

8108hw2

Ze Li

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

```
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 ($BMI \geq 25$), 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

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

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

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

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

```
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	

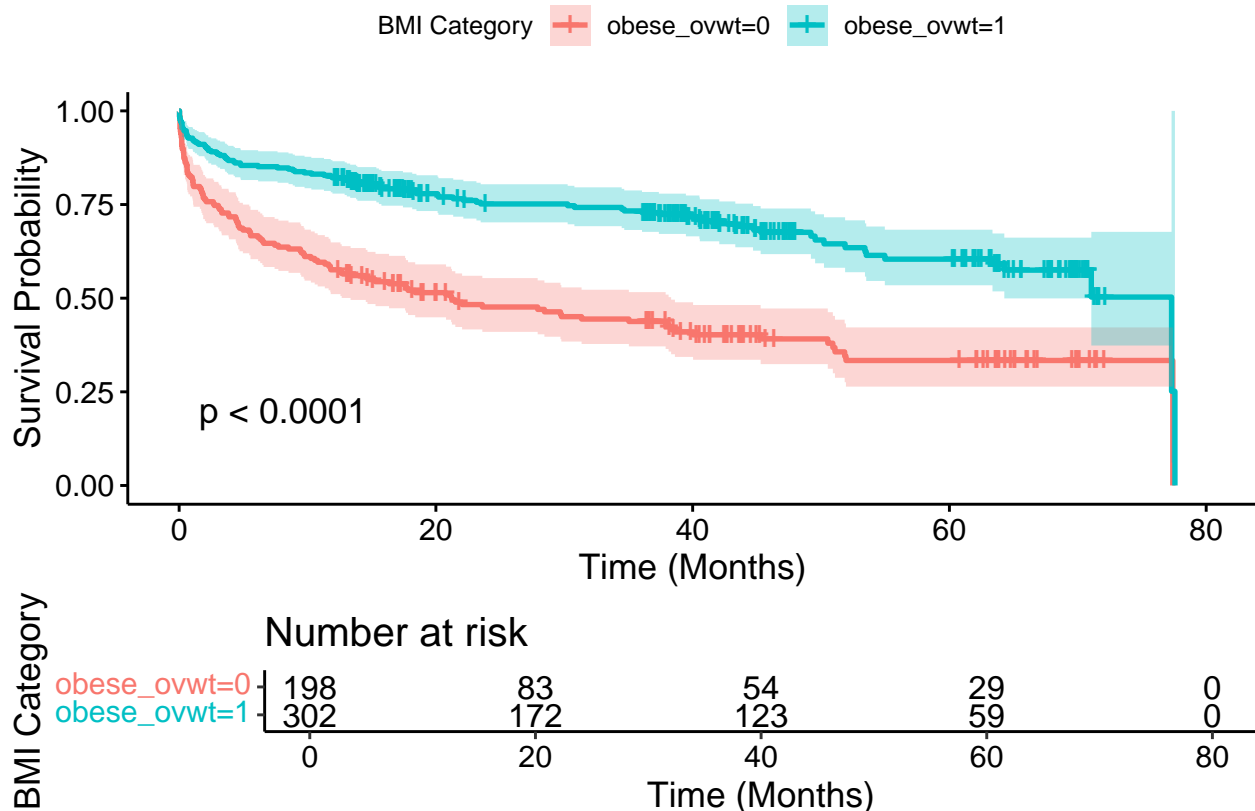
##	1.8092	155	1	0.778	0.02955	0.722	0.838
##	1.8750	154	2	0.768	0.03001	0.711	0.829
##	2.0066	152	1	0.763	0.03024	0.706	0.824
##	2.1053	151	1	0.758	0.03046	0.700	0.820
##	2.6645	150	1	0.753	0.03067	0.695	0.815
##	2.7303	149	1	0.747	0.03088	0.689	0.811
##	3.0592	148	1	0.742	0.03108	0.684	0.806
##	3.1250	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.						

##	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

```
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")
```

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)?

```
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)?

```
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
```

```
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)?

```
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
```

```
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
```

```
score_test
```

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

```
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 still 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.

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

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

```
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.

```
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
```

```
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.

```
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
```

```
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

```


Question 3: Myocardial Infarction Study

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

```
surv_object <- Surv(data$dthtime, data$dtthstat)
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.