# 8108hw2

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```r
library(dplyr)
library(survival)
library(survminer)
#if (!require("BiocManager", quietly = TRUE))
#    install.packages("BiocManager")
#BiocManager::install("Icens")a
```

```r
data=read.csv("MIstudy.csv",header=TRUE)
head(data)
```

```
##   id age gender hr sysbp diasbp      bmi cvd chf av3 miord mitype year los
## 1  1  83      0 89   152     78 25.54051   1   0   0     1      0    1   5
## 2  2  49      0 84   120     60 24.02398   1   0   0     0      1    1   5
## 3  3  70      1 83   147     88 22.14290   0   0   0     0      1    1   5
## 4  4  70      0 65   123     76 26.63187   1   1   0     0      1    1  10
## 5  5  70      0 63   135     85 24.41255   1   0   0     0      1    1   6
## 6  6  70      0 76    83     54 23.24236   1   0   1     0      0    1   1
##   dstat afib shock     dthtime dthstat obese overweight obese_ovwt bmicat
## 1     0    1     0 71.64473684       0     0          1          1      2
## 2     0    0     0 71.44736842       0     0          0          0      1
## 3     0    0     0 72.03947368       0     0          0          0      1
## 4     0    0     0  9.76973684       1     0          1          1      2
## 5     0    0     0 70.09868421       0     0          0          0      1
## 6     1    0     0  0.03289474       1     0          0          0      1
```

## Question 1: Logrank and Score Tests for MI Study

### (a) Produce a plot showing the estimated Kaplan-Meier survival functions for the endpoint of death for those who are obese or overweight (BMI>=25), as compared to those of normal weight (which we will define here as BMI<25). What percent of the 500 patients are either overweight or obese? What do you notice about the censoring pattern

```r
sum(data$bmicat %in% c(2, 3))
```

```
## [1] 302
```

```r
sum(data$obese_ovwt == 1)
```

```
## [1] 302
```

```r
data = data |>
  mutate(dthtime = as.numeric(dthtime))

surv_object <- Surv(data$dthtime, data$dthstat)
km_fit <- survfit(surv_object ~ obese_ovwt, data = data)
summary(km_fit)
```

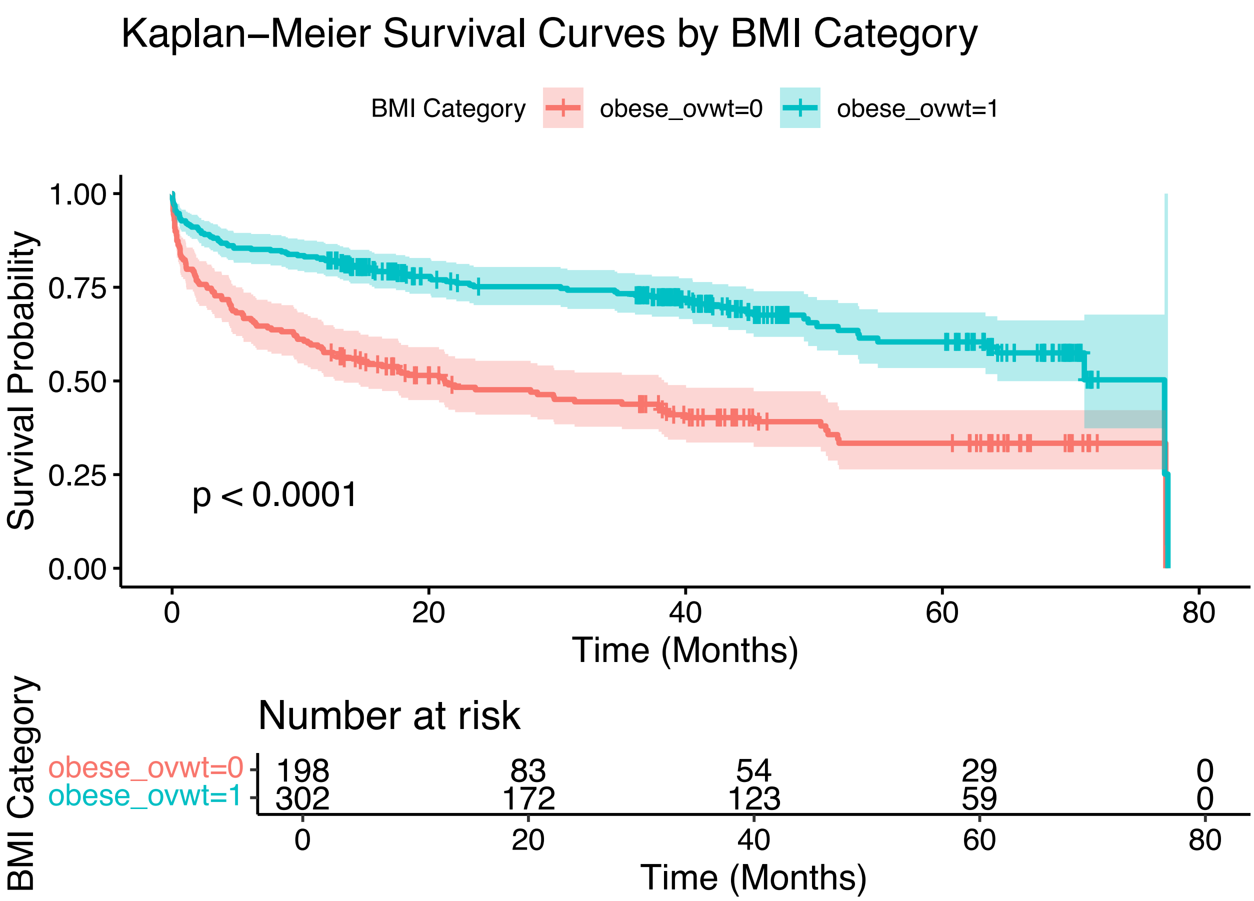
```
## Call: survfit(formula = surv_object ~ obese_ovwt, data = data)
##
##                 obese_ovwt=0
##     time n.risk n.event survival std.err lower 95% CI upper 95% CI
##   0.0329    198       3    0.985 0.00868        0.968        1.000
##   0.0658    195       6    0.955 0.01480        0.926        0.984
##   0.0987    189       2    0.944 0.01628        0.913        0.977
##   0.1316    187       1    0.939 0.01696        0.907        0.973
##   0.1645    186       2    0.929 0.01822        0.894        0.966
##   0.1974    184       4    0.909 0.02043        0.870        0.950
##   0.2303    180       2    0.899 0.02142        0.858        0.942
##   0.3289    178       2    0.889 0.02233        0.846        0.934
##   0.3618    176       3    0.874 0.02360        0.829        0.921
##   0.4605    173       2    0.864 0.02439        0.817        0.913
##   0.5263    171       1    0.859 0.02476        0.811        0.909
##   0.5921    170       1    0.854 0.02513        0.806        0.904
##   0.6250    169       3    0.838 0.02616        0.789        0.891
##   0.6579    166       1    0.833 0.02649        0.783        0.887
##   0.7237    165       1    0.828 0.02680        0.777        0.883
##   0.8553    164       1    0.823 0.02711        0.772        0.878
##   1.0197    163       1    0.818 0.02741        0.766        0.874
##   1.0526    162       1    0.813 0.02770        0.761        0.869
##   1.0855    161       2    0.803 0.02826        0.750        0.860
##   1.1184    159       1    0.798 0.02853        0.744        0.856
##   1.6118    158       1    0.793 0.02880        0.738        0.851
##   1.7105    157       1    0.788 0.02905        0.733        0.847
##   1.7434    156       1    0.783 0.02930        0.727        0.842
```

