Survival analysis with R (Part I)

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1 Introduction

Objectives

- Understand the concept of survival analysis
- Learn how to perform survival analysis (Kaplan-Meier estiamtor and log-rank test) with R
- Peform data analyses where the scientific question is to determine factor associated with time until event

2 Survival analysis

To illustrate how to carry out different survival data analyses a real dataset is going to be used. The database belongs to the data presented in a paper that analysed 686 women enrolled in a clinical trial on breast cancer. The reference is *W. Sauerbrei and P. Royston. Building multivariable prognostic and diagnostic models: transformation of the predictors by using fractional polynomials. Journal of the Royal Statistics Society, Series A, 1999;162:71-94.* The information available is:

- Running-ID
- Hormonal Therapy (0- no treatment, 1-treatment)
- age (X1; in years)
- menopausal status (X2; 1- premenopausal,2- postmenopausal)
- Tumour size (X3; in mm)
- Tumour grade (X4; 1,2,3)
- Number of positive nodes (X5)
- Progesterone receptor (X6; in fmol)
- Estrogen receptor (X7; in fmol)
- Survival time (in days)
- Censoring Indicator (0- censored, 1- event).

Data can be loaded by executing:

```
library(survival)
datos <- read.table("../data/sauerbre.txt", header=TRUE)
head(datos)
##   id therapy age meno.status tumor.size tumor.grade nodes progest estrog
## 1  1       0  70           2         21           2     3      48     66
## 2  2       1  56           2         12           2     7      61     77
## 3  3       1  58           2         35           2     9      52    271
## 4  4       1  59           2         17           2     4      60     29
## 5  5       0  73           2         35           2     1      26     65
## 6  6       0  32           1         57           3    24       0     13
##   time event
## 1 1814     1
## 2 2018     1
## 3  712     1
## 4 1807     1
## 5  772     1
## 6  448     1
```

Survival analysis requires an object of class Surv where "+" denotes the individual is right-censored.

```
Surv(datos$time, datos$event)
```

```
##  [1] 1814  2018   712  1807   772   448  2172+ 2161+  471  2014+  577
## [12]  184  1840+ 1842+ 1821+ 1371   707  1743+ 1781+  865  1684  1701+
## [23] 1701+ 1693+  379  1105   548  1296  1483+ 1570+ 1469+ 1472+ 1342+
## [34] 1349+ 1162  1342+  797  1232+ 1230+ 1205+
```

3 Survival time estimates using Kaplan-Meier estimator

The survival function can be estimated by using survfit function

```
ans <- survfit(Surv(time, event)~1, datos)
ans
## Call: survfit(formula = Surv(time, event) ~ 1, data = datos)
##
##       n  events  median 0.95LCL 0.95UCL
##     686     299    1807    1587    2030
```

