Survival Analysis of Heroin Addiction Treatment: A Comparative Study of Methadone Treatment Clinics

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5/10/2023

Introduction:

This report presents a survival analysis of the "addicts" dataset, which contains data on 238 heroin addicts undergoing treatment in two distinct methadone treatment clinics. Methadone, a synthetic opiate widely used to alleviate heroin addiction, serves to counteract the effects of heroin and successfully eradicate withdrawal symptoms. The primary goal of this analysis is to evaluate the duration that patients persist in methadone treatment, offering critical insights into the effectiveness of the different therapeutic approaches employed by each clinic.

The two clinics under study follow divergent patient management policies - one clinic maintains a live-in program, while the other does not necessitate residential commitments. By assessing the impact of these contrasting environments on the treatment's duration, this analysis aims to contribute valuable insights towards developing effective and sustainable interventions for heroin addiction.

```
library(survival)
library(survminer)
library(ggfortify)
library(tidyverse)
setwd("/Users/pranjalsrivastava/Desktop/Projects/Clinical_Trial_Study")
data <- read.csv("addicts.csv")
head(data)
```

```
##   ID clinic status survtime prison dose
## 1  1      1      1      428      0   50
## 2  2      1      1      275      1   55
## 3  3      1      1      262      0   55
## 4  4      1      1      183      0   30
## 5  5      1      1      259      1   65
## 6  6      1      1      714      0   55
```

Kaplan Meier estimates by clinic and separately, by prison record

```
## By Clinic
km_clin <- survfit(Surv(survtime,status) ~ clinic, data)
summary(km_clin)
```

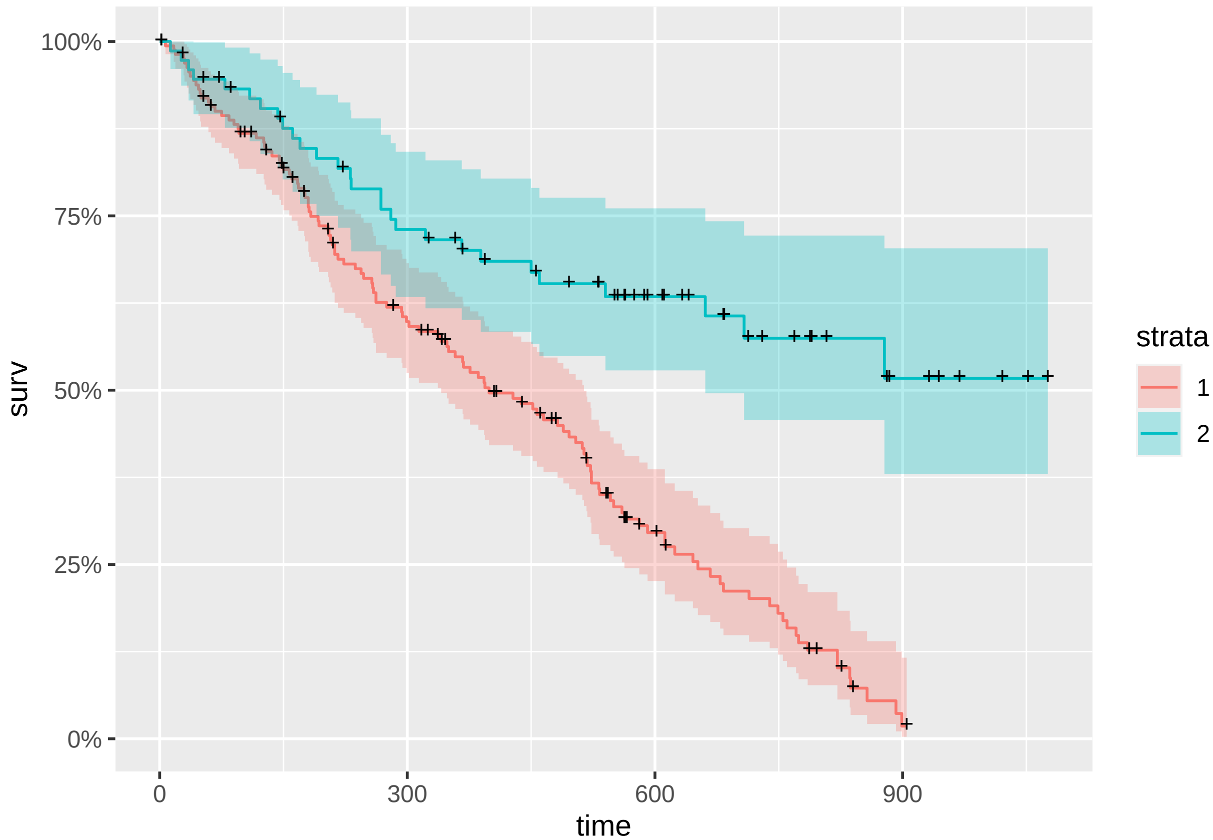
```
## Call: survfit(formula = Surv(survtime, status) ~ clinic, data = data)
```

```
##
##                 clinic=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     7    162       1   0.9938 0.00615      0.98184        1.000
##    17    161       1   0.9877 0.00868      0.97080        1.000
##    19    160       1   0.9815 0.01059      0.96094        1.000
##    29    157       1   0.9752 0.01223      0.95155        0.999
##    30    156       1   0.9690 0.01366      0.94258        0.996
##    33    155       1   0.9627 0.01493      0.93390        0.992
##    35    154       1   0.9565 0.01609      0.92545        0.989
##    37    153       1   0.9502 0.01716      0.91719        0.984
##    41    152       1   0.9440 0.01815      0.90907        0.980
##    44    151       1   0.9377 0.01907      0.90107        0.976
##    47    150       1   0.9315 0.01994      0.89319        0.971
##    49    149       1   0.9252 0.02077      0.88540        0.967
##    50    148       1   0.9190 0.02155      0.87769        0.962
##    59    146       1   0.9127 0.02230      0.87000        0.957
##    62    145       1   0.9064 0.02302      0.86237        0.953
##    67    143       1   0.9000 0.02371      0.85474        0.948
##    75    142       1   0.8937 0.02438      0.84718        0.943
##    84    141       1   0.8874 0.02502      0.83966        0.938
##    90    140       1   0.8810 0.02563      0.83220        0.933
##    95    139       1   0.8747 0.02622      0.82479        0.928
##    96    138       1   0.8683 0.02678      0.81741        0.922
##   117    134       1   0.8619 0.02735      0.80989        0.917
##   126    133       1   0.8554 0.02790      0.80241        0.912
##   127    132       1   0.8489 0.02844      0.79496        0.907
##   129    131       1   0.8424 0.02895      0.78756        0.901
##   136    129       1   0.8359 0.02945      0.78012        0.896
##   145    128       1   0.8294 0.02994      0.77272        0.890
##   147    127       1   0.8228 0.03040      0.76535        0.885
##   150    125       1   0.8163 0.03087      0.75795        0.879
##   157    123       1   0.8096 0.03132      0.75050        0.873
##   160    122       1   0.8030 0.03176      0.74309        0.868
##   167    120       1   0.7963 0.03219      0.73563        0.862
##   168    119       1   0.7896 0.03261      0.72820        0.856
##   175    118       1   0.7829 0.03301      0.72081        0.850
##   176    116       1   0.7762 0.03341      0.71336        0.844
##   180    115       2   0.7627 0.03416      0.69855        0.833
##   181    113       1   0.7559 0.03452      0.69119        0.827
##   183    112       1   0.7492 0.03487      0.68384        0.821
##   192    111       1   0.7424 0.03520      0.67653        0.815
##   193    110       1   0.7357 0.03552      0.66923        0.809
##   204    109       1   0.7289 0.03583      0.66196        0.803
##   205    107       1   0.7221 0.03614      0.65463        0.797
##   207    106       1   0.7153 0.03643      0.64733        0.790
##   209    105       1   0.7085 0.03672      0.64004        0.784
##   212    103       2   0.6947 0.03727      0.62538        0.772
##   216    101       1   0.6878 0.03753      0.61808        0.765
##   223    100       1   0.6810 0.03778      0.61080        0.759
##   237     99       1   0.6741 0.03802      0.60354        0.753
##   244     98       1   0.6672 0.03825      0.59629        0.747
##   247     97       1   0.6603 0.03847      0.58907        0.740
##   257     96       1   0.6534 0.03868      0.58187        0.734
```

```