```
##    1.8092    155       1    0.778 0.02955        0.722         0.838
##    1.8750    154       2    0.768 0.03001        0.711         0.829
##    2.0066    152       1    0.763 0.03024        0.706         0.824
##    2.1053    151       1    0.758 0.03046        0.700         0.820
##    2.6645    150       1    0.753 0.03067        0.695         0.815
##    2.7303    149       1    0.747 0.03088        0.689         0.811
##    3.0592    148       1    0.742 0.03108        0.684         0.806
##    3.1250    147       1    0.737 0.03127        0.679         0.801
##    3.2895    146       1    0.732 0.03146        0.673         0.797
##    3.3224    145       1    0.727 0.03165        0.668         0.792
##    3.8487    144       1    0.722 0.03183        0.662         0.787
##    3.8816    143       1    0.717 0.03201        0.657         0.783
##    4.4079    142       1    0.712 0.03218        0.652         0.778
##    4.4408    141       1    0.707 0.03234        0.646         0.773
##    4.5066    140       1    0.702 0.03250        0.641         0.769
##    4.6053    139       2    0.692 0.03281        0.631         0.759
##    4.7039    137       1    0.687 0.03296        0.625         0.755
##    4.9671    136       1    0.682 0.03310        0.620         0.750
##    5.4605    135       1    0.677 0.03324        0.615         0.745
##    5.5592    134       2    0.667 0.03350        0.604         0.736
##    6.1513    132       1    0.662 0.03363        0.599         0.731
##    6.3158    131       1    0.657 0.03375        0.594         0.726
##    6.4803    130       1    0.652 0.03386        0.588         0.721
##    6.5789    129       1    0.646 0.03397        0.583         0.717
##    7.4342    128       1    0.641 0.03408        0.578         0.712
##    7.7303    127       1    0.636 0.03419        0.573         0.707
##    8.5197    126       1    0.631 0.03429        0.568         0.702
##    9.4408    125       1    0.626 0.03438        0.562         0.697
##    9.5066    124       1    0.621 0.03447        0.557         0.693
##    9.7039    123       1    0.616 0.03456        0.552         0.688
##    9.7697    122       1    0.611 0.03464        0.547         0.683
##   10.2632    121       1    0.606 0.03472        0.542         0.678
##   10.5592    120       1    0.601 0.03480        0.537         0.673
##   10.7895    119       1    0.596 0.03487        0.531         0.668
##   11.3487    118       1    0.591 0.03494        0.526         0.664
##   11.6447    117       1    0.586 0.03501        0.521         0.659
##   11.7763    116       1    0.581 0.03507        0.516         0.654
##   11.8092    115       1    0.576 0.03512        0.511         0.649
##   12.5658    113       1    0.571 0.03518        0.506         0.644
##   12.6645    112       1    0.566 0.03523        0.501         0.639
##   13.3553    108       1    0.560 0.03529        0.495         0.634
##   14.5395    105       1    0.555 0.03536        0.490         0.629
##   14.6711    102       1    0.550 0.03543        0.484         0.624
##   15.2961    100       1    0.544 0.03550        0.479         0.618
##   16.3487     98       1    0.539 0.03557        0.473         0.613
##   17.5987     91       1    0.533 0.03566        0.467         0.607
##   17.6645     90       1    0.527 0.03576        0.461         0.602
##   17.8289     89       1    0.521 0.03584        0.455         0.596
##   18.3882     87       1    0.515 0.03593        0.449         0.590
##   20.7895     81       1    0.508 0.03604        0.442         0.584
##   21.1842     80       1    0.502 0.03614        0.436         0.578
##   21.2500     79       1    0.496 0.03624        0.430         0.572
##   21.5132     78       1    0.489 0.03633        0.423         0.566
##   22.0395     76       1    0.483 0.03642        0.417         0.560
```

