Survival Analysis of NHANES Romberg Balance Test

STAT 417, Sklar, Winter 2024
Jason Blake, Brendan Callender
Lucas Fonda, Martin Hsu

Introduction

In this report we will be performing survival analysis techniques on data from a balance test that was conducted by the US Center for Disease Control (CDC). More specifically, the test was conducted by the CDC from 2001 to 2002 and contains the results for 2238 participants as part of the National Health and Nutrition Examination Survey (NHANES). The data also contains information relating several other tests conducted, body measures, demographics, and questionnaire responses for each participant. The purpose of this experiment, as stated by the CDC, was to provide data for analysis on predictors of balance disorders within the population of U.S. adults.

The participants were sampled from the population of all U.S. adults ages 40 or older. Participants were excluded if they felt dizzy, were unable to stand on their own, weighed more than 275 pounds, or could not properly fit into personal safety equipment. Participants were also excluded if they could not stand on their own, were amputees, were experiencing dizziness, or were blind. The balance test administered was the Romberg Test, where four balance tests are administered in order of increasing difficulty. For our analysis, we will be specifically looking at the results of the first trial of the 4th and hardest balance test. This test involved the participant balancing on a foam pad with their eyes closed.

The time to event variable can be defined as time until failure in seconds with the test ending after 30 seconds. Failure was determined as the subject opening their eyes to maintain balance, moving their arms or feet to maintain balance, or needing assistance to maintain balance. Complete times in the data are represented by individuals who failed the balance test before 30 seconds. Right censored times occur in the data for individuals who passed the balance test and maintained balance for the 30 second duration of the test. Additional variables we included for our analysis include the participants weight, height, BMI, gender, and age in months.

Parametric Survival Analysis

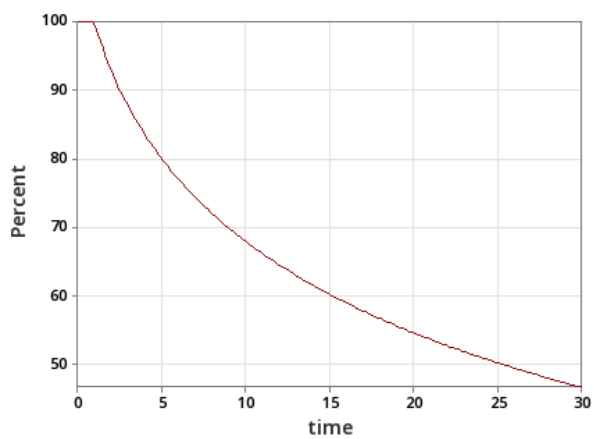
We fit several parametric models to the balance test results in order to determine a probability distribution which best modeled the time until loss of balance. Each distribution was fit to the data using maximum likelihood estimation to determine parameter estimates. Additionally, we observed the Anderson-Darling (AD) test statistic to measure the goodness of fit of the probability distribution to the data. Since lower values of the AD test statistic represent a better fit to the data, we selected the probability distribution which produced the lowest AD test statistic when fit to the data. *Table 1* contains a list of all the probability distributions fit to the data and their respective AD statistics. Fitting a three parameter Log Normal distribution to the data resulted in the lowest AD test statistic value of 7295.1.

Table 1. Anderson-Darling Test Statistics by Probability Distribution

Probability Distribution	**Anderson-Darling Test Statistic**
Weibull	7304.9
Exponential	7322.1
Log Normal	7299.3
Logistic	7327.8
Log Logistic	7299.4
Smallest Extreme Value	7336.6
3 Parameter Log Logistic	7297.3
2 Parameter Exponential	7336.3
3 Parameter Log Normal	7295.1
3 Parameter Weibull	7299.9