##    258     95        1   0.6466 0.03888       0.57469         0.727
##    259     94        1   0.6397 0.03907       0.56752         0.721
##    262     93        2   0.6259 0.03942       0.55325         0.708
##    275     91        1   0.6191 0.03958       0.54614         0.702
##    293     89        1   0.6121 0.03974       0.53896         0.695
##    294     88        1   0.6051 0.03990       0.53179         0.689
##    299     87        1   0.5982 0.04004       0.52464         0.682
##    302     86        1   0.5912 0.04017       0.51751         0.675
##    314     85        1   0.5843 0.04030       0.51040         0.669
##    337     82        1   0.5772 0.04043       0.50311         0.662
##    341     80        1   0.5699 0.04057       0.49573         0.655
##    348     77        1   0.5625 0.04071       0.48815         0.648
##    350     76        1   0.5551 0.04084       0.48059         0.641
##    358     75        1   0.5477 0.04096       0.47306         0.634
##    367     74        1   0.5403 0.04107       0.46554         0.627
##    368     73        1   0.5329 0.04117       0.45805         0.620
##    376     72        1   0.5255 0.04126       0.45058         0.613
##    386     71        1   0.5181 0.04134       0.44313         0.606
##    393     70        1   0.5107 0.04140       0.43569         0.599
##    394     69        1   0.5033 0.04146       0.42828         0.592
##    399     68        1   0.4959 0.04150       0.42089         0.584
##    428     65        1   0.4883 0.04156       0.41326         0.577
##    438     64        1   0.4807 0.04161       0.40566         0.570
##    452     62        1   0.4729 0.04165       0.39793         0.562
##    457     61        1   0.4652 0.04168       0.39023         0.554
##    465     59        1   0.4573 0.04172       0.38240         0.547
##    482     56        1   0.4491 0.04176       0.37428         0.539
##    489     55        1   0.4409 0.04179       0.36618         0.531
##    496     54        1   0.4328 0.04181       0.35812         0.523
##    504     53        1   0.4246 0.04181       0.35008         0.515
##    512     52        1   0.4164 0.04180       0.34208         0.507
##    514     51        1   0.4083 0.04177       0.33410         0.499
##    517     50        1   0.4001 0.04172       0.32615         0.491
##    518     48        1   0.3918 0.04168       0.31804         0.483
##    522     47        1   0.3834 0.04162       0.30997         0.474
##    523     46        2   0.3668 0.04144       0.29391         0.458
##    532     44        1   0.3584 0.04133       0.28593         0.449
##    533     43        1   0.3501 0.04120       0.27798         0.441
##    546     40        1   0.3413 0.04109       0.26961         0.432
##    550     39        1   0.3326 0.04096       0.26127         0.423
##    560     38        1   0.3238 0.04081       0.25298         0.415
##    563     37        1   0.3151 0.04063       0.24472         0.406
##    581     33        1   0.3055 0.04051       0.23563         0.396
##    591     31        1   0.2957 0.04038       0.22625         0.386
##    612     29        2   0.2753 0.04009       0.20694         0.366
##    624     26        1   0.2647 0.03992       0.19697         0.356
##    646     25        1   0.2541 0.03970       0.18709         0.345
##    652     24        1   0.2435 0.03943       0.17730         0.334
##    667     23        1   0.2329 0.03912       0.16761         0.324
##    679     22        1   0.2224 0.03874       0.15802         0.313
##    683     21        1   0.2118 0.03832       0.14853         0.302
##    714     20        1   0.2012 0.03784       0.13915         0.291
##    739     19        1   0.1906 0.03730       0.12987         0.280
##    749     18        1   0.1800 0.03670       0.12071         0.268
```

```
##   755     17       1   0.1694 0.03603      0.11166        0.257
##   760     16       1   0.1588 0.03530      0.10273        0.246
##   771     15       1   0.1482 0.03450      0.09394        0.234
##   774     14       1   0.1376 0.03362      0.08528        0.222
##   785     13       1   0.1271 0.03266      0.07677        0.210
##   821     10       2   0.1016 0.03068      0.05626        0.184
##   836      7       1   0.0871 0.02953      0.04484        0.169
##   837      6       1   0.0726 0.02795      0.03414        0.154
##   857      4       1   0.0545 0.02620      0.02120        0.140
##   892      3       1   0.0363 0.02291      0.01054        0.125
##   899      2       1   0.0182 0.01720      0.00283        0.116
##
##                 clinic=2
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    13     74       1    0.986  0.0134        0.961        1.000
##    26     73       1    0.973  0.0189        0.937        1.000
##    35     72       1    0.959  0.0229        0.916        1.000
##    41     71       1    0.946  0.0263        0.896        0.999
##    79     68       1    0.932  0.0294        0.876        0.991
##   109     66       1    0.918  0.0321        0.857        0.983
##   122     65       1    0.904  0.0346        0.838        0.974
##   143     64       1    0.890  0.0368        0.820        0.965
##   149     62       1    0.875  0.0389        0.802        0.955
##   161     61       1    0.861  0.0408        0.785        0.945
##   170     60       1    0.847  0.0426        0.767        0.934
##   190     59       1    0.832  0.0442        0.750        0.924
##   216     58       1    0.818  0.0457        0.733        0.913
##   231     56       1    0.803  0.0472        0.716        0.901
##   232     55       1    0.789  0.0486        0.699        0.890
##   268     54       2    0.759  0.0510        0.666        0.866
##   280     52       1    0.745  0.0520        0.650        0.854
##   286     51       1    0.730  0.0530        0.633        0.842
##   322     50       1    0.716  0.0539        0.617        0.830
##   366     47       1    0.700  0.0549        0.601        0.817
##   389     45       1    0.685  0.0558        0.584        0.804
##   450     43       1    0.669  0.0568        0.566        0.790
##   460     41       1    0.653  0.0577        0.549        0.776
##   540     35       1    0.634  0.0590        0.528        0.761
##   661     23       1    0.606  0.0625        0.495        0.742
##   708     19       1    0.575  0.0669        0.457        0.722
##   878     10       1    0.517  0.0812        0.380        0.703
```

```
autoplot(km_clin)
```




```
## By Prison record
km_pris <- survfit(Surv(survtime,status) ~ prison, data)
summary(km_pris)
```