```
##   23.6184     75        1    0.476 0.03650        0.410         0.554
##   27.9276     74        1    0.470 0.03657        0.404         0.547
##   28.4539     73        1    0.464 0.03663        0.397         0.541
##   29.7039     72        1    0.457 0.03668        0.391         0.535
##   29.7697     71        1    0.451 0.03673        0.384         0.529
##   31.3487     70        1    0.444 0.03676        0.378         0.522
##   35.0329     69        1    0.438 0.03679        0.371         0.516
##   37.8947     63        1    0.431 0.03685        0.364         0.510
##   38.1250     62        1    0.424 0.03691        0.357         0.503
##   38.3224     60        1    0.417 0.03696        0.350         0.496
##   38.6184     58        1    0.410 0.03702        0.343         0.489
##   40.0329     54        1    0.402 0.03710        0.336         0.482
##   45.2961     37        1    0.391 0.03766        0.324         0.472
##   50.5263     34        1    0.380 0.03827        0.312         0.463
##   50.9211     33        1    0.368 0.03880        0.300         0.453
##   51.0855     32        1    0.357 0.03926        0.287         0.443
##   51.8421     31        1    0.345 0.03964        0.276         0.432
##   51.9408     30        1    0.334 0.03995        0.264         0.422
##   77.4013      1        1    0.000     NaN           NA            NA
##
##                 obese_ovwt=1
##      time n.risk n.event survival std.err lower 95% CI upper 95% CI
##    0.0329    302       5    0.983 0.00734       0.9692        0.998
##    0.0658    297       2    0.977 0.00866       0.9600        0.994
##    0.0987    295       1    0.974 0.00924       0.9556        0.992
##    0.1316    294       1    0.970 0.00978       0.9512        0.990
##    0.1974    293       1    0.967 0.01030       0.9469        0.987
##    0.2303    292       4    0.954 0.01210       0.9302        0.978
##    0.3289    288       1    0.950 0.01250       0.9261        0.975
##    0.3618    287       1    0.947 0.01289       0.9221        0.973
##    0.5592    286       2    0.940 0.01362       0.9141        0.967
##    0.5921    284       2    0.934 0.01431       0.9061        0.962
##    0.6579    282       1    0.930 0.01464       0.9022        0.960
##    0.7237    281       1    0.927 0.01495       0.8983        0.957
##    1.0526    280       1    0.924 0.01526       0.8944        0.954
##    1.0855    279       1    0.921 0.01556       0.8905        0.952
##    1.2171    278       1    0.917 0.01586       0.8867        0.949
##    1.3816    277       1    0.914 0.01614       0.8828        0.946
##    1.5132    276       1    0.911 0.01642       0.8790        0.943
##    1.9737    275       1    0.907 0.01669       0.8752        0.941
##    2.0395    274       1    0.904 0.01695       0.8713        0.938
##    2.1053    273       1    0.901 0.01721       0.8676        0.935
##    2.2697    272       2    0.894 0.01771       0.8600        0.929
##    2.5000    270       1    0.891 0.01795       0.8562        0.927
##    2.8947    269       1    0.887 0.01819       0.8525        0.924
##    2.9934    268       1    0.884 0.01842       0.8487        0.921
##    3.1908    267       1    0.881 0.01865       0.8450        0.918
##    3.5526    266       1    0.877 0.01887       0.8413        0.915
##    3.5855    265       1    0.874 0.01908       0.8376        0.912
##    3.7171    264       1    0.871 0.01930       0.8338        0.910
##    3.8158    263       1    0.868 0.01951       0.8301        0.907
##    4.2434    262       1    0.864 0.01971       0.8265        0.904
##    4.3421    261       1    0.861 0.01991       0.8228        0.901
##    4.7697    260       1    0.858 0.02011       0.8191        0.898
```

```
##   4.8026    259        1    0.854 0.02030       0.8154         0.895
##   6.1513    258        1    0.851 0.02049       0.8118         0.892
##   7.6645    257        1    0.848 0.02068       0.8081         0.889
##   8.5197    256        1    0.844 0.02086       0.8045         0.886
##   8.8487    255        1    0.841 0.02104       0.8008         0.883
##   9.0132    254        1    0.838 0.02122       0.7972         0.880
##   9.7697    253        1    0.834 0.02139       0.7936         0.877
##  10.2961    252        1    0.831 0.02156       0.7899         0.874
##  11.2829    251        1    0.828 0.02173       0.7863         0.872
##  11.8092    250        1    0.825 0.02189       0.7827         0.869
##  11.9408    249        1    0.821 0.02205       0.7791         0.866
##  12.8947    239        1    0.818 0.02222       0.7753         0.862
##  13.0592    238        1    0.814 0.02239       0.7716         0.859
##  13.3224    234        1    0.811 0.02257       0.7678         0.856
##  13.7829    227        1    0.807 0.02275       0.7639         0.853
##  13.8816    225        1    0.804 0.02293       0.7600         0.850
##  15.3618    204        1    0.800 0.02315       0.7556         0.846
##  15.5592    203        1    0.796 0.02337       0.7513         0.843
##  15.7566    200        1    0.792 0.02359       0.7469         0.839
##  17.4342    190        1    0.788 0.02383       0.7423         0.836
##  18.1579    181        1    0.783 0.02409       0.7375         0.832
##  18.4868    179        1    0.779 0.02435       0.7326         0.828
##  20.1316    172        1    0.774 0.02463       0.7276         0.824
##  20.1974    171        1    0.770 0.02490       0.7226         0.820
##  21.3487    169        1    0.765 0.02516       0.7175         0.816
##  22.1382    167        1    0.761 0.02543       0.7125         0.812
##  23.1579    165        1    0.756 0.02569       0.7074         0.808
##  23.4868    164        1    0.752 0.02594       0.7023         0.804
##  30.2632    162        1    0.747 0.02619       0.6973         0.800
##  30.7895    161        1    0.742 0.02644       0.6922         0.796
##  34.4737    160        1    0.738 0.02668       0.6871         0.792
##  34.6711    159        1    0.733 0.02691       0.6821         0.788
##  36.0526    158        1    0.728 0.02714       0.6770         0.783
##  37.3684    144        1    0.723 0.02741       0.6715         0.779
##  39.4737    126        1    0.718 0.02779       0.6651         0.774
##  40.5263    122        1    0.712 0.02818       0.6585         0.769
##  40.5592    119        1    0.706 0.02857       0.6518         0.764
##  42.0724    103        1    0.699 0.02910       0.6440         0.758
##  43.3224     98        1    0.692 0.02967       0.6359         0.752
##  44.7039     88        1    0.684 0.03035       0.6268         0.746
##  45.2961     85        1    0.676 0.03104       0.6176         0.739
##  49.2105     66        1    0.666 0.03222       0.6053         0.732
##  49.5395     65        1    0.655 0.03331       0.5932         0.724
##  50.2303     64        1    0.645 0.03433       0.5812         0.716
##  51.8750     63        1    0.635 0.03528       0.5693         0.708
##  53.4211     62        1    0.625 0.03616       0.5576         0.700
##  53.5197     61        1    0.614 0.03699       0.5460         0.691
##  54.9671     60        1    0.604 0.03776       0.5344         0.683
##  63.3553     44        1    0.590 0.03932       0.5181         0.673
##  64.2763     38        1    0.575 0.04124       0.4994         0.662
##  71.0526      8        1    0.503 0.07629       0.3736         0.677
##  77.3026      2        1    0.251 0.18187       0.0609         1.000
##  77.5658      1        1    0.000     NaN           NA            NA
```