The Kaplan-Meier table can be obtained by:

```
summary(ans)
## Call: survfit(formula = Surv(time, event) ~ 1, data = datos)
##
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    72    672       1    0.999 0.00149        0.996        1.000
##    98    671       1    0.997 0.00210        0.993        1.000
##   113    670       1    0.996 0.00257        0.991        1.000
##   120    668       1    0.994 0.00297        0.988        1.000
##   160    666       1    0.993 0.00332        0.986        0.999
##   169    664       1    0.991 0.00363        0.984        0.998
##   171    663       1    0.990 0.00392        0.982        0.997
##   173    662       1    0.988 0.00419        0.980        0.996
##   175    661       1    0.987 0.00445        0.978        0.995
```

```
##    177     660        2     0.984 0.00491          0.974          0.993
##    180     657        1     0.982 0.00512          0.972          0.992
##    181     656        1     0.981 0.00533          0.970          0.991
##    184     655        1     0.979 0.00553          0.968          0.990
##    191     653        1     0.978 0.00572          0.966          0.989
##    195     652        1     0.976 0.00590          0.965          0.988
##    205     650        1     0.975 0.00608          0.963          0.987
##    223     648        1     0.973 0.00626          0.961          0.985
##    227     647        1     0.972 0.00643          0.959          0.984
##    233     645        1     0.970 0.00659          0.957          0.983
##    238     644        1     0.969 0.00675          0.955          0.982
##    241     643        1     0.967 0.00691          0.954          0.981
##    242     642        1     0.966 0.00706          0.952          0.979
##    247     641        1     0.964 0.00720          0.950          0.978
##    249     640        1     0.963 0.00735          0.948          0.977
##    251     639        1     0.961 0.00749          0.946          0.976
##    272     638        2     0.958 0.00776          0.943          0.973
##    275     635        1     0.957 0.00790          0.941          0.972
##    281     633        2     0.953 0.00816          0.938          0.970
##    285     631        2     0.950 0.00841          0.934          0.967
##    286     629        1     0.949 0.00853          0.932          0.966
##    288     628        1     0.947 0.00865          0.931          0.965
##    293     627        1     0.946 0.00876          0.929          0.963
##    305     625        1     0.944 0.00888          0.927          0.962
##    307     624        1     0.943 0.00899          0.925          0.961
##    308     623        2     0.940 0.00922          0.922          0.958
##    316     620        1     0.938 0.00932          0.920          0.957
##    329     617        1     0.937 0.00943          0.919          0.956
##    336     616        1     0.935 0.00954          0.917          0.954
##    338     615        3     0.931 0.00985          0.912          0.950
##    343     612        1     0.929 0.00995          0.910          0.949
##    344     611        1     0.928 0.01005          0.908          0.948
##    348     610        1     0.926 0.01015          0.907          0.946
##    350     609        1     0.925 0.01024          0.905          0.945
##    353     608        1     0.923 0.01034          0.903          0.944
##    357     607        1     0.922 0.01043          0.901          0.942
##    358     606        1     0.920 0.01053          0.900          0.941
##    359     605        2     0.917 0.01071          0.896          0.938
##    360     603        1     0.916 0.01080          0.895          0.937
##    369     601        1     0.914 0.01089          0.893          0.936
##    370     600        2     0.911 0.01106          0.890          0.933
##    371     598        1     0.909 0.01115          0.888          0.932
##    372     597        1     0.908 0.01123          0.886          0.930
##    374     596        1     0.906 0.01132          0.885          0.929
##    375     595        1     0.905 0.01140          0.883          0.928
##    377     594        1     0.903 0.01148          0.881          0.926
##    379     593        1     0.902 0.01156          0.879          0.925
##    385     592        1     0.900 0.01164          0.878          0.923
##    392     591        1     0.899 0.01172          0.876          0.922
##    394     590        1     0.897 0.01180          0.874          0.921
##    403     589        1     0.896 0.01188          0.873          0.919
##    410     588        1     0.894 0.01196          0.871          0.918
##    415     587        1     0.893 0.01203          0.869          0.917
##    417     586        1     0.891 0.01211          0.868          0.915
```

```
##    420    585        2    0.888 0.01226          0.864          0.912
##    426    582        2    0.885 0.01240          0.861          0.910
##    436    578        1    0.884 0.01248          0.859          0.908
##    438    577        1    0.882 0.01255          0.858          0.907
##    446    576        1    0.880 0.01262          0.856          0.906
##    448    575        1    0.879 0.01269          0.854          0.904
##    449    574        1    0.877 0.01276          0.853          0.903
##    455    573        1    0.876 0.01283          0.851          0.901
##    456    572        1    0.874 0.01290          0.849          0.900
##    460    571        1    0.873 0.01297          0.848          0.899
##    465    568        1    0.871 0.01303          0.846          0.897
##    471    567        1    0.870 0.01310          0.844          0.896
##    473    566        1    0.868 0.01317          0.843          0.894
##    475    565        1    0.867 0.01323          0.841          0.893
##    476    564        2    0.864 0.01337          0.838          0.890
##    481    562        1    0.862 0.01343          0.836          0.889
##    486    561        1    0.861 0.01349          0.834          0.887
##    490    559        1    0.859 0.01356          0.833          0.886
##    491    558        3    0.854 0.01374          0.828          0.882
##    495    555        1    0.853 0.01380          0.826          0.880
##    498    554        1    0.851 0.01387          0.825          0.879
##    500    553        1    0.850 0.01393          0.823          0.878
##    502    552        1    0.848 0.01398          0.821          0.876
##    503    551        1    0.847 0.01404          0.820          0.875
##    504    550        1    0.845 0.01410          0.818          0.873
##    515    549        1    0.844 0.01416          0.816          0.872
##    518    548        1    0.842 0.01422          0.815          0.870
##    525    547        1    0.841 0.01428          0.813          0.869
##    529    545        1    0.839 0.01433          0.811          0.868
##    530    543        1    0.837 0.01439          0.810          0.866
##    533    542        1    0.836 0.01445          0.808          0.865
##    535    541        1    0.834 0.01450          0.806          0.863
##    536    540        1    0.833 0.01456          0.805          0.862
##    537    539        1    0.831 0.01461          0.803          0.860
##    540    538        1    0.830 0.01467          0.801          0.859
##    542    536        1    0.828 0.01472          0.800          0.858
##    544    535        2    0.825 0.01483          0.797          0.855
##    545    533        1    0.824 0.01488          0.795          0.853
##    547    531        1    0.822 0.01493          0.793          0.852
##    548    530        3    0.817 0.01509          0.788          0.847
##    550    527        2    0.814 0.01519          0.785          0.845
##    552    525        2    0.811 0.01529          0.782          0.842
##    554    522        2    0.808 0.01539          0.778          0.839
##    557    520        1    0.806 0.01543          0.777          0.837
##    559    519        1    0.805 0.01548          0.775          0.836
##    563    518        1    0.803 0.01553          0.773          0.834
##    564    517        1    0.802 0.01558          0.772          0.833
##    571    513        1    0.800 0.01563          0.770          0.831
##    573    512        1    0.799 0.01567          0.769          0.830
##    575    511        1    0.797 0.01572          0.767          0.829
##    577    510        1    0.796 0.01577          0.765          0.827
##    578    509        1    0.794 0.01581          0.764          0.826
##    579    508        1    0.792 0.01586          0.762          0.824
##    586    507        1    0.791 0.01591          0.760          0.823
```