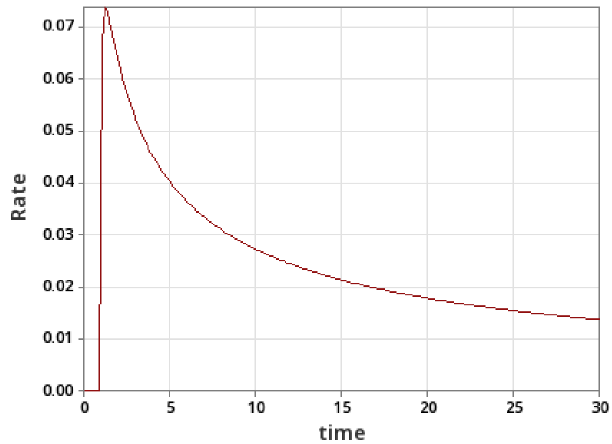
The resulting estimated survival function using a three parameter log normal distribution can be seen below in *Figure 1.* From the curve we see that the probability of maintaining balance up to time t begins decreasing after 1 second. Additionally, we see the probability of maintaining balance up to time decreases most quickly between 1 and 5 seconds and decreases at a slower rate between 5 and 30 seconds. Finally, we see that the curve approximates around 46% of participants to pass the balance test meaning they maintained balance up to 30 seconds.

Figure 1. Estimated Survival Function for 3 Parameter Log Normal Distribution



The estimated hazard curve using a three parameter log normal distribution can be seen below in *Figure 2.* From the curve we see the hazard of losing balance at time t given a participant maintained balanced up to time t rapidly increases from 1 to 2 seconds. From there, the hazard decreases rapidly between 2 to 5 seconds, and decreases at a slower rate between 5 and 30 seconds.

Figure 2. Estimated Hazard Function for 3 Parameter Log Normal Distribution



The estimated survival functions for both males and females can be seen in *Figure 3* below. From the curves we see that for any time t, the probability of maintaining balance up to time t is higher for males compared to females. *Figure 4* contains the estimated hazard curves for both males and females. We see the hazard curves follow the same pattern with a rapid increase between 1 and 2 seconds. Additionally, we see that the hazard of losing balance at time t, given an individual has not lost balance up to time t is higher for females compared to males. Finally, we can compare the survival experiences using summary statistics contained in *Table 2.* We see that men tend to lose balance later than women since the median time to lose balance for men is 25.21 seconds compared to 21.97 seconds for women.