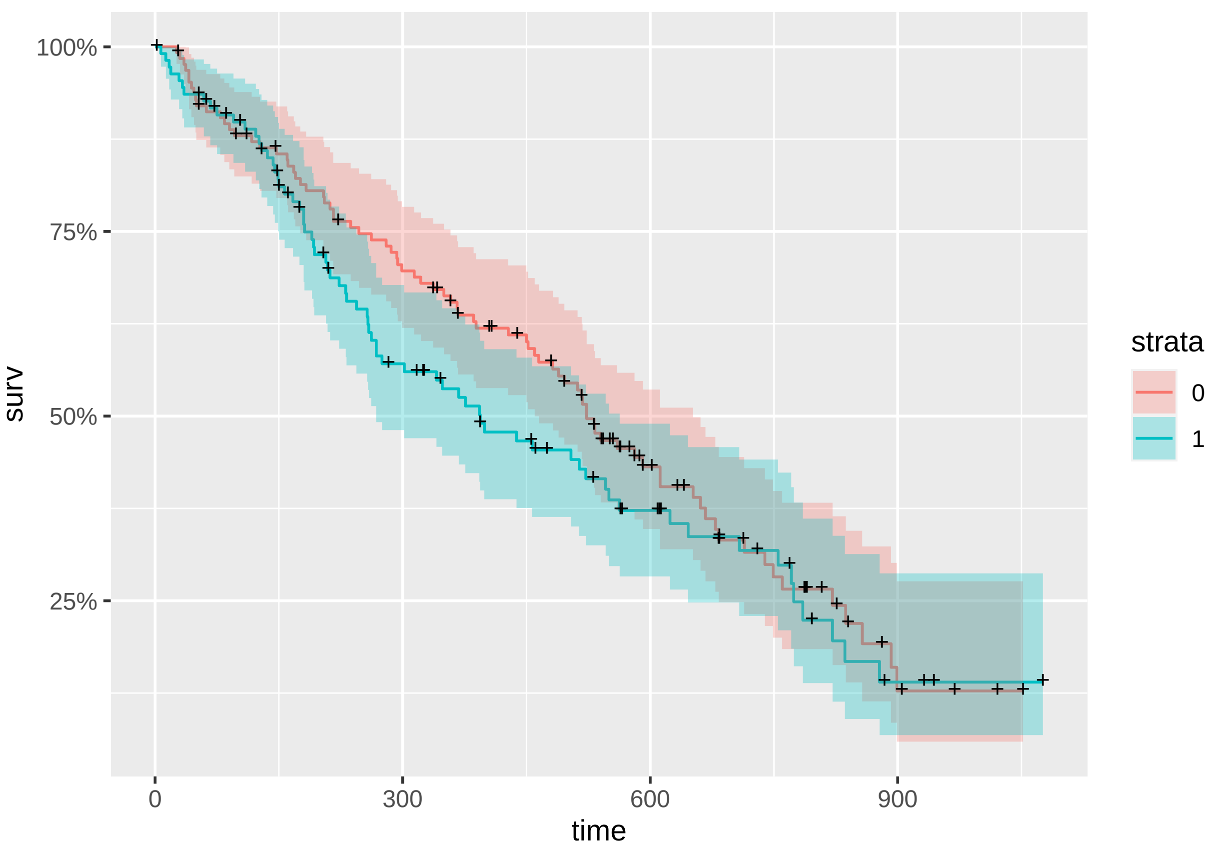
```
## Call: survfit(formula = Surv(survtime, status) ~ prison, data = data)
##
##                 prison=0
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    26    127       1    0.992 0.00784       0.9769        1.000
##    30    124       1    0.984 0.01114       0.9625        1.000
##    35    123       1    0.976 0.01362       0.9498        1.000
##    37    122       1    0.968 0.01568       0.9379        0.999
##    41    121       2    0.952 0.01907       0.9155        0.990
##    44    119       1    0.944 0.02052       0.9047        0.985
##    47    118       1    0.936 0.02185       0.8943        0.980
##    49    117       1    0.928 0.02309       0.8840        0.974
##    50    116       1    0.920 0.02423       0.8738        0.969
##    62    114       1    0.912 0.02533       0.8637        0.963
##    79    113       1    0.904 0.02636       0.8538        0.957
##    84    112       1    0.896 0.02733       0.8439        0.951
##    90    111       1    0.888 0.02825       0.8342        0.945
##    96    110       1    0.880 0.02913       0.8245        0.939
##   117    107       1    0.872 0.02999       0.8147        0.932
##   127    106       1    0.863 0.03081       0.8050        0.926
##   147    104       1    0.855 0.03162       0.7952        0.919
##   160    103       1    0.847 0.03238       0.7856        0.913
```

```
##   161    102         1     0.838 0.03311       0.7760         0.906
##   168    101         1     0.830 0.03381       0.7664         0.899
##   170    100         1     0.822 0.03447       0.7569         0.892
##   176     99         1     0.814 0.03511       0.7475         0.885
##   183     98         1     0.805 0.03572       0.7382         0.878
##   204     97         1     0.797 0.03630       0.7288         0.871
##   205     96         1     0.789 0.03686       0.7196         0.864
##   212     95         1     0.780 0.03740       0.7103         0.857
##   216     94         2     0.764 0.03840       0.6920         0.843
##   237     91         1     0.755 0.03888       0.6828         0.836
##   247     90         1     0.747 0.03935       0.6736         0.828
##   262     89         1     0.739 0.03979       0.6645         0.821
##   280     88         1     0.730 0.04021       0.6554         0.813
##   286     87         1     0.722 0.04062       0.6464         0.806
##   293     86         1     0.713 0.04100       0.6373         0.798
##   294     85         1     0.705 0.04137       0.6284         0.791
##   299     84         1     0.697 0.04172       0.6194         0.783
##   314     83         1     0.688 0.04205       0.6105         0.776
##   322     82         1     0.680 0.04237       0.6016         0.768
##   337     81         1     0.671 0.04267       0.5928         0.760
##   350     78         1     0.663 0.04298       0.5837         0.753
##   358     77         1     0.654 0.04328       0.5746         0.745
##   366     75         1     0.645 0.04357       0.5655         0.737
##   367     74         1     0.637 0.04385       0.5563         0.729
##   386     72         1     0.628 0.04412       0.5471         0.721
##   389     71         1     0.619 0.04438       0.5379         0.712
##   428     68         1     0.610 0.04465       0.5284         0.704
##   450     66         1     0.601 0.04492       0.5188         0.696
##   452     65         1     0.591 0.04517       0.5092         0.687
##   460     64         1     0.582 0.04540       0.4997         0.678
##   465     63         1     0.573 0.04561       0.4902         0.670
##   482     61         1     0.564 0.04582       0.4806         0.661
##   489     60         1     0.554 0.04601       0.4710         0.652
##   496     59         1     0.545 0.04617       0.4614         0.643
##   512     57         1     0.535 0.04634       0.4517         0.634
##   517     56         1     0.526 0.04649       0.4420         0.625
##   518     54         1     0.516 0.04664       0.4322         0.616
##   523     53         2     0.496 0.04687       0.4126         0.597
##   532     51         1     0.487 0.04695       0.4029         0.588
##   533     49         1     0.477 0.04703       0.3930         0.578
##   540     48         1     0.467 0.04709       0.3831         0.569
##   560     43         1     0.456 0.04723       0.3722         0.559
##   581     38         1     0.444 0.04748       0.3601         0.548
##   591     35         1     0.431 0.04779       0.3471         0.536
##   612     32         2     0.404 0.04846       0.3197         0.511
##   652     28         1     0.390 0.04883       0.3051         0.498
##   661     27         1     0.375 0.04911       0.2906         0.485
##   667     26         1     0.361 0.04930       0.2763         0.472
##   679     25         1     0.347 0.04940       0.2621         0.458
##   683     24         1     0.332 0.04941       0.2482         0.445
##   714     20         1     0.316 0.04965       0.2318         0.430
##   739     19         1     0.299 0.04974       0.2158         0.414
##   749     18         1     0.282 0.04967       0.2000         0.399
##   760     17         1     0.266 0.04945       0.1845         0.383
```

```
##   821     12       1    0.244 0.05004       0.1629        0.364
##   837     10       1    0.219 0.05062       0.1394        0.345
##   857      8       1    0.192 0.05117       0.1137        0.324
##   892      6       1    0.160 0.05167       0.0848        0.301
##   899      5       1    0.128 0.05027       0.0592        0.276
##
##                 prison=1
##  time n.risk n.event survival std.err lower 95% CI upper 95% CI
##     7    109       1    0.991 0.00913       0.9731        1.000
##    13    108       1    0.982 0.01285       0.9568        1.000
##    17    107       1    0.972 0.01567       0.9422        1.000
##    19    106       1    0.963 0.01801       0.9286        0.999
##    29    105       1    0.954 0.02004       0.9157        0.994
##    33    104       1    0.945 0.02185       0.9031        0.989
##    35    103       1    0.936 0.02348       0.8909        0.983
##    59    101       1    0.927 0.02501       0.8788        0.977
##    67     99       1    0.917 0.02645       0.8668        0.970
##    75     97       1    0.908 0.02782       0.8548        0.964
##    95     95       1    0.898 0.02912       0.8429        0.957
##   109     93       1    0.888 0.03036       0.8309        0.950
##   122     92       1    0.879 0.03153       0.8192        0.943
##   126     91       1    0.869 0.03263       0.8075        0.936
##   129     90       1    0.860 0.03367       0.7960        0.928
##   136     88       1    0.850 0.03467       0.7844        0.920
##   143     87       1    0.840 0.03562       0.7730        0.913
##   145     86       1    0.830 0.03652       0.7616        0.905
##   149     84       1    0.820 0.03740       0.7502        0.897
##   150     83       1    0.810 0.03824       0.7389        0.889
##   157     81       1    0.800 0.03905       0.7274        0.881
##   167     79       1    0.790 0.03985       0.7159        0.872
##   175     78       1    0.780 0.04061       0.7045        0.864
##   180     76       2    0.760 0.04205       0.6815        0.847
##   181     74       1    0.749 0.04272       0.6702        0.838
##   190     73       1    0.739 0.04335       0.6589        0.829
##   192     72       1    0.729 0.04395       0.6476        0.820
##   193     71       1    0.719 0.04451       0.6364        0.811
##   207     69       1    0.708 0.04507       0.6251        0.802
##   209     68       1    0.698 0.04559       0.6139        0.793
##   212     66       1    0.687 0.04611       0.6025        0.784
##   223     65       1    0.677 0.04660       0.5912        0.774
##   231     64       1    0.666 0.04705       0.5799        0.765
##   232     63       1    0.655 0.04748       0.5687        0.755
##   244     62       1    0.645 0.04788       0.5576        0.746
##   257     61       1    0.634 0.04824       0.5465        0.736
##   258     60       1    0.624 0.04858       0.5354        0.727
##   259     59       1    0.613 0.04890       0.5245        0.717
##   262     58       1    0.603 0.04918       0.5135        0.707
##   268     57       2    0.581 0.04968       0.4918        0.687
##   275     55       1    0.571 0.04989       0.4810        0.678
##   302     53       1    0.560 0.05010       0.4701        0.667
##   341     49       1    0.549 0.05036       0.4584        0.657
##   348     47       1    0.537 0.05062       0.4464        0.646
##   368     46       1    0.525 0.05085       0.4346        0.635
##   376     45       1    0.514 0.05104       0.4228        0.624
```

```
##   393     44       1   0.502 0.05120      0.4110       0.613
##   394     43       1   0.490 0.05132      0.3994       0.602
##   399     41       1   0.478 0.05145      0.3874       0.591
##   438     40       1   0.466 0.05153      0.3756       0.579
##   457     38       1   0.454 0.05162      0.3634       0.567
##   504     35       1   0.441 0.05175      0.3505       0.555
##   514     34       1   0.428 0.05183      0.3377       0.543
##   522     33       1   0.415 0.05185      0.3251       0.530
##   546     29       1   0.401 0.05201      0.3109       0.517
##   550     28       1   0.387 0.05208      0.2969       0.503
##   563     27       1   0.372 0.05208      0.2830       0.490
##   624     21       1   0.355 0.05253      0.2652       0.474
##   646     20       1   0.337 0.05281      0.2477       0.458
##   708     18       1   0.318 0.05309      0.2293       0.441
##   755     16       1   0.298 0.05336      0.2100       0.423
##   771     12       1   0.273 0.05440      0.1851       0.404
##   774     11       1   0.249 0.05483      0.1613       0.383
##   785     10       1   0.224 0.05469      0.1385       0.361
##   821      8       1   0.196 0.05454      0.1133       0.338
##   836      7       1   0.168 0.05343      0.0898       0.313
##   878      6       1   0.140 0.05132      0.0681       0.287
```

```
autoplot(km_pris)
```