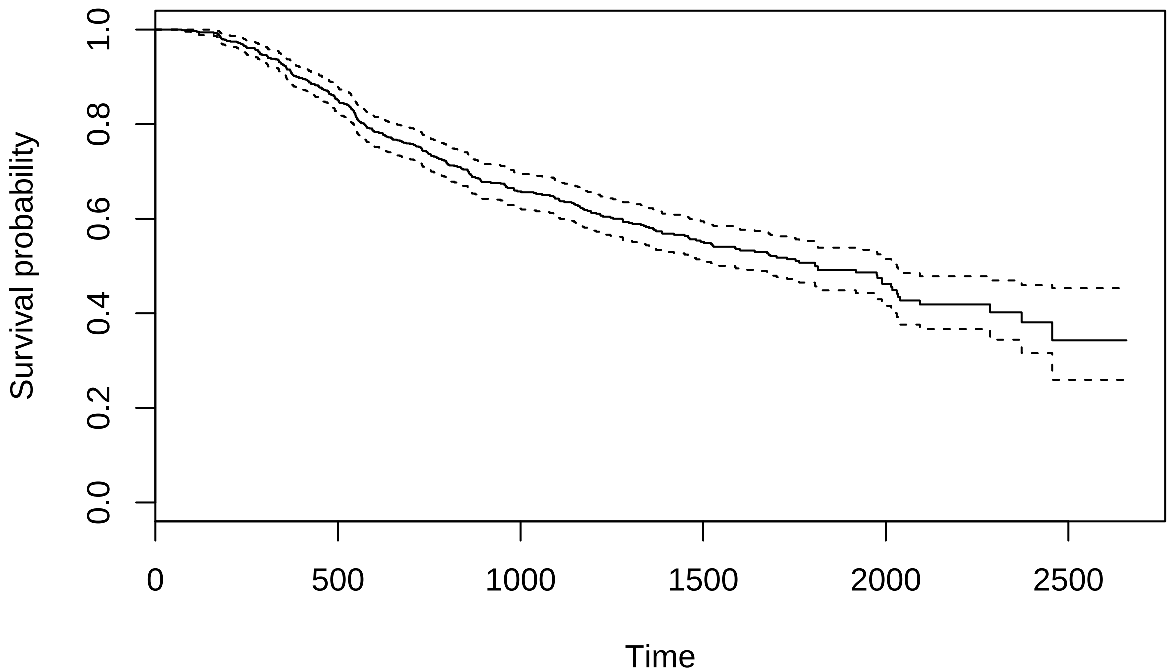
```
##    594     506          2     0.788 0.01600         0.757          0.820
##    595     504          1     0.786 0.01604         0.755          0.818
##    598     502          1     0.785 0.01608         0.754          0.817
##    600     501          1     0.783 0.01613         0.752          0.815
##    612     500          1     0.781 0.01617         0.750          0.814
##    622     498          1     0.780 0.01622         0.749          0.812
##    624     495          2     0.777 0.01630         0.745          0.809
##    629     492          1     0.775 0.01635         0.744          0.808
##    632     489          1     0.774 0.01639         0.742          0.806
##    637     488          1     0.772 0.01643         0.740          0.805
##    646     486          1     0.770 0.01647         0.739          0.803
##    648     485          1     0.769 0.01652         0.737          0.802
##    650     484          1     0.767 0.01656         0.735          0.800
##    662     479          1     0.766 0.01660         0.734          0.799
##    670     477          1     0.764 0.01664         0.732          0.797
##    675     476          1     0.762 0.01669         0.730          0.796
##    679     474          1     0.761 0.01673         0.729          0.794
##    687     473          1     0.759 0.01677         0.727          0.793
##    698     470          1     0.758 0.01681         0.725          0.791
##    707     469          1     0.756 0.01685         0.724          0.790
##    712     468          1     0.754 0.01689         0.722          0.788
##    714     467          1     0.753 0.01694         0.720          0.787
##    722     464          1     0.751 0.01698         0.719          0.785
##    727     461          1     0.749 0.01702         0.717          0.784
##    729     460          1     0.748 0.01706         0.715          0.782
##    730     459          1     0.746 0.01710         0.713          0.781
##    731     458          1     0.745 0.01714         0.712          0.779
##    732     457          1     0.743 0.01718         0.710          0.777
##    742     449          1     0.741 0.01722         0.708          0.776
##    745     448          1     0.740 0.01726         0.707          0.774
##    747     447          1     0.738 0.01730         0.705          0.773
##    748     445          1     0.736 0.01734         0.703          0.771
##    754     442          1     0.735 0.01738         0.701          0.770
##    755     441          1     0.733 0.01742         0.700          0.768
##    762     437          1     0.731 0.01746         0.698          0.766
##    769     434          1     0.730 0.01750         0.696          0.765
##    772     432          1     0.728 0.01755         0.694          0.763
##    776     430          1     0.726 0.01759         0.693          0.762
##    784     428          1     0.725 0.01763         0.691          0.760
##    790     427          1     0.723 0.01767         0.689          0.758
##    795     425          1     0.721 0.01771         0.687          0.757
##    797     424          2     0.718 0.01779         0.684          0.753
##    799     421          1     0.716 0.01783         0.682          0.752
##    801     420          1     0.714 0.01786         0.680          0.750
##    805     419          1     0.713 0.01790         0.678          0.749
##    819     417          1     0.711 0.01794         0.677          0.747
##    827     415          1     0.709 0.01798         0.675          0.745
##    836     413          1     0.708 0.01802         0.673          0.744
##    838     412          1     0.706 0.01806         0.671          0.742
##    842     410          1     0.704 0.01809         0.669          0.740
##    855     407          2     0.701 0.01817         0.666          0.737
##    857     404          1     0.699 0.01821         0.664          0.736
##    859     401          2     0.695 0.01828         0.660          0.732
##    861     398          1     0.694 0.01832         0.659          0.731
```