Figure 3. Estimated Survival Functions by Gender

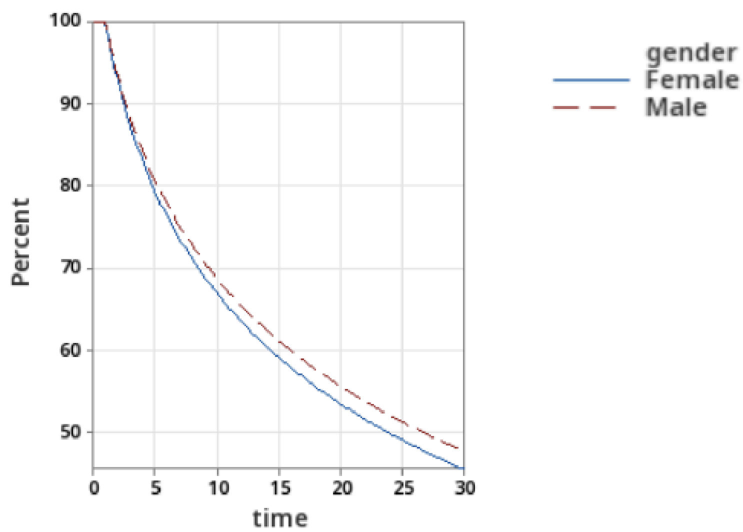


Figure 4. Estimated Hazard Functions by Gender

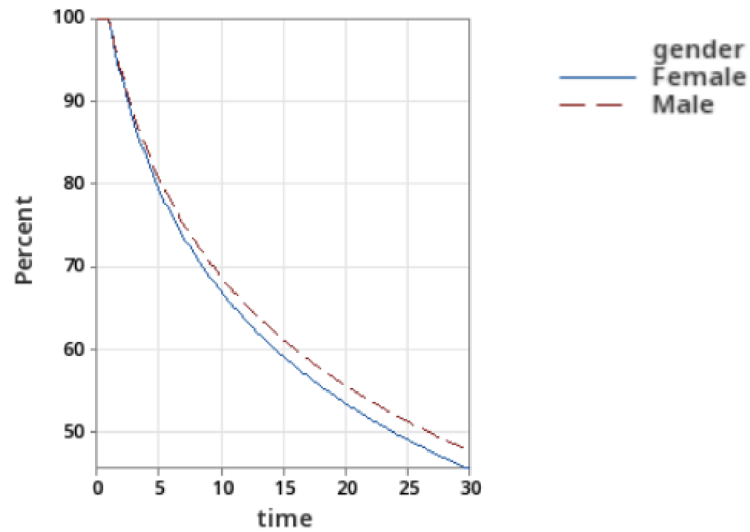


Table 2. Survival Summary Statistics by Gender

Gender	Mean	Median
Male	251.41	25.21
Female	215.18	21.97

Table 3. BMI to Weight Category Mappings

BMI Range	Weight Category
<18.5	Underweight
18.5 – 24.9	Healthy Weight
25.0 – 29.9	Overweight
>30.0	Obese

We binned different ranges of BMI into different weight categories to create a new categorical variable with 4 levels in the data. These mappings can be found in *Table 3* above. Looking at the estimated survival functions below in *Figure 5,* we see the survival probabilities differ visually between the four groups. For any time t, the probability of maintaining balance beyond time t is the highest for obese individuals. On the other hand, it is the smallest for underweight individuals for any time t. *Figure 6* contains the hazard functions for each of the four weight categories. We see the hazard of losing balance at time t, given an individual has maintained balance up to time t, is extremely high between 1 and 2 seconds for underweight individuals compared to the other weight categories. We also observe that the hazard of losing balance at any time t is the lowest for obese individuals compared to the other weight categories. These observations are backed by *Table 4* which contain the summary statistics relating to the different weight categories. We observe that underweight individuals have the shortest medium time until losing balance followed by healthy weight individuals. Obese individuals have the longest median time until balance is lost followed by overweight individuals.

