8	4
0.88000	0.2500	0.7500	0.1250	9	3
0.92000	0.1667	0.8333	0.1076	10	2
1.10000	0.0833	0.9167	0.0798	11	1
1.24000	0	1.0000	0	12	0

Summary Statistics for Time Variable survtime

Quartile Estimates

Percent	Point Estimate	95% Confidence Interval [Lower	Upper)
75	0.90000	0.61000	1.10000
50	0.66500	0.38000	0.88000
25	0.37500	0.30000	0.72000

```
                          Mean    Standard Error
                       0.67667           0.09262


                          Stratum 3: trt = 3
                    Product-Limit Survival Estimates

                                        Survival
                                        Standard     Number      Number
 survtime     Survival    Failure       Error       Failed       Left
  0.00000       1.0000           0           0        0          12
  0.22000       0.9167      0.0833      0.0798        1          11
  0.23000       0.8333      0.1667      0.1076        2          10
  0.24000       0.7500      0.2500      0.1250        3           9
  0.25000       0.6667      0.3333      0.1361        4           8
  0.31000       0.5833      0.4167      0.1423        5           7
  0.35000       0.5000      0.5000      0.1443        6           6
  0.40000       0.4167      0.5833      0.1423        7           5
  0.43000       0.3333      0.6667      0.1361        8           4
  0.44000       0.2500      0.7500      0.1250        9           3
  0.45000       0.1667      0.8333      0.1076       10           2
  0.63000       0.0833      0.9167      0.0798       11           1
  0.79000            0      1.0000           0       12           0

               Summary Statistics for Time Variable survtime
                           Quartile Estimates
                           Point     95% Confidence Interval
                Percent    Estimate      [Lower      Upper)
                     75     0.44500     0.35000     0.63000
                     50     0.37500     0.25000     0.44000
                     25     0.24500     0.23000     0.40000

                          Mean    Standard Error
                       0.39500           0.04998


                          Stratum 4: trt = 4
                    Product-Limit Survival Estimates

                                        Survival
                                        Standard     Number      Number
 survtime     Survival    Failure       Error       Failed       Left
  0.00000       1.0000           0           0        0          12
  0.30000       0.9167      0.0833      0.0798        1          11
  0.31000       0.8333      0.1667      0.1076        2          10
  0.33000       0.7500      0.2500      0.1250        3           9
  0.36000       0.6667      0.3333      0.1361        4           8
  0.38000       0.5833      0.4167      0.1423        5           7
  0.45000       0.5000      0.5000      0.1443        6           6
  0.56000       0.4167      0.5833      0.1423        7           5
  0.62000       0.3333      0.6667      0.1361        8           4
  0.66000       0.2500      0.7500      0.1250        9           3
  0.71000            .           .           .       10           2
  0.71000       0.0833      0.9167      0.0798       11           1
  1.02000            0      1.0000           0       12           0

               Summary Statistics for Time Variable survtime
                           Quartile Estimates
                           Point     95% Confidence Interval
                Percent    Estimate      [Lower      Upper)
                     75     0.68500     0.45000     0.71000
                     50     0.50500     0.36000     0.66000
```

25	0.34500	0.31000	0.56000

Mean	Standard Error
0.53417	0.06335

Summary of the Number of Censored and Uncensored Values

Stratum	trt	Total	Failed	Censored	Percent Censored
1	1	12	12	0	0.00
2	2	12	12	0	0.00
3	3	12	12	0	0.00
4	4	12	12	0	0.00
Total		48	48	0	0.00

Testing Homogeneity of Survival Curves for survtime over Strata

Rank Statistics

trt	Log-Rank	Wilcoxon
1	6.7993	235.00
2	-8.9057	-217.00
3	3.7690	93.00
4	-1.6625	-111.00

Covariance Matrix for the Log-Rank Statistics

trt	1	2	3	4
1	4.16057	-1.54498	-1.13291	-1.48268
2	-1.54498	9.65729	-2.79897	-5.31334
3	-1.13291	-2.79897	6.31571	-2.38383
4	-1.48268	-5.31334	-2.38383	9.17985

Covariance Matrix for the Wilcoxon Statistics

trt	1	2	3	4
1	5396.70	-1928.80	-1563.59	-1904.30
2	-1928.80	7912.08	-2555.28	-3428.00
3	-1563.59	-2555.28	6600.75	-2481.87
4	-1904.30	-3428.00	-2481.87	7814.17

Test of Equality over Strata

Test	Chi-Square	DF	Pr > Chi-Square
Log-Rank	17.9121	3	0.0005
Wilcoxon	14.9222	3	0.0019
-2Log(LR)	4.0428	3	0.2569