2 Graphical evaluation of the proportional hazards assumption for clinic and separately, for prison.

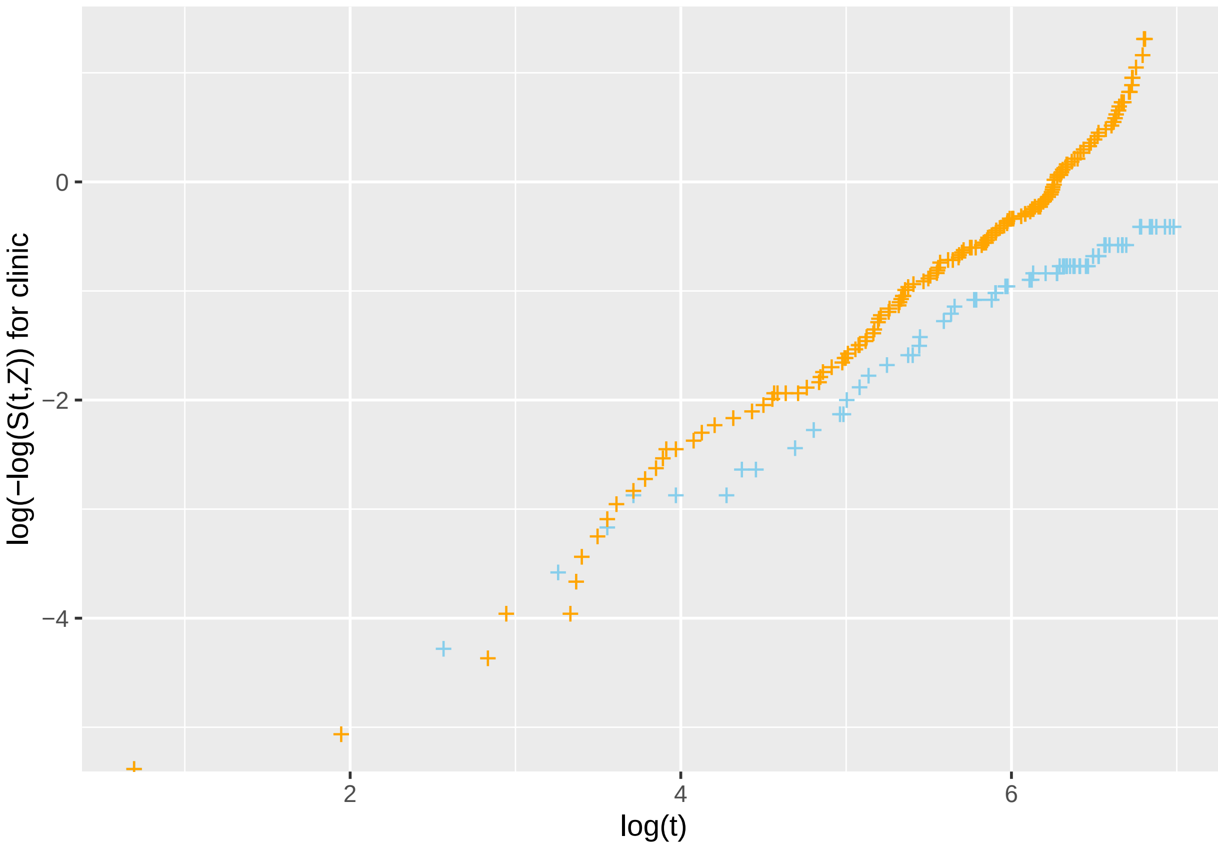
```
## I will be evaluating the proportional hazards assumption using KM estimates


## By Clinic
lmod1 <- coxph(Surv(survtime, status) ~ strata(clinic), data = data, ties="breslow")
fit0=basehaz(lmod1,centered=FALSE)
fit01=fit0[fit0$strata=="clinic=1",]
fit00=fit0[fit0$strata=="clinic=2",]

# Create a data frame with the log-transformed time and hazard values for fit00
data_fit00 <- data.frame(time = log(fit00$time), hazard = log(fit00$hazard))

# Create a data frame with the log-transformed time and hazard values for fit01
data_fit01 <- data.frame(time = log(fit01$time), hazard = log(fit01$hazard))

# Create the plot
ggplot() +
geom_point(data = data_fit00, aes(x = time, y = hazard),
             shape = "+" , size = 4,
             color = "skyblue") +
geom_point(data = data_fit01, aes(x = time, y = hazard),
             shape = "+" , size = 4,
             color = "orange") +
ylab("log(-log(S(t,Z)) for clinic") +
xlab("log(t)")
```



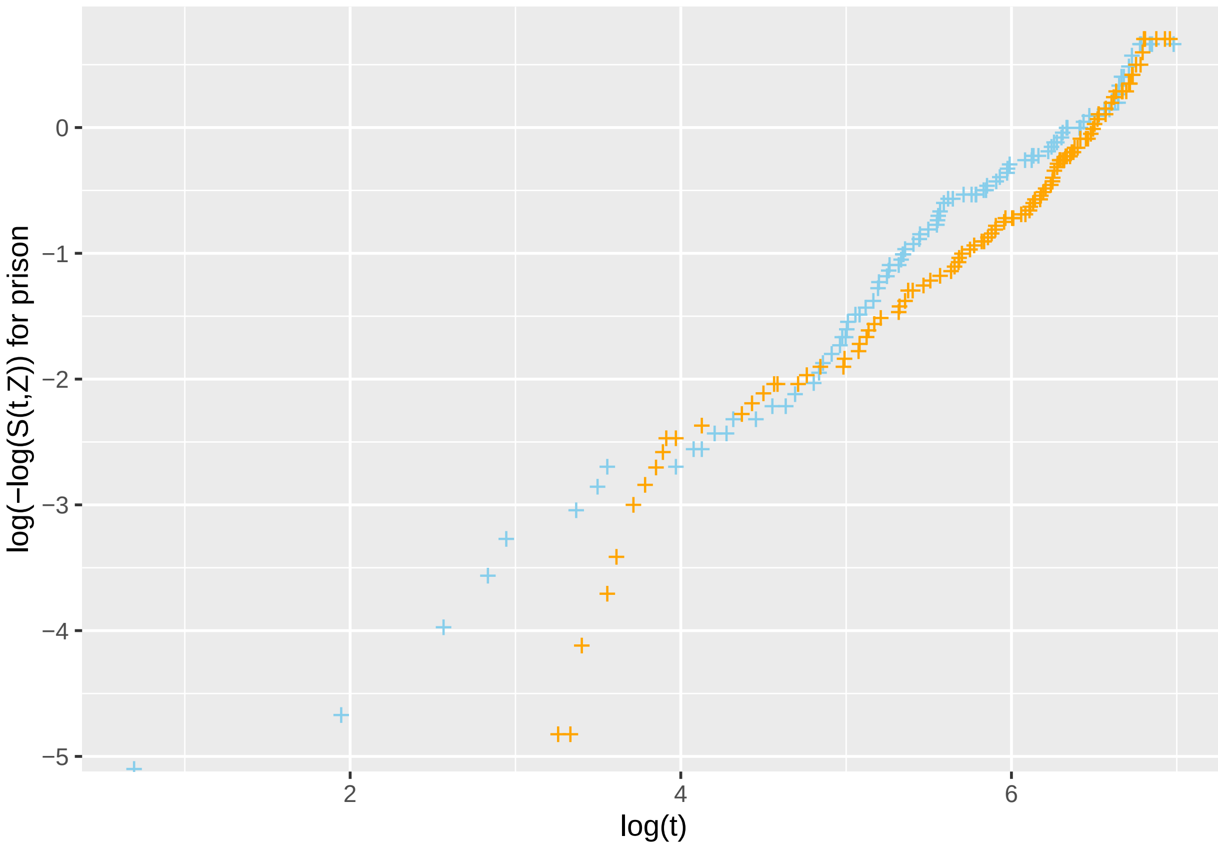

```r
## By Prison

lmod2 <- coxph(Surv(survtime, status) ~ strata(prison), data = data, ties="breslow")
fit0=basehaz(lmod2,centered=FALSE)
fit01=fit0[fit0$strata=="prison=0",]
fit00=fit0[fit0$strata=="prison=1",]

# Create a data frame with the log-transformed time and hazard values for fit00
data_fit00 <- data.frame(time = log(fit00$time), hazard = log(fit00$hazard))

# Create a data frame with the log-transformed time and hazard values for fit01
data_fit01 <- data.frame(time = log(fit01$time), hazard = log(fit01$hazard))

# Create the plot
ggplot() +
geom_point(data = data_fit00, aes(x = time, y = hazard),
             shape = "+" , size = 4, color = "skyblue") +
geom_point(data = data_fit01, aes(x = time, y = hazard),
             shape = "+" , size = 4, color = "orange") +
ylab("log(-log(S(t,Z)) for prison") +
xlab("log(t)")
```