Figure 5. Estimated Survival Functions by Weight Category

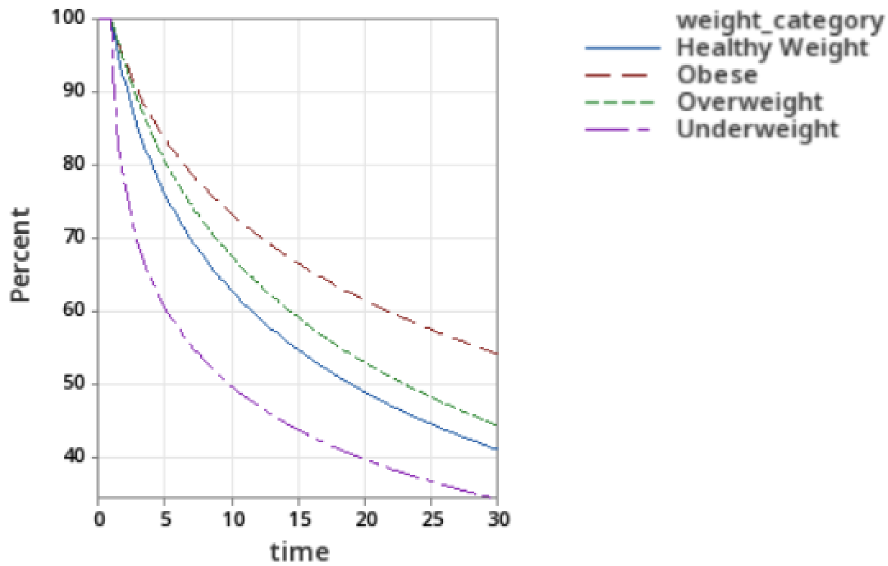


Figure 6. Estimated Hazard Functions by Weight Category

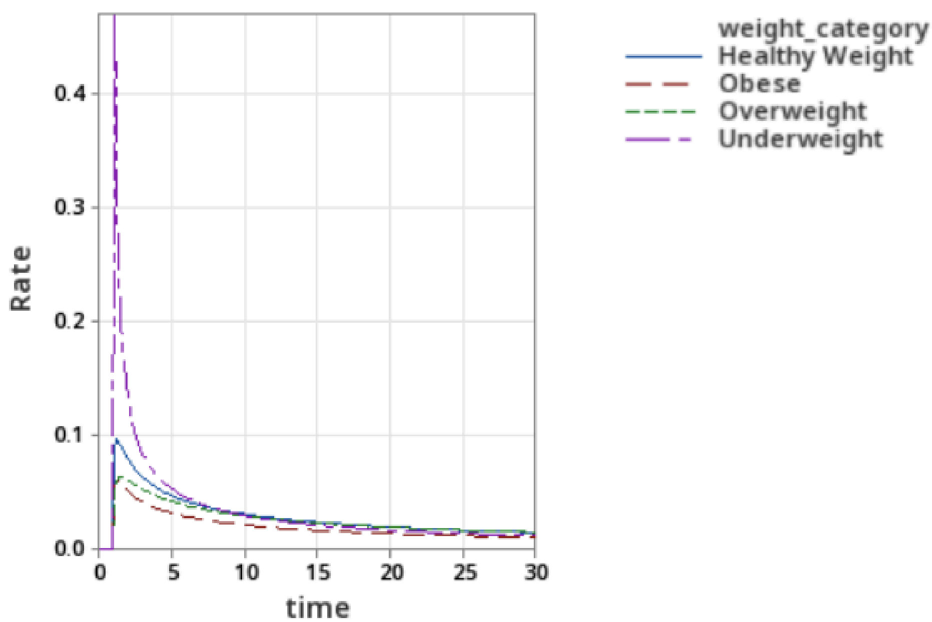


Table 4. Survival Summary Statistics by Weight Category

Weight Status	**Mean**	**Median**
Underweight	651.20	9.87
Healthy Weight	167.53	19.07
Overweight	150.31	23.11
Obese	467.10	37.96

Non-parametric Survival Analysis

The estimated Kaplan-Meier survival curve for all participants can be seen below in *Figure 7*. From the curve we see that the probability of maintaining balance up to time t begins to decrease after about 1 second. The probability of maintaining balance up to time t decreases the quickest between 1 and 5 seconds, and then begins to taper off from between 5 and 30 seconds. The curve approximates about 48% of participants to pass the balance test, which means successfully balancing for the full 30 seconds.

Figure 7. Estimated Kaplan-Meier Survival Curve for all Participants

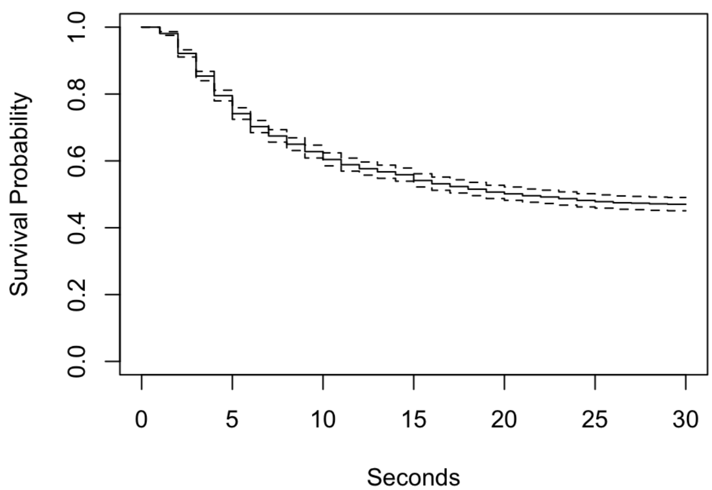
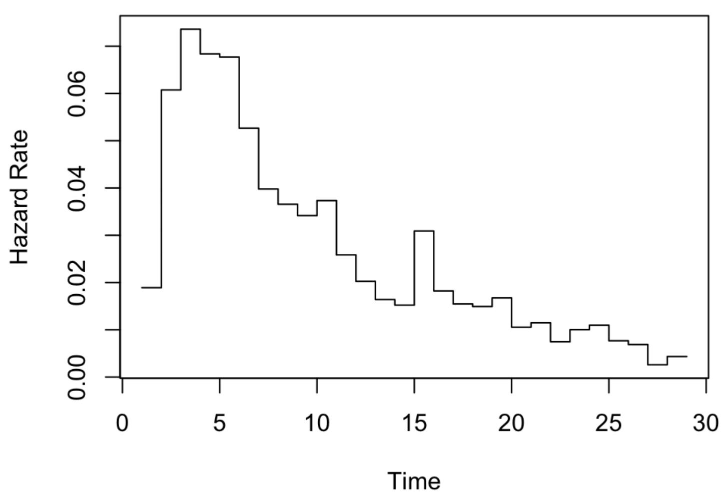