```r
ggsurvplot(km_fit, data = data,
           risk.table = TRUE,
           pval = TRUE,
           conf.int = TRUE,
           xlab = "Time (Months)",
           ylab = "Survival Probability",
           legend.title = "BMI Category",
           title = "Kaplan-Meier Survival Curves by BMI Category")
```




The percentage of the 500 patients are either overweight or obese is 60.4%.

there are tick marks along the curves and are distributed across the timeline, showing that censored observations occur at different time points. There are three parts of censoring data that around 15, 40, and 65.

**(b) Calculate both a logrank test and Wilcoxon test of the effect of being overweight/obese on the risk of death, using either the CMH approach or a linear rank test (state which approach you have used). Which of these two tests yields a larger test statistic? Could you have predicted that based on the KM plot from (a)?**

```r
logrank_test <- survdiff(surv_object ~ obese_ovwt, data = data)
wilcoxon_test <- survdiff(surv_object ~ obese_ovwt, data = data, rho = 1) # rho = 1 gives the Wilcoxon
```

```
logrank_test
```

```
## Call:
## survdiff(formula = surv_object ~ obese_ovwt, data = data)
##
##                N Observed Expected (O-E)^2/E (O-E)^2/V
## obese_ovwt=0 198      119     74.3      26.9      41.4
## obese_ovwt=1 302       96    140.7      14.2      41.4
##
##  Chisq= 41.4  on 1 degrees of freedom, p= 1e-10
```

```
wilcoxon_test
```

```
## Call:
## survdiff(formula = surv_object ~ obese_ovwt, data = data, rho = 1)
##
##                N Observed Expected (O-E)^2/E (O-E)^2/V
## obese_ovwt=0 198     94.5     58.5      22.2      42.6
## obese_ovwt=1 302     72.1    108.1      12.0      42.6
##
##  Chisq= 42.6  on 1 degrees of freedom, p= 7e-11
```

The logrank test and Wilcoxon test are both linear rank tests.

We can see that logrank test results in 41.4 chisq and Wilcoxon test results in 42.6. Thus, the Wilcoxon test yields a slightly larger test statistic compared to the log-rank test.

The Normal Weight group (red curve) shows a steeper decline in survival probability early on, starting within the first few months; while the Obese or Overweight group (blue curve) has a less steep initial decline, suggesting that fewer events are happening early. The Wilcoxon test weight more on early so that we can see from the graph that it should be larger than logrank test.

### (c) Calculate the Fleming-Harrington test statistic for comparing survival distributions under several different combinations of p and q:

i. Setting p and q both to 0
ii. Setting p to 1 and q to 0
iii. Setting p and q both to 1

### How do these compare to the logrank tests and Wilcoxon tests in (b)? When would you expect them to be more or less powerful than the logrank test in (b)?

```r
surv_object <- Surv(data$dthtime, data$dthstat)
fh_test_1 <- FHtest::FHtestrcc(surv_object ~ obese_ovwt,
                               data = data, rho = 0, lambda = 0)
fh_test_2 <- FHtest::FHtestrcc(surv_object ~ obese_ovwt,
                               data = data, rho = 0, lambda = 1)
fh_test_3 <- FHtest::FHtestrcc(surv_object ~ obese_ovwt,
                               data = data, rho = 1, lambda = 1)

fh_test_1
```

```
##
##  Two-sample test for right-censored data
##
## Parameters: rho=0, lambda=0
## Distribution: counting process approach
##
## Data: surv_object by obese_ovwt
##
##                N Observed Expected   O-E (O-E)^2/E (O-E)^2/V
## obese_ovwt=0 198      119     74.3  44.7      26.9      41.4
## obese_ovwt=1 302       96    140.7 -44.7      14.2      41.4
##
## Statistic Z= -6.4, p-value= 1.22e-10
## Alternative hypothesis: survival functions not equal
```

```
fh_test_2
```

```
##
##  Two-sample test for right-censored data
##
## Parameters: rho=0, lambda=1
## Distribution: counting process approach
##
## Data: surv_object by obese_ovwt
##
##                N Observed Expected   O-E (O-E)^2/E (O-E)^2/V
## obese_ovwt=0 198     24.5     15.9  8.67      4.74      22.9
## obese_ovwt=1 302     23.9     32.6 -8.67      2.30      22.9
##
## Statistic Z= -4.8, p-value= 1.74e-06
## Alternative hypothesis: survival functions not equal
```