From the graph for clinic, we can see that the lines cross in the initial point and then move parallel which shows the assumption of Proportional Hazard holds.

While from the graph for prison, the lines are crossing each other at multiple points and are not parallel to each other. Which violates the Proportional hazard assumption.

A Cox PH model to assess the unadjusted effect of clinic on time to treatment drop and provide the estimated Hazard ratio and a 95% confidence interval for Clinic 1 vs Clinic 2.

```
# Fit the Cox proportional hazards model
cox_model <- coxph(Surv(survtime, status) ~ factor(clinic), data = data, ties="breslow")

# Get the hazard ratio and 95% confidence interval for Clinic 1 vs Clinic 2
cox_summary <- summary(cox_model)

# Extract the hazard ratio and confidence intervals
hazard_ratio <- exp(cox_model$coefficients)

ci <- c(cox_summary$conf.int[3], cox_summary$conf.int[4])
```

```r
# Print the results
cat("Hazard Ratio (Clinic 1 vs Clinic 2):", round(hazard_ratio, 3), "\n")
```

```
## Hazard Ratio (Clinic 1 vs Clinic 2): 0.341
```

```r
cat("95% Confidence Interval:", round(ci, 3))
```

```
## 95% Confidence Interval: 0.225 0.517
```

Based on the unadjusted model, the predicted probability (the Breslow estimator) of remaining in treatment at Clinic 1 for at least 60 days and the probability of remaining in treatment for at least 60 days at Clinic 2?

```r
#The predicted probability (the Breslow estimator) for Clinic 1

fit1 = predict(cox_model, newdata=list(survtime = 60,
                        status = 1, clinic="1"),
                data=data, type="expected")
p1 = exp(-fit1)

# The predicted probability (the Breslow estimator) for Clinic 2

fit2 = predict(cox_model, newdata=list(survtime = 60,
                        status = 1, clinic="2"),
                data=data, type="expected")
p2 = exp(-fit2)

cat("The predicted probability (the Breslow estimator) for Clinic 1:", p1, "\n")
```

```
## The predicted probability (the Breslow estimator) for Clinic 1: 0.9041755
```

```r
cat("The predicted probability (the Breslow estimator) for Clinic 2:", p2, "\n")
```

```
## The predicted probability (the Breslow estimator) for Clinic 2: 0.9662661
```

Likelihood Ratio Test on different models.

```r
Likelihood = c(1411.70, 1380.60, 1410.56, 1374.91, 1378.03,
                1350.85, 1373.70, 1347.35, 1344.82, 1346.65, 1346.84)
parameter = c(0, 1, 1, 1, 2, 2, 2, 3, 4, 4, 4)

parameter_alpha = 2*parameter
```

```r
Models = c(1:11)

AIC = Likelihood + parameter_alpha

table = data.frame(Models, Likelihood, AIC)
print(table)
```

```
##    Models Likelihood     AIC
## 1       1    1411.70 1411.70
## 2       2    1380.60 1382.60
## 3       3    1410.56 1412.56
## 4       4    1374.91 1376.91
## 5       5    1378.03 1382.03
## 6       6    1350.85 1354.85
## 7       7    1373.70 1377.70
## 8       8    1347.35 1353.35
## 9       9    1344.82 1352.82
## 10     10    1346.65 1354.65
## 11     11    1346.84 1354.84
```

The strongest predictor of time to treatment dropout in this study

To determine the strongest predictor of time to treatment dropout, I performed the LR test by comparing the likelihoods of the model with the predictors, to the likelihoods of the null model. Specifically, we will compare the model 1 with model 2, model 3 and model 4.

1. Lets start with performing LR test on model 1 that is "Null Model" and Model 2 (Clinic).

```
Here are the relevant models to consider:

Model 1: Includes no predictor.
Model 2: Includes only the "clinic" variable.

From the table, we have the log-likelihood values:

Log-likelihood of Model 1: 1411.70
Log-likelihood of Model 2: 1380.60

Substituting these values into the formula, we get:

X2LR = 1411.70 - 1380.60
     = 31.1

The degrees of freedom for the likelihood ratio test is 1.
p_value = 1 - pchisq(31.1, df = 1)
        = 2.450714e-08 < 0.001
```

2. Similarly, for model 3 and model 1,

```
Here are the relevant models to consider:
```

```
Model 1: Includes no predictor.
Model 3: Includes only the "prison" variable.

From the table, we have the log-likelihood values:

Log-likelihood of Model 1: 1411.70
Log-likelihood of Model 3: 1410.56

Substituting these values into the formula, we get:

X2LR = 1411.70 - 1410.56
     = 1.14

The degrees of freedom for the likelihood ratio test is 1.
p_value = 1 - pchisq(1.14, df = 1)
        = 0.286
```

3. For model 4 and model 1,

```
Here are the relevant models to consider:

Model 1: Includes no predictor.
Model 4: Includes only the "maxdose" variable.

From the table, we have the log-likelihood values:

Log-likelihood of Model 1: 1411.70
Log-likelihood of Model 4: 1374.91

Substituting these values into the formula, we get:

X2LR = 1411.70 - 1374.91
     = 36.79

The degrees of freedom for the likelihood ratio test is 1.
p_value = 1 - pchisq(36.79, df = 1)
        = 1.315634e-09 < 0.001
```

From the LR test results, it is shown that the model 2 and model 4 are significant. Having lowest p-value, we can conclude that, model 4 with predictor "maxdose" is the most important variable in predicting time to treatment dropout in this study.

To check whether prior priosn record should be adusted or not, while comparing the effects of 2 clinics; we will compare model 2 (only clinic) with model 5(clinic and prison)

```
Here are the relevant models to consider:

Model 2: Includes only the "clinic" variable.
Model 5: Includes both the "clinic" and "prison" variables.

From the table, we have the log-likelihood values:

Log-likelihood of Model 2: 1380.60
```

```
                    Log-likelihood of Model 5: 1378.03

                   Substituting these values into the formula, we get:

                          X2LR = 1380.60 - 1378.03
                                 = 2.57

          the degrees of freedom for the likelihood ratio test is 1.
                    p_value = 1 - pchisq(2.57, df = 1)
                              = 0.1089077
```

Since, the p-value is not significant, we can conclude that adjusting for prison is not making any significant change here based on the likelihood ratio test.

Best Model on the basis of AIC value.

```
table$Models[which.min(table$AIC)]
```

```
## [1] 9
```

Comparing the AIC values from the table above, we can see that model 9 has the lowest AIC value, tat concludes that Model has the best fit, which includes the clinic variable, prison variable, maxdose variable, and the interaction between clinic and prison.

The interaction term in model 9 has the best model fit as compared to other models without interaction term, as we can notice from the AIC criterion. The AIC values are comparatively lower for the model with interaction time

Fitting model (9) to the data to find the estimated coefficients and estimated hazard ratio for dropping out for someone in Clinic 1 with a prior prison record and maxdose of 55 versus someone in Clinic 2 with a prior prison record and maxdose of 55.