```
##    865    397         1     0.692 0.01836         0.657         0.729
##    866    396         1     0.690 0.01839         0.655         0.727
##    867    395         1     0.688 0.01843         0.653         0.726
##    876    392         1     0.687 0.01847         0.651         0.724
##    883    390         1     0.685 0.01850         0.650         0.722
##    889    388         1     0.683 0.01854         0.648         0.720
##    890    387         1     0.681 0.01857         0.646         0.719
##    891    386         1     0.680 0.01861         0.644         0.717
##    893    384         1     0.678 0.01865         0.642         0.715
##    918    382         1     0.676 0.01868         0.640         0.714
##    945    374         1     0.674 0.01872         0.639         0.712
##    956    372         2     0.671 0.01879         0.635         0.708
##    959    370         1     0.669 0.01883         0.633         0.707
##    960    369         1     0.667 0.01886         0.631         0.705
##    964    368         1     0.665 0.01890         0.629         0.703
##    981    358         1     0.663 0.01894         0.627         0.702
##    982    357         1     0.661 0.01898         0.625         0.700
##    983    356         1     0.660 0.01901         0.623         0.698
##    991    354         1     0.658 0.01905         0.621         0.696
##   1002    352         1     0.656 0.01909         0.620         0.694
##   1036    350         1     0.654 0.01913         0.618         0.693
##   1043    349         1     0.652 0.01916         0.616         0.691
##   1059    348         1     0.650 0.01920         0.614         0.689
##   1080    344         1     0.648 0.01924         0.612         0.687
##   1090    340         1     0.646 0.01927         0.610         0.685
##   1093    337         1     0.645 0.01931         0.608         0.684
##   1094    335         1     0.643 0.01935         0.606         0.682
##   1105    330         2     0.639 0.01943         0.602         0.678
##   1108    328         1     0.637 0.01947         0.600         0.676
##   1120    322         1     0.635 0.01951         0.598         0.674
##   1140    320         1     0.633 0.01955         0.596         0.672
##   1146    319         1     0.631 0.01958         0.594         0.670
##   1150    318         1     0.629 0.01962         0.592         0.669
##   1157    315         1     0.627 0.01966         0.589         0.667
##   1162    314         1     0.625 0.01970         0.587         0.665
##   1164    312         1     0.623 0.01974         0.585         0.663
##   1170    309         1     0.621 0.01978         0.583         0.661
##   1174    307         1     0.619 0.01982         0.581         0.659
##   1183    304         1     0.617 0.01986         0.579         0.657
##   1192    302         1     0.615 0.01989         0.577         0.655
##   1193    300         1     0.613 0.01993         0.575         0.653
##   1207    297         1     0.611 0.01997         0.573         0.651
##   1218    294         1     0.609 0.02001         0.571         0.649
##   1219    293         1     0.606 0.02005         0.568         0.647
##   1225    289         1     0.604 0.02009         0.566         0.645
##   1246    282         1     0.602 0.02013         0.564         0.643
##   1253    280         1     0.600 0.02018         0.562         0.641
##   1279    277         1     0.598 0.02022         0.560         0.639
##   1280    276         2     0.594 0.02030         0.555         0.635
##   1296    273         1     0.591 0.02035         0.553         0.633
##   1306    271         1     0.589 0.02039         0.551         0.631
##   1329    268         1     0.587 0.02043         0.548         0.628
##   1337    265         1     0.585 0.02047         0.546         0.626
##   1343    260         1     0.583 0.02052         0.544         0.624
```