```
fh_test_3
```

```
##
##  Two-sample test for right-censored data
##
## Parameters: rho=1, lambda=1
## Distribution: counting process approach
##
## Data: surv_object by obese_ovwt
##
##                N Observed Expected  O-E (O-E)^2/E (O-E)^2/V
## obese_ovwt=0 198     17.3     10.9  6.4      3.75        30
## obese_ovwt=1 302     15.5     21.9 -6.4      1.87        30
##
## Statistic Z= -5.5, p-value= 4.22e-08
## Alternative hypothesis: survival functions not equal
```

All the FH tests yield similar Z-statistic and p-value. This consistency implies that survival differences are robust across all parts of the survival curve.

When all time intervals are equally weighted rho=0 lambda =0, the strongest signal is detected. When focusing on late events rho=0, lambda=1, the signal is still significant but slightly weaker. A balanced approach rho=1, lambda=1 captures significant differences across both early and late times, but with a slightly reduced Z-statistic.

The FH test 1 directly corresponds to the logrank test, and the results match exactly. The Wilcoxon test gives more weight to early events, similar to the FH test 2.

### (d) Ignoring the times of death, conduct a test of whether the proportions of deaths during follow-up differ for those who are overweight/obese versus those of normal weight (using a logistic regression model or based on analysis of a 2x2 table). Does this test yield similar conclusions to the tests in parts (b) and (c)? When would you expect the survival analysis to be more powerful than the comparison of proportions of deaths in the two subgroups?

```
table_bmi_death <- table(data$obese_ovwt, data$dthstat)
fisher_test <- fisher.test(table_bmi_death)
fisher_test
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  table_bmi_death
## p-value = 4.758e-10
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.2092458 0.4573153
## sample estimates:
## odds ratio
##  0.3101566
```

```
logistic_model <- glm(dthstat ~ obese_ovwt,
                      data = data, family = binomial)
summary(logistic_model)
```

```
##
## Call:
## glm(formula = dthstat ~ obese_ovwt, family = binomial, data = data)
##
## Coefficients:
##             Estimate Std. Error z value Pr(>|z|)
## (Intercept)   0.4097     0.1451   2.823  0.00476 **
## obese_ovwt   -1.1732     0.1906  -6.155 7.51e-10 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##     Null deviance: 683.31  on 499  degrees of freedom
## Residual deviance: 644.01  on 498  degrees of freedom
## AIC: 648.01
##
## Number of Fisher Scoring iterations: 4
```

```r
exp(cbind(Odds_Ratio = coef(logistic_model), confint(logistic_model)))
```

```
## Waiting for profiling to be done...
```

```
##             Odds_Ratio    2.5 %    97.5 %
## (Intercept)  1.5063291 1.135961 2.0084030
## obese_ovwt   0.3093742 0.212210 0.4482543
```

Under fisher test, we have p-value is 0 which is smaller than 0.05 with odd ratio of 0.31. The test indicates that there is a significant difference in the proportions of deaths between the Normal Weight and Obese groups. The odd ratio of 0.31 suggests that those in the Obese group had much lower odds of dying compared to those in the Normal Weight group.

Since tests in (b) also suggest a significant difference in survival between the two groups with very small p-value. Thus, test in (d) has similar conclusion with tests in (b), both indicate a strong association between BMI category and risk of death. Furthermore, the Obese group has a lower risk of death compared to the Normal Weight group.

Survival analysis is more powerful when the timing of the event matters. This is because survival analysis takes into account both the occurrence and timing of deaths.

## Question 2: Cox Model for Myocardial Infarction Study

**(a) Fit a Cox proportional hazards model to evaluate the association of being overweight/obese with survival time, with 'obese ovwt' as the only covariate (i.e. unadjusted). Use the discrete option for ties. Provide the Wald, Score, and LR tests for the comparison of survival distributions after MI for overweight/obese vs normal weight. Are any of these test statistics the same as either the logrank or Wilcoxon test statistics from 1(b)?**

```r
cox_model <- coxph(Surv(data$dthtime, data$dthstat) ~ obese_ovwt,
                   data = data, ties = "exact")
summary(cox_model)
```

```
## Call:
## coxph(formula = Surv(data$dthtime, data$dthstat) ~ obese_ovwt,
##     data = data, ties = "exact")
##
##   n= 500, number of events= 215
##
##                coef exp(coef) se(coef)      z Pr(>|z|)
## obese_ovwt -0.8621    0.4223   0.1380 -6.245 4.23e-10 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##            exp(coef) exp(-coef) lower .95 upper .95
## obese_ovwt    0.4223      2.368    0.3222    0.5535
##
## Concordance= 0.615  (se = 0.017 )
## Likelihood ratio test= 39.07  on 1 df,   p=4e-10
## Wald test            = 39  on 1 df,   p=4e-10
## Score (logrank) test = 41.43  on 1 df,   p=1e-10
```

```r
wald_test <- summary(cox_model)$waldtest
score_test <- summary(cox_model)$sctest
lr_test <- summary(cox_model)$logtest
wald_test
```

```
##         test           df       pvalue
## 3.900000e+01 1.000000e+00 4.228419e-10
```

```r
score_test
```

```
##         test           df       pvalue
## 4.143012e+01 1.000000e+00 1.221603e-10
```

```r
lr_test
```

```
##         test           df       pvalue
## 3.906512e+01 1.000000e+00 4.099022e-10
```

The wald test is about 39, the score test is about 41.4. and the LR test is about 39.06, which all have p-value close to 0.

We can see that the score test is close to 1(b), they are testing the same whether there is a significant difference in survival distributions between the normal weight and overweight/obese groups.

However, the Wald test examines the estimated coefficient in the Cox model, which is the effect of being overweight/obese on the hazard of death. And the Likelihood Ratio test compares the fit of the full model to a null model that without any covariates. But they stil have similar results with 1(b).

### (b) Now fit an adjusted Cox proportional hazards model for evaluating the effect of 'obese ovwt', adjusting for the effects of age, gender, systolic blood pressure (sysbp), and type of MI (mitype). Summarize the effect of overweight/obesity on survival of MI patients using both the unadjusted and adjusted hazard ratios and 95% confidence intervals. Write a short (1-2 sentence) interpretation of the HR for overweight/obesity on mortality making sure to indicate both the magnitude and direction of effect (protective or adverse effect), and whether adjustment for other covariates makes any difference.