Figure 8. Estimated Kaplan-Meier Hazard Function for all Participants

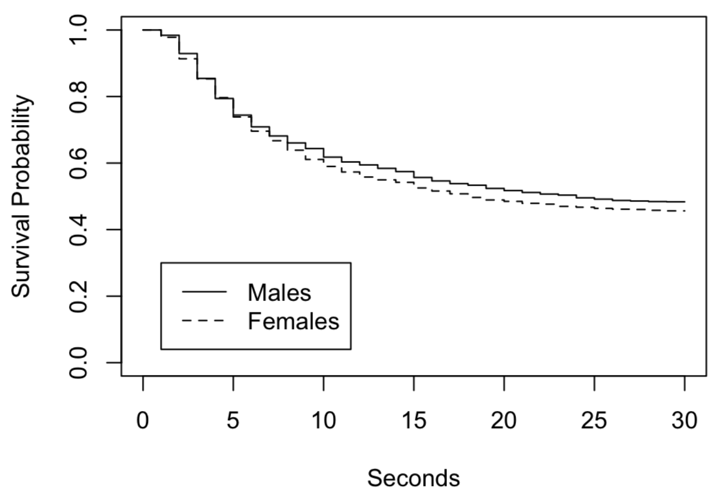


The estimated Kaplan-Meier hazard function for all participants is displayed above in *Figure 8*. From the curve, we see that given a participant has maintained balance up to time t, the probability of losing balance per a specific interval of time quickly increases from 1 to 2 seconds and is at its highest between 2 and 6 seconds. From there, the Kaplan-Meier estimate for hazard decreases promptly between 5 to about 15 seconds. Interestingly see a spike in the estimated hazard at 15 seconds with a slow decrease afterwards between 16 and 30 seconds.

Table 5. Survival Summary Statistics by Gender Category

Gender	**Mean**	**Median**
Male	18.64	24
Female	17.92	18

Figure 9. Estimated Kaplan-Meier Survival Curve by Gender



From *Figure 9* above we see that from 0 to 5 seconds, the probability of maintaining balance up to time t is almost equal for males and females. From 5 to 30 seconds, the probability of maintaining balance up to time t is higher for males compared to females. This phenomenon is further backed up by the summary statistics found in *Table 5*. The mean time to failure for men is 18.64 seconds compared to 17.92 for females indicating participants who are male tend to maintain balance longer than participants who are female. In *Figure 10* below, the estimated Kaplan-Meier Hazard functions based on gender are similar for both males and females. Given a participant maintained balance up to time t, the probability of losing balance per a specific time interval quickly increases from 1 to 4 seconds for both males and females. The estimated hazard then speedily decreased, with spikes at 10, 15, 20, and 25 seconds for males. Additionally, the estimated hazard for females decreases quickly at 5 seconds, with a noticeable spike at 15 seconds.