```
##   1352    255        1     0.580 0.02056         0.541          0.622
##   1363    248        1     0.578 0.02061         0.539          0.620
##   1366    246        1     0.576 0.02066         0.536          0.618
##   1371    245        1     0.573 0.02071         0.534          0.615
##   1387    244        1     0.571 0.02076         0.532          0.613
##   1388    243        1     0.569 0.02081         0.529          0.611
##   1420    241        1     0.566 0.02085         0.527          0.609
##   1449    232        1     0.564 0.02091         0.524          0.606
##   1459    231        1     0.561 0.02096         0.522          0.604
##   1460    229        1     0.559 0.02101         0.519          0.602
##   1463    228        1     0.556 0.02106         0.517          0.599
##   1481    223        1     0.554 0.02111         0.514          0.597
##   1493    218        1     0.551 0.02117         0.511          0.594
##   1502    214        1     0.549 0.02122         0.509          0.592
##   1521    209        1     0.546 0.02128         0.506          0.590
##   1525    208        1     0.544 0.02134         0.503          0.587
##   1528    206        1     0.541 0.02140         0.501          0.585
##   1587    200        1     0.538 0.02147         0.498          0.582
##   1589    199        1     0.535 0.02153         0.495          0.579
##   1601    196        1     0.533 0.02159         0.492          0.577
##   1641    185        1     0.530 0.02167         0.489          0.574
##   1675    177        1     0.527 0.02175         0.486          0.571
##   1679    175        1     0.524 0.02183         0.483          0.568
##   1684    173        1     0.521 0.02191         0.480          0.566
##   1701    168        1     0.518 0.02200         0.476          0.563
##   1730    150        1     0.514 0.02212         0.473          0.560
##   1753    144        1     0.511 0.02226         0.469          0.556
##   1763    140        1     0.507 0.02240         0.465          0.553
##   1806    132        1     0.503 0.02255         0.461          0.549
##   1807    131        1     0.499 0.02271         0.457          0.546
##   1814    129        2     0.492 0.02300         0.449          0.539
##   1918     94        1     0.486 0.02335         0.443          0.534
##   1975     84        1     0.481 0.02378         0.436          0.530
##   1977     82        1     0.475 0.02420         0.430          0.525
##   1989     77        1     0.469 0.02466         0.423          0.520
##   1990     76        1     0.462 0.02509         0.416          0.514
##   2015     68        1     0.456 0.02563         0.408          0.509
##   2018     66        1     0.449 0.02615         0.400          0.503
##   2030     63        1     0.442 0.02669         0.392          0.497
##   2034     61        1     0.434 0.02722         0.384          0.491
##   2039     60        1     0.427 0.02771         0.376          0.485
##   2093     51        1     0.419 0.02840         0.367          0.478
##   2286     25        1     0.402 0.03182         0.344          0.469
##   2372     19        1     0.381 0.03651         0.316          0.460
##   2456     10        1     0.343 0.04884         0.259          0.453
```