```r
data$mitype <- as.factor(data$mitype)

cox_adjusted <- coxph(Surv(data$dthtime, data$dthstat) ~ obese_ovwt + age + gender + sysbp + mitype, da
summary(cox_adjusted)
```

```
## Call:
## coxph(formula = Surv(data$dthtime, data$dthstat) ~ obese_ovwt +
##     age + gender + sysbp + mitype, data = data)
##
##   n= 500, number of events= 215
##
##                 coef exp(coef)  se(coef)      z Pr(>|z|)
## obese_ovwt -0.447085  0.639490  0.146392 -3.054  0.00226 **
## age         0.059592  1.061403  0.006366  9.360  < 2e-16 ***
## gender     -0.119640  0.887240  0.142079 -0.842  0.39975
## sysbp      -0.003533  0.996473  0.002184 -1.618  0.10569
## mitype1    -0.333083  0.716711  0.171947 -1.937  0.05273 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##            exp(coef) exp(-coef) lower .95 upper .95
## obese_ovwt    0.6395     1.5637    0.4800     0.852
## age           1.0614     0.9421    1.0482     1.075
## gender        0.8872     1.1271    0.6716     1.172
## sysbp         0.9965     1.0035    0.9922     1.001
## mitype1       0.7167     1.3953    0.5117     1.004
##
## Concordance= 0.744  (se = 0.017 )
## Likelihood ratio test= 159  on 5 df,   p=<2e-16
## Wald test            = 139.3  on 5 df,   p=<2e-16
## Score (logrank) test = 148.2  on 5 df,   p=<2e-16
```

```r
unadjusted_hr <- exp(cbind(HR = coef(cox_model), confint(cox_model)))
exp(cbind(HR = coef(cox_adjusted), confint(cox_adjusted)))
```

```
##                   HR     2.5 %    97.5 %
## obese_ovwt 0.6394898 0.4799813 0.8520065
## age        1.0614030 1.0482413 1.0747300
## gender     0.8872396 0.6715878 1.1721388
## sysbp      0.9964731 0.9922171 1.0007474
## mitype1    0.7167106 0.5116608 1.0039348
```

In the unadjusted model, the hazard ratio of 0.42 indicates that overweight/obese individuals have a 58% lower risk of death compared to normal weight individuals. This suggests a protective effect of being overweight/obese on survival following MI, and the effect is statistically significant as the confidence interval does not include 1.

After adjusting for age, gender, systolic blood pressure, and type of MI, the hazard ratio for overweight/obesity increases to 0.64, indicating that overweight/obese individuals still have a 36% lower risk of death compared to those with normal weight. The protective effect remains statistically significant as the confidence interval (0.48, 0.85) does not include 1. However, the effect is less pronounced after adjusting for these covariates, suggesting that part of the initial protective effect observed in the unadjusted model is explained by the other factors.

### (c) Compare the following test statistics for the effect of overweight/obesity on the risk of death by fitting the following models (don't worry about adjusting for any other covariates):

i. Test for 'obese ovwt' from Cox PH model, stratifying by gender.
ii. Test for 'obese ovwt' from Cox PH model, controlling for gender.
iii. Logrank test for 'obese ovwt', stratifying by gender.

### For each part, state which test statistic you use (Score, LR, Wald). How do the test statistics from (i)-(iii) compare? Do we gain any power by controlling for gender rather than stratifying by it?

**i. Test for 'obese ovwt' from Cox PH model, stratifying by gender.**

```r
cox_stratified <- coxph(surv_object ~ obese_ovwt + strata(gender), data = data)
summary(cox_stratified)
```

```
## Call:
## coxph(formula = surv_object ~ obese_ovwt + strata(gender), data = data)
##
##   n= 500, number of events= 215
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## obese_ovwt -0.8170    0.4417   0.1405 -5.814 6.11e-09 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
```

```
##             exp(coef) exp(-coef) lower .95 upper .95
## obese_ovwt    0.4417      2.264    0.3354    0.5818
##
## Concordance= 0.608  (se = 0.018 )
## Likelihood ratio test= 33.92  on 1 df,   p=6e-09
## Wald test            = 33.8  on 1 df,   p=6e-09
## Score (logrank) test = 35.48  on 1 df,   p=3e-09
```

```r
score_test_stratified <- summary(cox_stratified)$sctest
score_test_stratified
```

```
##         test           df       pvalue
## 3.548233e+01 1.000000e+00 2.573745e-09
```

The Score test is used because it compares the observed events death to the expected events within each stratum, while accounting for the fact that the baseline hazards may be different between stratum.

**ii. Test for 'obese ovwt' from Cox PH model, controlling for gender.**

```r
cox_control_gender <- coxph(surv_object ~ obese_ovwt + gender, data = data)
summary(cox_control_gender)
```

```
## Call:
## coxph(formula = surv_object ~ obese_ovwt + gender, data = data)
##
##   n= 500, number of events= 215
##
##                coef exp(coef) se(coef)      z Pr(>|z|)
## obese_ovwt -0.8178    0.4414   0.1407 -5.814 6.11e-09 ***
## gender      0.2206    1.2468   0.1404  1.572    0.116
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##             exp(coef) exp(-coef) lower .95 upper .95
## obese_ovwt    0.4414      2.265    0.3351    0.5815
## gender        1.2468      0.802    0.9470    1.6416
##
## Concordance= 0.625  (se = 0.019 )
## Likelihood ratio test= 41.52  on 2 df,   p=1e-09
## Wald test            = 41.51  on 2 df,   p=1e-09
## Score (logrank) test = 43.99  on 2 df,   p=3e-10
```