Estimated hazard ratio for dropping out for someone in Clinic 1 with no prior prison record and maxdose of 55 versus someone in Clinic 2 with no prior prison record

```
## Model Fitting for model 9
mod9 <- coxph(Surv(survtime, status) ~ clinic + prison +
                dose + clinic*prison, data = data, ties="breslow")

## Estimated Coefficients
summary(mod9)$coef
```

```
##                      coef exp(coef)    se(coef)         z     Pr(>|z|)
## clinic        -0.66412463 0.5147239 0.289006757 -2.297955 2.156433e-02
## prison         1.13132971 3.0997756 0.540334391  2.093758 3.628150e-02
## dose          -0.03680163 0.9638673 0.006497039 -5.664369 1.475665e-08
## clinic:prison -0.68186673 0.5056722 0.429280914 -1.588393 1.121975e-01
```

The Cox model with terms for clinic variable, prison variable, maxdose variable, and the interaction between clinic and prison can be written in terms of the hazard functions as:

$$\lambda(t;) = \lambda_o(t) * exp(\beta_1 * Clinic + \beta_2 * Prison + \beta_3 * Dose + \beta_4 * Clinic * Prison)$$
$$\lambda(t;) = \lambda_o(t) * exp((-0.664) * Clinic + 1.131 * Prison + (-0.0368) * Dose + (-0.682) * Clinic * Prison)$$

where $\lambda(t;)$ is the hazard function at time t for an individual with covariate values x, $\lambda_o(t)$ is the baseline hazard at time t, and β_1, β_2, β_3, and β_4 are the regression coefficients for clinic, prison record, maxdose and the interaction between clinic and prison, respectively.

Estimated hazard ratio for dropping out for someone in Clinic 1 with a prior prison record and maxdose of 55 versus someone in Clinic 2 with a prior prison record and maxdose of 55

For patient in clinic 1 with prior prison record, when maxdose = 55
$$\lambda_{clinic1} = \lambda_o(t) * exp((-0.664) * 1 + 1.131 * 1 + (-0.0368) * 55 + (-0.682) * 1 * 1)$$
$$\lambda_{clinic1} = \lambda_o(t) * exp(-2.239)$$
For patient in clinic 2 with prior prison record, when maxdose = 55
$$\lambda_{clinic2} = \lambda_o(t) * exp((-0.664) * 2 + 1.131 * 1 + (-0.0368) * 55 + (-0.682) * 2 * 1)$$
$$\lambda_{clinic2} = \lambda_o(t) * exp(-3.585)$$
$$\phi = \lambda_{clinic1}/\lambda_{clinic2}$$
$$\phi = 0.067564/0.0854042$$
$$\phi = 3.842027$$

Estimated hazard ratio for dropping out for someone in Clinic 1 with no prior prison record and maxdose of 55 versus someone in Clinic 2 with no prior prison record and maxdose of 55

For patient in clinic 1 with no prior prison record, when maxdose = 55
$$\lambda_{clinic1} = \lambda_o(t) * exp((-0.664) * 1 + 1.131 * 0 + (-0.0368) * 55 + (-0.682) * 1 * 1)$$
$$\lambda_{clinic1} = \lambda_o(t) * exp(-3.37)$$
For patient in clinic 2 with no prior prison record, when maxdose = 55
$$\lambda_{clinic2} = \lambda_o(t) * exp((-0.664) * 2 + 1.131 * 0 + (-0.0368) * 55 + (-0.682) * 2 * 1)$$
$$\lambda_{clinic2} = \lambda_o(t) * exp(-4.716)$$
$$\phi = \lambda_{clinic1}/\lambda_{clinic2}$$
$$\phi = 0.03438964/0.008950911$$
$$\phi = 3.842027$$

checking the assumption of proportional hazards for "clinic", adjusting for "prison" and "maxdose".

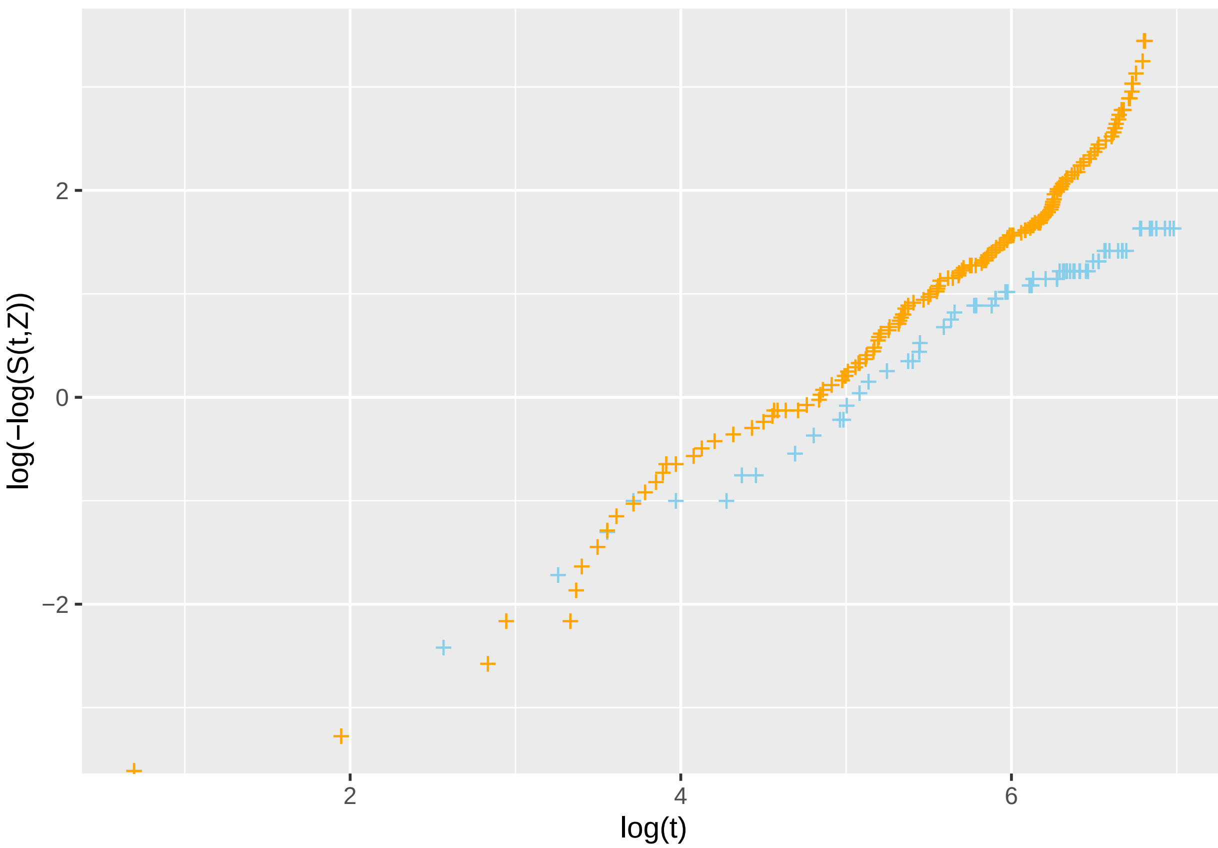
```r
## Model Fitting for model 8 (main effects)
mod8 <- coxph(Surv(survtime, status) ~  (prison+dose) + strata(clinic), data = data, ties="breslow")
fit0=basehaz(mod8,centered=FALSE)
fit01=fit0[fit0$strata=="clinic=1",]
```

```r
fit00=fit0[fit0$strata=="clinic=2",]

# Create a data frame with the log-transformed time and hazard values for fit00
data_fit00 <- data.frame(time = log(fit00$time), hazard = log(fit00$hazard))

# Create a data frame with the log-transformed time and hazard values for fit01
data_fit01 <- data.frame(time = log(fit01$time), hazard = log(fit01$hazard))

# Create the plot
ggplot() +
  geom_point(data = data_fit00, aes(x = time, y = hazard), shape = "+" , size = 4, color = "skyblue") +
  geom_point(data = data_fit01, aes(x = time, y = hazard), shape = "+" , size = 4, color = "orange") +
  ylab("log(-log(S(t,Z))") +
  xlab("log(t)")
```



The groups in the graph looks mostly parallel, so we can conclude that the assumption for proportional hazard holds.

7b An alternative way to test for proportional hazards is to include a clinic × g(t) interaction term.