The survival curve can be visualized by

```
plot(ans, xlab="Time", ylab="Survival probability")
```



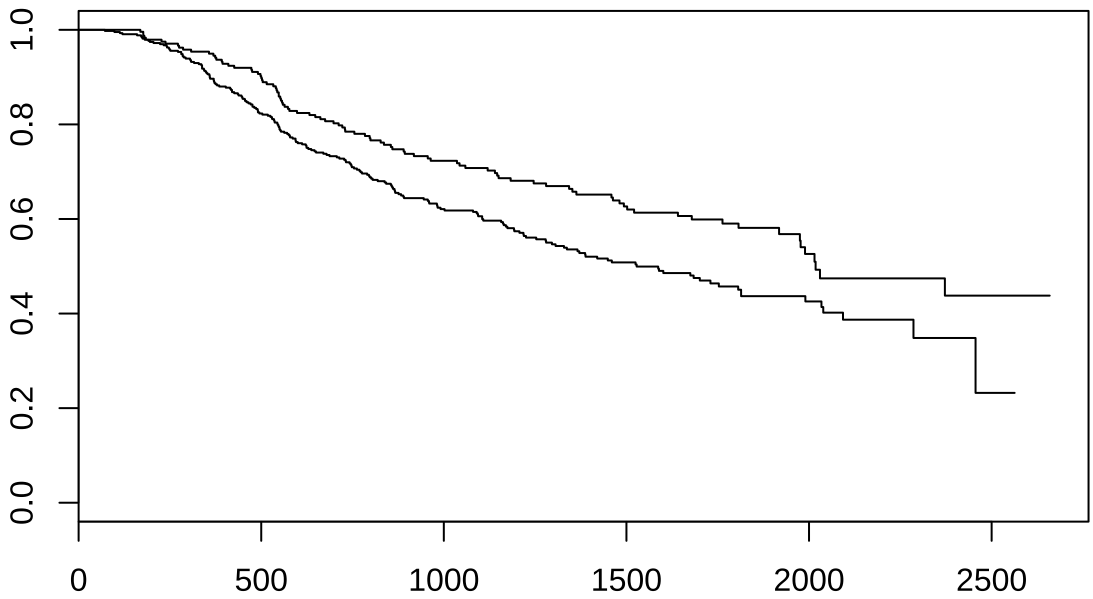
4 Comparing survival curves

Let us illustrate how to compare survival curves for two groups. Researchers are interested in comparing the survival between patients who received or not a new thepary. The R code is:

```
ans.ther <- survfit(Surv(time, event)~as.factor(therapy), datos)
ans.ther
## Call: survfit(formula = Surv(time, event) ~ as.factor(therapy), data = datos)
##
##                        n events median 0.95LCL 0.95UCL
## as.factor(therapy)=0 440    205   1528    1296    1814
## as.factor(therapy)=1 246     94   2018    1918      NA
```

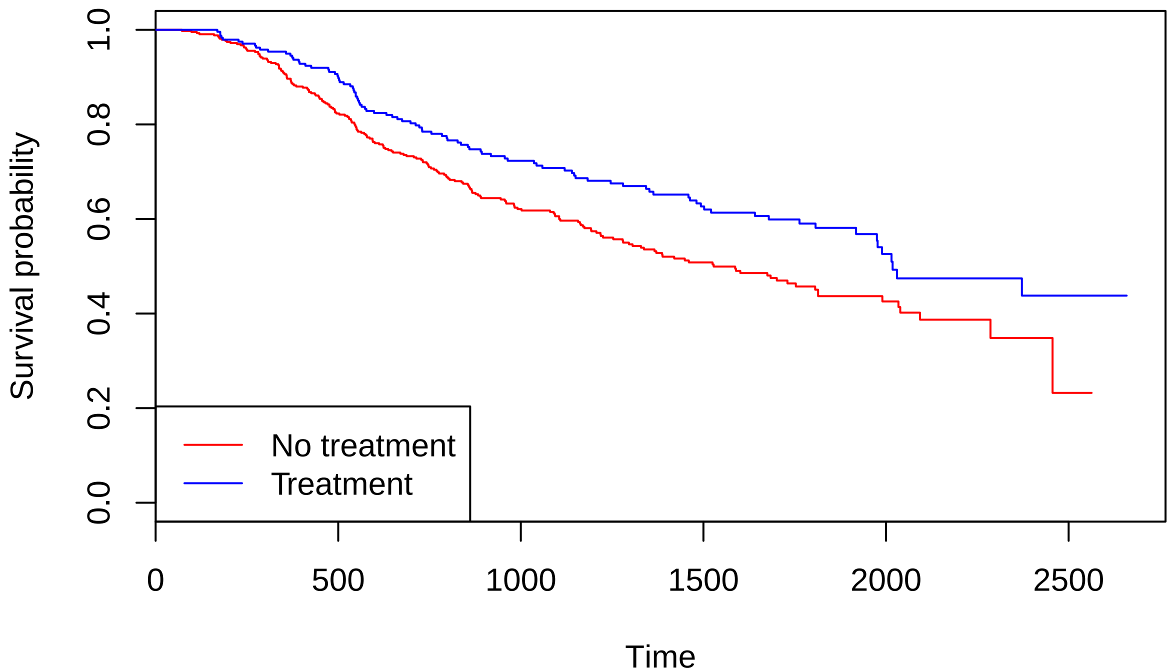
In this case we observe that there are statistically significant differences between the median survival of the two groups since their confidence intervals do not overlap. However we are normally interested in determining differences at any time. This can be visualized by comparing survival curves between groups

```
plot(ans.ther)
```



The plot can be improved by

```
plot(ans.ther, xlab="Time", ylab="Survival probability",
               col=c("red", "blue"))
legend("bottomleft", c("No treatment", "Treatment"),
               col=c("red", "blue"), lty=c(1,1))
```



The comparison across time is computed by using log-rank test

```
ans.logrank<-survdiff(Surv(time, event)~as.factor(therapy), datos,
                              rho=0)
ans.logrank
## Call:
## survdiff(formula = Surv(time, event) ~ as.factor(therapy), data = datos,
##     rho = 0)
##
##                          N Observed Expected (O-E)^2/E (O-E)^2/V
## as.factor(therapy)=0 440      205      180      3.37      8.56
## as.factor(therapy)=1 246       94      119      5.12      8.56
##
##  Chisq= 8.6  on 1 degrees of freedom, p= 0.00343
```