```r
wald_test_controlled <- summary(cox_control_gender)$waldtest
wald_test_controlled
```

```
##         test           df       pvalue
## 4.151000e+01 2.000000e+00 9.683354e-10
```

The Wald test is used to test the significance of the coefficients in this model, including the effect of obese_ovwt. Since we control the gender variable, we use the Wald test.

**iii. Logrank test for 'obese ovwt', stratifying by gender.**

```
logrank_test_stratified <- survdiff(surv_object ~ obese_ovwt + strata(gender), data = data)

logrank_statistic <- logrank_test_stratified$chisq
logrank_statistic
```

```
## [1] 35.46875
```

i and iii are both stratify by gender, and the test statistics (35.48 and 35.47) are nearly identical. However, ii has higher test statistics than the other 2 methods, suggesting that controlling for gender yields a higher test statistic.

Controlling for gender provides more power than stratifying by it. When we control for gender, we assume that its effect is consistent across all individuals, which allows us to estimate a single baseline hazard for the entire cohort. This approach uses the data more efficiently and maximizes the information from the sample, leading to a higher test statistic. By contrast, when we stratify by gender, the model estimates a different baseline hazard for each gender, which divides the dataset into strata and reduces the overall sample size for each stratum.

## (d) Briefly comment on any advantages or disadvantages of stratifying by gender rather than controlling for gender in part (c) above. Are there any additional analyses you would suggest doing to check whether the stratified analysis is appropriate?

Stratifying by gender allows the model to accommodate different baseline hazards for each gender, providing flexibility and robustness when the risk of death is expected to differ significantly between male and female. However, stratification can lead to a loss of statistical power, as the dataset is divided into separate strata, reducing the effective sample size for each group.

Controlling for gender as a covariate in the model allows for the use of the entire dataset when estimating the baseline hazard, which increases statistical power. Nevertheless, it requires assuming that the effect of gender is proportional and consistent across all individuals, which may not be appropriate in all cases. If the proportional hazards assumption for gender is violated, this model could produce biased estimates.

```
# check proportional hazards assumption for the model controlling for gender
cox.zph(cox_control_gender)
```

```
##            chisq df    p
## obese_ovwt 1.378  1 0.24
## gender     0.745  1 0.39
## GLOBAL     2.630  2 0.27
```

```
# fit a Cox model with interaction between gender and obese_ovwt
cox_interaction <- coxph(surv_object ~ obese_ovwt * gender, data = data)
summary(cox_interaction)
```

```
## Call:
## coxph(formula = surv_object ~ obese_ovwt * gender, data = data)
##
```

```
##   n= 500, number of events= 215
##
##                        coef exp(coef) se(coef)      z Pr(>|z|)
## obese_ovwt        -0.84780   0.42836  0.19039 -4.453 8.47e-06 ***
## gender             0.19225   1.21197  0.18530  1.038    0.299
## obese_ovwt:gender  0.06568   1.06789  0.28095  0.234    0.815
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##                   exp(coef) exp(-coef) lower .95 upper .95
## obese_ovwt           0.4284     2.3345    0.2949    0.6221
## gender               1.2120     0.8251    0.8429    1.7427
## obese_ovwt:gender    1.0679     0.9364    0.6157    1.8521
##
## Concordance= 0.625  (se = 0.019 )
## Likelihood ratio test= 41.57  on 3 df,   p=5e-09
## Wald test            = 41.27  on 3 df,   p=6e-09
## Score (logrank) test = 44.15  on 3 df,   p=1e-09
```

3. Model Interpretation - Myocardial Infarction Study

Table 2 below shows the results of fitting one particular multivariable Cox proportional hazards model for time to death using some of the covariates described above. You should be able to answer the questions below using only the provided output (eg., without fitting any additional models).

| Variable Name | Estimate | s.e. | P-value |
|---|---|---|---|
| Age | 0.0500 | 0.0066 | $< 0.0001$ |
| Heart rate | 0.0112 | 0.0029 | 0.0001 |
| Diastolic BP | $-0.0107$ | 0.0035 | 0.0024 |
| Sex (0=male, 1=female) | $-0.2732$ | 0.1442 | 0.0581 |
| Congestive heart failure | 0.7816 | 0.1469 | $< 0.0001$ |
| BMI | $-0.0453$ | 0.0163 | 0.0055 |

Table 2: Coefficient Estimate Table of Multivariable Model

(a) Write out the estimated hazard for death ($\lambda(t, Z)$) in the form of a Cox proportional hazards model, using the output from fitting the model to supply the parameter estimates.

(b) How is the "baseline" group (i.e., with hazard $\lambda_0(t)$) defined in this model in terms of all of the covariates? Does the baseline group correspond to any of the actual observations in the dataset?

(c) What is the estimated hazard ratio (HR) for death associated with a BMI of 30 as compared to a BMI of 24, holding all other covariates constant? Also provide a 95% confidence interval for the HR for a BMI of 30 vs BMI of 24, adjusting for the other covariates, and interpret.

(d) What is the estimated hazard ratio of death for a subject aged 60 years versus a subject aged 50 years, holding all other variables constant? Construct a 95% confidence interval for this estimated HR (comparing age 60 vs 50).

(e) Based on this model, calculate the estimated hazard ratio of death for a female subject aged 60 with BMI=24 versus a male subject aged 50 with BMI=30.

(f) Based on this model, describe the association of sex (male or female) with risk of death.

(a) Write out the estimated hazard for death ($\lambda(t, Z)$) in the form of a Cox proportional hazards model, using the output from fitting the model to supply the parameter estimates.

$$\lambda(t,z) = \lambda_0(t)\exp(\beta_1 z_1 + \cdots + \beta_p z_p)$$

$$\lambda(t,z) = \lambda_0(t)\exp(0.05\,Age + 0.0112\,\text{Heart rate} - 0.0107\,\text{DiastolicBP}$$
$$- 0.2732\,sex + 0.7816\,\text{congestive heart failure} - 0.0453\,BMI)$$

(b) How is the "baseline" group (i.e., with hazard $\lambda_0(t)$) defined in this model in terms of all of the covariates? Does the baseline group correspond to any of the actual observations in the dataset?

We can define baseline group: age=0, heart rate=0. diastolicBP=0

sex=0 (male), CHF = 0 . BMI=0

No, since we set values to 0, it's hypothetical and used as a reference.

(c) What is the estimated hazard ratio (HR) for death associated with a BMI of 30 as compared to a BMI of 24, holding all other covariates constant? Also provide a 95% confidence interval for the HR for a BMI of 30 vs BMI of 24, adjusting for the other covariates, and interpret.

$$HR = \exp(-0.0453(BMI_{30} - BMI_{24}))$$
$$= \exp(-0.0453(30-24)) \approx 0.762$$

$$CI = \exp(-0.0453(30-24) \pm 1.96 \times 0.0163 \times (30-24))$$
$$= \exp(-0.2718 \pm 0.1919)$$
$$= (0.629, 0.923)$$

People with BMI of 30 have 24% lower hazard of death compared with those with BMI of 24, holding all other covariates constant.

We are 95% confident that the true HR is between (0.629, 0.923).

(d) What is the estimated hazard ratio of death for a subject aged 60 years versus a subject aged 50 years, holding all other variables constant? Construct a 95% confidence interval for this estimated HR (comparing age 60 vs 50).

$HR = \exp(0.05(Age_{60} - Age_{50})) = \exp(0.5) \approx 1.649$

$CI = \exp(0.05 \times (60-50) \pm 1.96 \times 0.0066 \times (60-50))$

$= \exp(0.5 \pm 0.1294)$

$= (1.448, 1.876)$

A subject aged 60 has 1.65 times higher hazard of death compared to a subject aged 50, holding all other covariates constant.

We are 95% confident that the true HR is between (1.448, 1.876)

(e) Based on this model, calculate the estimated hazard ratio of death for a female subject aged 60 with BMI=24 versus a male subject aged 50 with BMI=30.

$LP_{female} = 0.05 \times 60 - 0.2732 \times 1 - 0.0453 \times 24 \approx 1.6396$

$LP_{male} = 0.05 \times 50 - 0.2732 \times 0 - 0.0453 \times 30 \approx 1.141$

$\approx 1.646$

$HR = \exp(LP_{female} - LP_{male}) = \exp(1.6396 - 1.141) = \exp(0.4986)$

The female aged 60 with BMI 24 has 1.65 times higher hazard of death compared to the male aged 50 with BMI 30.

(f) Based on this model, describe the association of sex (male or female) with risk of death.

The female has 24% lower hazard of death compared to male.

However, p-value = 0.0581 > 0.05, the effect is not statistical significant.

It suggests that evidence is not strong enough to conclude sex difference in risk of death.

$HR_{sex} = \exp(-0.2732) \approx 0.761$

# Question 4: Impact of Ties on Cox Model Estimation and Testing