Fitting the Cox model including this time- dependent covariate, where g(t) = (t − 500)/90, so that the resulting effect can be interpreted as the change in log(HR) for the "clinic" effect for each additional 3 months in the treatment program.

```
# Create a time-dependent dataset using tmerge
data_time_dependent <- tmerge(data, data, id = ID, tstart = survtime, tstop = survtime + 3*30)

head(data_time_dependent)
```

```
##   ID clinic status survtime prison dose tstart tstop
## 1  1      1      1      428      0   50    428   518
## 2  2      1      1      275      1   55    275   365
## 3  3      1      1      262      0   55    262   352
## 4  4      1      1      183      0   30    183   273
## 5  5      1      1      259      1   65    259   349
## 6  6      1      1      714      0   55    714   804
```

```
# Create the time-dependent covariate
data_time_dependent$g_t <- (data_time_dependent$tstop - 500) / 90

# Fit the Cox model with time-dependent covariate
fit_time_dependent <- coxph(Surv(tstart, tstop, status) ~
                              factor(clinic) + factor(prison) + dose + g_t:clinic, data = data_time_dependent)

summary(fit_time_dependent)
```

```
## Call:
## coxph(formula = Surv(tstart, tstop, status) ~ factor(clinic) +
##     factor(prison) + dose + g_t:clinic, data = data_time_dependent)
##
##   n= 238, number of events= 150
##
##                       coef exp(coef)  se(coef)      z Pr(>|z|)
## factor(clinic)2 -3.254345  0.038606  0.610323 -5.332 9.70e-08 ***
## factor(prison)1 -0.054668  0.946800  0.177934 -0.307    0.759
## dose            -0.002848  0.997156  0.007055 -0.404    0.686
## g_t:clinic      -1.398387  0.246995  0.191578 -7.299 2.89e-13 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                 exp(coef) exp(-coef) lower .95 upper .95
## factor(clinic)2   0.03861     25.903   0.01167    0.1277
## factor(prison)1   0.94680      1.056   0.66804    1.3419
```

```
## dose               0.99716      1.003   0.98346    1.0110
## g_t:clinic         0.24699      4.049   0.16967    0.3596
##
## Concordance= 0.891  (se = 0.016 )
## Likelihood ratio test= 121.1  on 4 df,   p=<2e-16
## Wald test            = 62.21  on 4 df,   p=1e-12
## Score (logrank) test = 73.78  on 4 df,   p=4e-15
```

```r
## At 100,
fit100 = predict(fit_time_dependent, newdata=list(tstart = 0,
                     tstop=100,prison=0,dose=0,
        status = 1, clinic = 1, g_t = 0),
        data=data_time_dependent, type="expected")

exp(-fit100)
```

```
## [1] 0.9999671
```

```r
## At 500,
fit500 = predict(fit_time_dependent, newdata=list(tstart = 0,
          tstop=500,prison=0,dose=0, status = 1, clinic = 1, g_t = 0),
          data=data_time_dependent, type="expected")

exp(-fit500)
```

```
## [1] 0.2019964
```

```r
## At 700,
fit700 = predict(fit_time_dependent, newdata=list(tstart = 0,
             tstop=700,prison=0,dose=0, status = 1, clinic = 1, g_t = 0),
             data=data_time_dependent, type="expected")

exp(-fit700)
```

```
## [1] 3.457024e-10
```

The coefficient for the clinic variable is -3.254345, which indicates that individuals from the second clinic have a significantly lower hazard (higher survival probability) compared to individuals from the first clinic (reference category).

The hazard ratio (HR) is calculated as exp(coef), which is 0.038606. This means that the hazard of treatment dropout is 96.14% lower for individuals from the second clinic compared to the first clinic, adjusting for other covariates in the model.

Time-Dependent Effect: The coefficient for the interaction term clinic:g_t is -1.398387. This indicates that the effect of clinic on the hazard of treatment dropout changes over time. Specifically, for each additional 3 months in the treatment program (g_t), the hazard ratio of the clinic effect decreases by a factor of exp(coef), which is 0.246995. In other words, the difference in hazard between the two clinics becomes smaller as time progresses.

Since "maxdose" is a continuous variable, we would like to make sure that the relationship with log(HR) is a linear function of "maxdose". One way to do this is to divide the maximum dose into 4 categories: (0,50] (values between 0 and 50, including 50), (50, 60], (60, 75], and > 75 then evaluate trends over these categories.

```
library(dplyr)
library(lmtest)
```

```
## Warning: package 'lmtest' was built under R version 4.1.2
```

```
## Loading required package: zoo
```

```
## Warning: package 'zoo' was built under R version 4.1.2
```

```
##
## Attaching package: 'zoo'
```

```
## The following objects are masked from 'package:base':
##
##     as.Date, as.Date.numeric
```

```
# Ordinal
data <- data %>%
  dplyr::mutate(dose_ord = case_when(
    dose <= 50 ~ 1,
    dose <= 60 ~ 2,
    dose <= 75 ~ 3,
    TRUE ~ 4
  ))

data$dose_ord<- as.numeric(data$dose_ord)

# categorical as factor of ordinal
```

```r
data$dose_cat_factor<- 0
data$dose_cat_factor<- as.factor(data$dose_ord)

head(data)
```

```
##   ID clinic status survtime prison dose dose_ord dose_cat_factor
## 1  1      1      1      428      0   50        1               1
## 2  2      1      1      275      1   55        2               2
## 3  3      1      1      262      0   55        2               2
## 4  4      1      1      183      0   30        1               1
## 5  5      1      1      259      1   65        3               3
## 6  6      1      1      714      0   55        2               2
```

```r
## Fitting the model (Ordinal)

Mod_ord <- coxph(Surv(survtime, status) ~ clinic + prison +
                dose_ord, data = data, ties="breslow")
summary(Mod_ord)
```

```
## Call:
## coxph(formula = Surv(survtime, status) ~ clinic + prison + dose_ord,
##     data = data, ties = "breslow")
##
##   n= 238, number of events= 150
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## clinic   -0.98767   0.37244  0.21432 -4.608 4.06e-06 ***
## prison    0.27261   1.31338  0.16628  1.639    0.101
## dose_ord -0.40012   0.67024  0.08258 -4.845 1.27e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##          exp(coef) exp(-coef) lower .95 upper .95
## clinic      0.3724     2.6850    0.2447    0.5669
## prison      1.3134     0.7614    0.9481    1.8194
## dose_ord    0.6702     1.4920    0.5701    0.7880
##
## Concordance= 0.653  (se = 0.025 )
## Likelihood ratio test= 58.14  on 3 df,   p=1e-12
## Wald test            = 48.79  on 3 df,   p=1e-10
## Score (logrank) test = 52.73  on 3 df,   p=2e-11
```

```r
## Fitting the model (Categorical_factored)
Mod_cat <- coxph(Surv(survtime, status) ~ clinic + prison +
                dose_cat_factor, data = data, ties="breslow")

summary(Mod_cat)
```

```
## Call:
## coxph(formula = Surv(survtime, status) ~ clinic + prison + dose_cat_factor,
##     data = data, ties = "breslow")
##
```

```
##   n= 238, number of events= 150
##
##                      coef exp(coef) se(coef)      z Pr(>|z|)
## clinic           -0.8901    0.4106   0.2198 -4.049 5.15e-05 ***
## prison            0.2310    1.2599   0.1673  1.381   0.1673
## dose_cat_factor2 -0.2086    0.8117   0.2045 -1.020   0.3076
## dose_cat_factor3 -0.4871    0.6144   0.2304 -2.114   0.0345 *
## dose_cat_factor4 -1.4592    0.2324   0.3158 -4.620 3.83e-06 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                  exp(coef) exp(-coef) lower .95 upper .95
## clinic              0.4106     2.4353    0.2669    0.6318
## prison              1.2599     0.7937    0.9077    1.7487
## dose_cat_factor2    0.8117     1.2320    0.5437    1.2119
## dose_cat_factor3    0.6144     1.6276    0.3912    0.9651
## dose_cat_factor4    0.2324     4.3027    0.1251    0.4316
##
## Concordance= 0.661  (se = 0.024 )
## Likelihood ratio test= 62.17  on 5 df,   p=4e-12
## Wald test            = 47.26  on 5 df,   p=5e-09
## Score (logrank) test = 53.76  on 5 df,   p=2e-10
```

```r
## Performing LR Test

LL_diff<- (-2*(logLik(Mod_ord)-logLik(Mod_cat)))


df<- 5-3 # from the degrees of freedom in the above mod

p_value <-  pchisq(LL_diff, df, lower.tail=F)

cat("p value of the LR Test:", p_value, "\n")
```

```
## p value of the LR Test: 0.1337253
```

Since the test is not significant at 95 % confidence interval with p_value being 0.1337, we conclude that there is no evidence of non-linearity.