We observe that the differences we observe in the curves, are statistically significant at 5% level. Notice that the argument `rho` is not necessary since it is the default value. It corresponds to the log-rank test. Wilcoxon test is computed by setting `rho=1`

```
ans.wilcox<-survdiff(Surv(time, event)~as.factor(therapy), datos,
                              rho=1)
ans.wilcox
## Call:
## survdiff(formula = Surv(time, event) ~ as.factor(therapy), data = datos,
##     rho = 1)
##
##                          N Observed Expected (O-E)^2/E (O-E)^2/V
```

```
## as.factor(therapy)=0 440    157.8    138.6      2.66      8.71
## as.factor(therapy)=1 246     69.3     88.5      4.16      8.71
##
##  Chisq= 8.7  on 1 degrees of freedom, p= 0.00316
```

We observe that both tests are providing the same conclusion.

5 Adjusting for other covariates: stratified analysis

In some occassions researchers are interested in comparing survival curves between two groups of patients but they know that there are differences in the survival due to a third variable. For instance, in this data, menopausal status influence survival. Therefore, observed differences between women receiven therapy or not must be adjusted for this third variable. This can be performed by using an stratified test

```
ans.strat<-survdiff(Surv(time, event)~as.factor(therapy)
                      +strata(meno.status), datos)
ans.strat
## Call:
## survdiff(formula = Surv(time, event) ~ as.factor(therapy) + strata(meno.status),
##     data = datos)
##
##                        N Observed Expected (O-E)^2/E (O-E)^2/V
## as.factor(therapy)=0 440      205      180      3.52      9.51
## as.factor(therapy)=1 246       94      119      5.31      9.51
##
##  Chisq= 9.5  on 1 degrees of freedom, p= 0.00204

ans.logrank
## Call:
## survdiff(formula = Surv(time, event) ~ as.factor(therapy), data = datos,
##     rho = 0)
##
##                        N Observed Expected (O-E)^2/E (O-E)^2/V
## as.factor(therapy)=0 440      205      180      3.37      8.56
## as.factor(therapy)=1 246       94      119      5.12      8.56
##
##  Chisq= 8.6  on 1 degrees of freedom, p= 0.00343
```

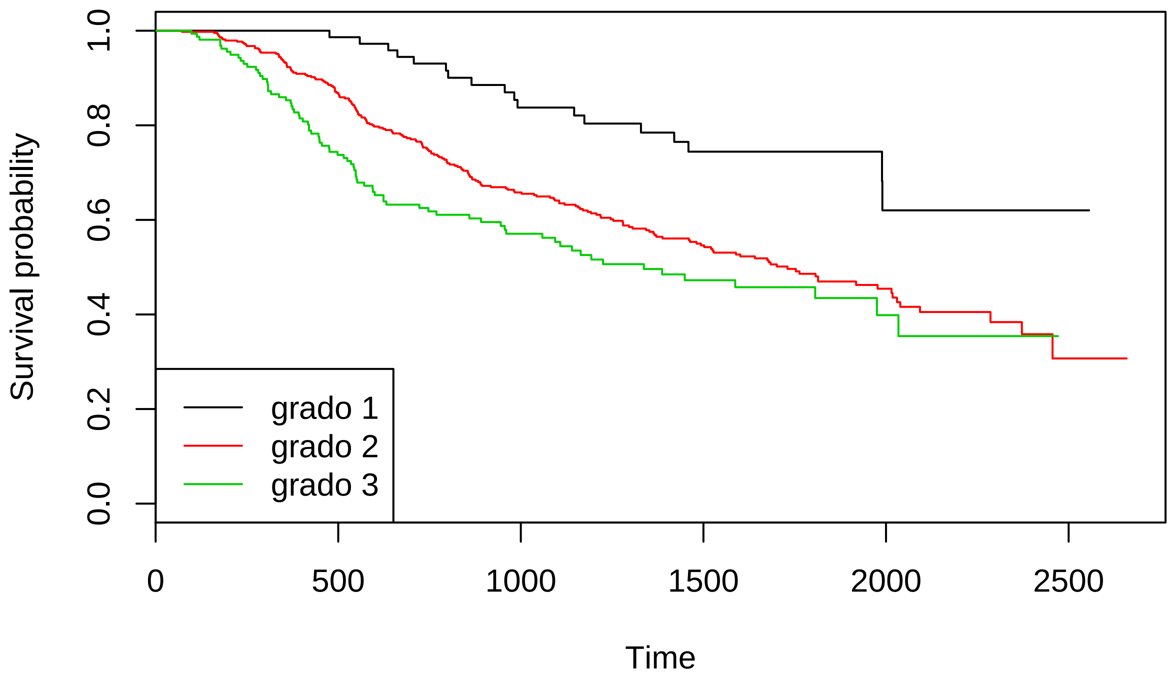
We can observe as both tests are providing similar answer. In both cases the differences in survival times after receiving or not the therapy are statistically significant. This implies that the menopausal status is not confounding the results.