```
surv_object <- Surv(data$dthtime, data$dthstat)
cox_breslow <- coxph(surv_object ~ gender, data = data, ties = "breslow")
cox_efron <- coxph(surv_object ~ gender, data = data, ties = "efron")
cox_exact <- coxph(surv_object ~ gender, data = data, ties = "exact")
summary(cox_breslow)
```

```
## Call:
## coxph(formula = surv_object ~ gender, data = data, ties = "breslow")
##
##   n= 500, number of events= 215
##
##          coef exp(coef) se(coef)     z Pr(>|z|)
## gender 0.3813    1.4641   0.1376 2.771  0.00559 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##        exp(coef) exp(-coef) lower .95 upper .95
## gender     1.464      0.683     1.118     1.917
##
## Concordance= 0.542  (se = 0.018 )
## Likelihood ratio test= 7.59  on 1 df,   p=0.006
## Wald test            = 7.68  on 1 df,   p=0.006
## Score (logrank) test = 7.77  on 1 df,   p=0.005
```

```
summary(cox_efron)
```

```
## Call:
## coxph(formula = surv_object ~ gender, data = data, ties = "efron")
##
##   n= 500, number of events= 215
##
##          coef exp(coef) se(coef)     z Pr(>|z|)
## gender 0.3815    1.4645   0.1376 2.773  0.00556 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##        exp(coef) exp(-coef) lower .95 upper .95
## gender     1.464     0.6828     1.118     1.918
##
## Concordance= 0.542  (se = 0.018 )
## Likelihood ratio test= 7.6  on 1 df,   p=0.006
## Wald test            = 7.69  on 1 df,   p=0.006
## Score (logrank) test = 7.78  on 1 df,   p=0.005
```

```
summary(cox_exact)
```

```
## Call:
## coxph(formula = surv_object ~ gender, data = data, ties = "exact")
##
```

```
##   n= 500, number of events= 215
##
##          coef exp(coef) se(coef)     z Pr(>|z|)
## gender 0.3822    1.4655   0.1378 2.775  0.00553 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##        exp(coef) exp(-coef) lower .95 upper .95
## gender     1.466     0.6824     1.119      1.92
##
## Concordance= 0.542  (se = 0.018 )
## Likelihood ratio test= 7.61  on 1 df,   p=0.006
## Wald test            = 7.7  on 1 df,   p=0.006
## Score (logrank) test = 7.79  on 1 df,   p=0.005
```

The coefficient for gender, HR, and the test statistics Likelihood Ratio, Wald, and Score tests are very similar across all three methods.

The HR values range from 1.464 to 1.466, and the p-values for the Wald test are all approximately 0.006, indicating a statistically significant effect of gender on survival.

The small differences in test statistics and parameter estimates across the methods suggest that ties are not an important issue in this study.