Now lets fit the Exponential, Weibull, and Lognormal models to the same outcome with three main effects (clinic, prison, maxdose)

```r
## Exponential
fitexp=survreg(Surv(survtime, status)~clinic + prison +
                dose,data=data,dist="exponential")

## Weibull
fitweib=survreg(Surv(survtime, status)~clinic + prison +
                dose,data=data,dist="weibull")
```

```r
## Lognormal

fitLog=survreg(Surv(survtime, status)~clinic + prison +
                dose,data=data,dist="lognormal")


df <- data.frame(models = rep(c("Exponential", "Weibull", "Lognormal"), each = 5))
df$Parameters <- c("Intercept", "clinic", "prison", "maxdose", "Scale", "Intercept", "clinic",
                   "prison", "maxdose", "Scale", "Intercept", "clinic", "prison", "maxdose", "Scale")

df$Estimates <- c(3.66425626,  0.88623275, -0.24286726,  0.02897405,NA,
                  4.07169587,0.71984592, -0.22319158,  0.02466327, -0.30059,
                  3.34800051, 0.59624691, -0.28815075,  0.03394836,0.08569)

df$SE <- c(0.43006, 0.21058, 0.16485, 0.00613, NA, 0.33228, 0.15951, 0.12245,
           0.00464, 0.06759,0.40205, 0.17844, 0.15597, 0.00574,0.05931)

df$p_value <- c("2e-16", "2.6e-05", "0.14", "2.3e-06", NA,
                "2e-16","6.4e-06", "0.068", "1.1e-07", "8.7e-06","2e-16",
                "0.00083", "0.06468", "3.3e-09", "0.14851")

df$Likelihood <- c(-1093.1, NA, NA, NA, NA, -1084.4, NA, NA, NA, NA,-1097.2, NA, NA, NA, NA)

print(df)
```

```
##         models Parameters   Estimates      SE p_value Likelihood
## 1  Exponential  Intercept  3.66425626 0.43006   2e-16    -1093.1
## 2  Exponential     clinic  0.88623275 0.21058 2.6e-05         NA
## 3  Exponential     prison -0.24286726 0.16485    0.14         NA
## 4  Exponential    maxdose  0.02897405 0.00613 2.3e-06         NA
## 5  Exponential      Scale          NA      NA    <NA>         NA
## 6      Weibull  Intercept  4.07169587 0.33228   2e-16    -1084.4
## 7      Weibull     clinic  0.71984592 0.15951 6.4e-06         NA
## 8      Weibull     prison -0.22319158 0.12245   0.068         NA
## 9      Weibull    maxdose  0.02466327 0.00464 1.1e-07         NA
## 10     Weibull      Scale -0.30059000 0.06759 8.7e-06         NA
## 11   Lognormal  Intercept  3.34800051 0.40205   2e-16    -1097.2
## 12   Lognormal     clinic  0.59624691 0.17844 0.00083         NA
## 13   Lognormal     prison -0.28815075 0.15597 0.06468         NA
## 14   Lognormal    maxdose  0.03394836 0.00574 3.3e-09         NA
## 15   Lognormal      Scale  0.08569000 0.05931 0.14851         NA
```

Writing the hazard as a function of the covariates based on the exponential model, including the estimated parameter values and calculating the estimated hazard rate for each clinic for those without prior prison record and at the maximum dose of 60 mg/day.

```r
library(eha)
```

```
## Warning: package 'eha' was built under R version 4.1.2
```

```r
## Exponential
phexp <- phreg(Surv(survtime, status)~clinic + prison +
                dose,data=data,dist="weibull", shape = 1)
# A special case like "exponential" in phreg can be obtained using "weibull" in combination with scale = 1.

summary(phexp)
```

```
## Covariate             Mean       Coef     Rel.Risk   S.E.    LR p
## clinic                1.380    -0.886     0.412     0.211   0.0000
## prison                0.420     0.243     1.275     0.165   0.1424
## dose                 64.355    -0.029     0.971     0.006   0.0000
##
## Events                    150
## Total time at risk         95422
## Max. log. likelihood      -1093.1
## LR test statistic         50.35
## Degrees of freedom        3
## Overall p-value           6.72564e-11
```

The model with terms for clinic variable, prison variable, and maxdose variable can be written in terms of the hazard functions as:

$$\lambda(t;) = \lambda_o(t) * exp(\beta_1 * Clinic + \beta_2 * Prison + \beta_3 * Dose$$
$$\lambda(t;) = \lambda_o(t) * exp((-0.886) * Clinic + 0.243 * Prison + (-0.029) * Dose)$$

where $\lambda(t;)$ is the hazard function at time t for an individual with covariate values x, $\lambda_o(t)$ is the baseline hazard at time t, and β_1, β_2, and β_3 are the regression coefficients for clinic, prison record, and maxdose, respectively

The estimated hazard rate for each clinic for those without prior prison record and at the maximum dose of 60 mg/day.

$$\text{For patient in clinic 1 without prior prison record, when maxdose} = 60$$
$$\lambda_{clinic1} = \lambda_o(t) * exp((-0.886) * 1 + 0.243 * 0 + (-0.029) * 60)$$
$$\lambda_{clinic1} = \lambda_o(t) * exp(-2.626)$$
$$\text{For patient in clinic 2 without prior prison record, when maxdose} = 60$$
$$\lambda_{clinic2} = \lambda_o(t) * exp((-0.886) * 2 + 0.243 * 0 + (-0.029) * 60)$$
$$\lambda_{clinic2} = \lambda_o(t) * exp(-3.512)$$
$$\phi = \lambda_{clinic1}/\lambda_{clinic2}$$
$$\phi = 0.07236735/0.02983718$$
$$\phi = 2.425$$

For individuals without prior prison records and at the maximum dose of 60 mg/day: Clinic 1 has an estimated hazard rate that is 2.425 times higher than Clinic 2. This means that individuals in Clinic 1, who do not have a prior prison record and are receiving a maximum dose of 60 mg/day, have a 2.425 times higher risk of experiencing the event (such as dropout) compared to individuals in Clinic 2 with the same characteristics.

Let's check if the Weibull model provide a better fit to the data than the Exponential model. Of the three models considered, which seems to provide the best fit?

```r
## Likelihood Ratio Test between Weibull model and Exponential model
lrtest(fitexp, fitweib)
```

```
## Likelihood ratio test
##
## Model 1: Surv(survtime, status) ~ clinic + prison + dose
## Model 2: Surv(survtime, status) ~ clinic + prison + dose
##   #Df  LogLik Df Chisq Pr(>Chisq)
## 1   4 -1093.1
## 2   5 -1084.4  1 17.39  3.044e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
## Likelihood Ratio Test between Weibull model and Lognormal model
lrtest(fitLog, fitweib)
```

```
## Likelihood ratio test
##
## Model 1: Surv(survtime, status) ~ clinic + prison + dose
## Model 2: Surv(survtime, status) ~ clinic + prison + dose
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   5 -1097.2
## 2   5 -1084.4  0 25.565  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
## Likelihood Ratio Test between Exponential model and Lognormal model
lrtest(fitLog, fitexp)
```

```
## Likelihood ratio test
##
## Model 1: Surv(survtime, status) ~ clinic + prison + dose
## Model 2: Surv(survtime, status) ~ clinic + prison + dose
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1   5 -1097.2
## 2   4 -1093.1 -1 8.1752   0.004247 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

From the result of the Likelihood Ratio Test using both models, it is depicted that the Weibull model has the better fit than the Exponential model as the p-value is less than 0.001 which demonstrates that the reults are significant at 5% confidence interval.

Among the 3 models, again the Weibull model has the best fit among all models, as being shown by all the LR tests performed. The p-value in the test was always lower for Weibull model as compared to Exponential model and Lognormal model.

A randomized clinical trial is planned to investigate the effect of adaptive servo-ventilation on the mortality and morbidity of patients with stable heart failure. Patients will be randomized into either control (optimal medical management) or active treatment (optimal medical treatment plus use of adaptive servoventilation). The primary outcome is a time to first event of either all cause mortality or heart failure related hospitalization.

Assuming that the probability of the event within the first year is 35% and the intervention reduces the hazard rate by 20%. Assuming that the hazard rate is constant over time (i.e., exponential distributions). What are the corresponding hazard rates and the median survival times in the control and intervention groups?

Let's denote the hazard rate in the control group as $\lambda_{control}$ and the hazard rate in the intervention group as $\lambda_{intervention}$. We are given that the probability of the event within the first year is 35

$$\lambda = -ln(1 - probability)/time$$

1. Control Group: The probability of the event within the first year in the control group is 0.35. Therefore, we can calculate the hazard rate in the control group as follows:

$$\lambda_{control} = -ln(1 - 0.35)/1$$

2.Intervention Group: The intervention reduces the hazard rate by 20

$$\lambda_{intervention} = \lambda_{control} * (1 - 0.20)$$

$$\text{Median survival time} = -ln(0.5)/\lambda$$

Now, let's calculate the hazard rates and median survival times:

$$\text{Control Group: } \lambda_{control} = -ln(1 - 0.35)/1$$
$$= 0.4307829$$

$$\text{Median survival time in the control group} = -ln(0.5)/\lambda_{control}$$
$$= 1.609041$$

Intervention Group:

$$\lambda_{intervention} = \lambda_{control} * (1 - 0.20)$$
$$= 0.3446263$$

$$\text{Median survival time in the intervention group} = -ln(0.5)/\lambda_{intervention}$$
$$= 2.011301$$