6 Trend test

In other occassions researchers are interested in addressing the next scientific question: Is there any linear relationship between the survival and the tumor grade? In other words, the worse tumor grade implies worse survival? This question makes sense in the situations where the independent variable has any order. In this figure we also check whether this question is well addressed.

```
ans.grade<-survfit(Surv(time, event)~as.factor(tumor.grade), datos)
plot(ans.grade, xlab="Time", ylab="Survival probability", col=1:3)
```

```
legend("bottomleft", c("grado 1", "grado 2", "grado 3"),
                     col=1:3, lty=1)
```



The statistical test is performed by considering `tumor.grade` variable as numeric. This cannot be performed by using `survfit` function since it assumes that the covariates are categorical. These type of question can be answered by fitting Cox proportional hazards models (this will be seen in Part II). Here can also addressed he question: Are there statistical differences between tumoral grades?

```
survdiff(Surv(time, event)~as.factor(tumor.grade), datos)
## Call:
## survdiff(formula = Surv(time, event) ~ as.factor(tumor.grade),
##     data = datos)
##
##                            N Observed Expected (O-E)^2/E (O-E)^2/V
## as.factor(tumor.grade)=1  81       18     42.2   13.8469    16.159
## as.factor(tumor.grade)=2 444      202    198.2    0.0725     0.215
## as.factor(tumor.grade)=3 161       79     58.6    7.0788     8.848
##
##  Chisq= 21.1  on 2 degrees of freedom, p= 2.63e-05
```

Further information about survival data analysis with R can be found in this tutorial Tutorial Survival Analysis.

7 Exercise (to deliver)

Data for exercises are in the repository https://github.com/isglobal-brge/TeachingMaterials/tree/master/Longitudinal_data_analysis/data

File *pulmon.sav* contains data about a survival study about lung cancer (NOTE: data can be loaded into Rby using `read.spss` function available at `foreign` library - use argument *to.data.frame=TRUE*). Colums contain this information:

- TIEMPO Supervivencia (meses)
- ESTADO: 0 VIVO, 1 MORT
- EDAD4 Age at diagnosis in years (quartiles)
- SEXO: HOMBRES, MUJERES
- ESTCLIN Estadio clinico: EST 0/I, EST II, EST IIIA, EST IIIB, EST IV
- IK Indice de estado general (100 estado perfecto, 0 muerte)
- CIRUGIA: 1 No operado, 2 Cirugia no radical, 3 Cirugia Radical
- QUIMIO: 1 No Quimio, 2 Platino
- RADIOTER: 1 No RT, 2 <60 Gy, 3 >60 Gy

Exercise 1: Survival function estimation

- Estimate global survival time
- Draw survival curve
- Estimate median survival time and its confidence interval
- Which is the time where 75% of people have died?
- Estimate survival curve for the covariates sex, surgery, chemotherapy and radiotherapy

Exercise 2: Comparing survival curves

- Draw survival curves of patients receiveing chemotherapy and not
- Compare survival curves of patients receiving chemotherapy, radiotherapy, surgery and clinical stage by using log-rank test. Identify those variables significantly assoicuated with survival
- Are there statistical differences depending on chemotherapy after adjusting by clinical stage?
- Is there any trend in the survival with regard to the Karnofski index. Answer this question by visualy inspecting the required plot \end{enumerate}

---

8 References

- The [`survival`] package (https://cran.r-project.org/web/packages/survival/)

9 Session information

```
## R version 3.3.2 (2016-10-31)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 10 x64 (build 14393)
##
## locale:
## [1] LC_COLLATE=Spanish_Spain.1252  LC_CTYPE=Spanish_Spain.1252
## [3] LC_MONETARY=Spanish_Spain.1252 LC_NUMERIC=C
## [5] LC_TIME=Spanish_Spain.1252
##
## attached base packages:
## [1] stats     graphics  grDevices utils     datasets  methods   base
##
## other attached packages:
```

```
## [1] survival_2.40-1 knitr_1.15.1    BiocStyle_2.2.1
##
## loaded via a namespace (and not attached):
##  [1] Rcpp_0.12.9     lattice_0.20-34 digest_0.6.11   rprojroot_1.2
##  [5] grid_3.3.2      backports_1.0.5 magrittr_1.5    evaluate_0.10
##  [9] stringi_1.1.2   Matrix_1.2-7.1  rmarkdown_1.3   splines_3.3.2
## [13] tools_3.3.2     stringr_1.2.0   yaml_2.1.14     htmltools_0.3.5
```