Figure 10. Estimated Kaplan-Meier Hazard Functions by Gender

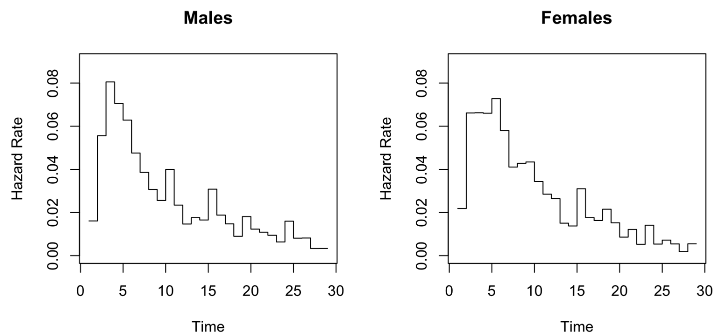


Table 7. Log-Rank Test for Gender

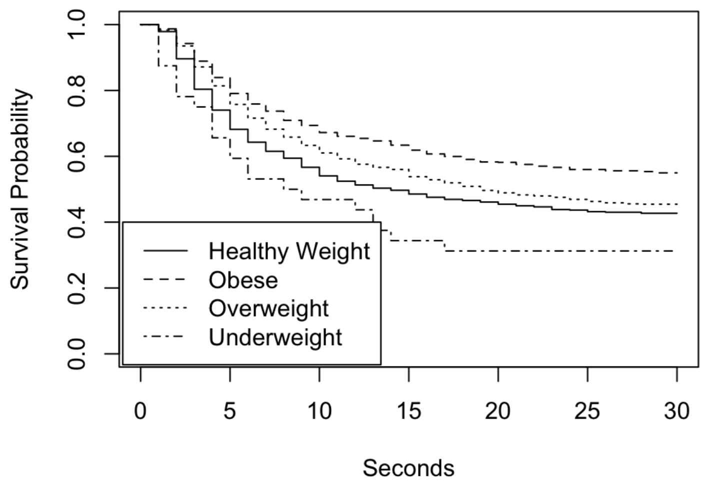
Log-Rank Test Statistic	**DF**	**p-value**
1.9	1	.2

Table 7 contains the results for a log-rank test which is the formal test for determining whether the survival experiences differ between two groups. More specifically, the test was conducted to determine whether there are significant differences in the survival experiences between men and women. The null hypothesis is that the probability of maintaining one's balance beyond time t is the same regardless of gender. Based on the rather low test statistic of 1.9 and high p-value of 0.2 for this log-rank test, we fail to reject this null hypothesis at any reasonable significance level. Therefore, there is not enough evidence to conclude that the probability of a participant maintaining their balance beyond time t differs for any time t between males and females.

Table 6. Survival Summary Statistics by Weight Category

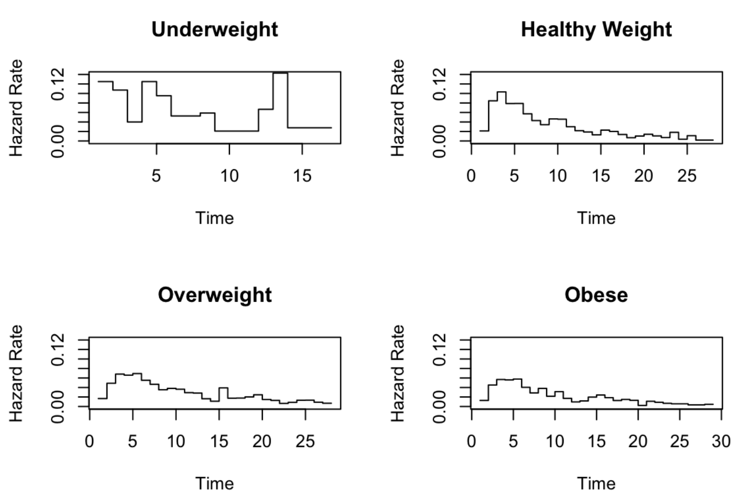
Weight Status	**Mean**	**Median**
Underweight	13.53	8.5
Healthy Weight	16.83	14
Overweight	18.23	19
Obese	20.24	30

Figure 11. Estimated Kaplan-Meier Hazard Functions by Weight Classification



We were able to model the survival experiences of different weight categories using Kaplan-Meier curves. The categories were created by binning the BMI variable. (See *Table 3)* A plot containing the overlaid curves for each category can be found above in *Figure 11.* Much like the estimated survival curves using parametric methods, the plot above shows that for any time t, the probability of maintaining balance beyond time t is the highest for obese individuals. On the other hand, for any time t, the probability of maintaining balance beyond time t is the lowest for underweight individuals. This is further backed up by *Table 6* which contains summary statistics for each weight category. We see that obese individuals have the highest mean time until balance is lost, that being 20.24 seconds, while underweight individuals have the lowest, 13.53 seconds.

Figure 12. Estimated Kaplan-Meier Hazard Functions by Weight Classification



The estimated Kaplan-Meier hazard functions by weight classification are shown above in *Figure* 12. Given an individual has not lost balance up to time t, the conditional probability of losing balance per an interval of time is similar for healthy weight, overweight, and obese individuals. For these participants, the estimated hazard increases for the first five seconds, after which the hazard of losing balance at time t seconds gradually decreases for the remainder of the time period. The estimated hazard function for participants who are underweight deviates from this trend, and there are notably three large spikes at approximately the first three seconds, around 5 seconds, and at about 13 seconds. However, it is important to note that a very small proportion of the sample was considered to be underweight, so there is less data for inference on this group.

Table 8. Log-Rank Test for Weight Classification

Log-Rank Test Statistic	**DF**	**p-value**
34.1	3	<.0001

We performed a log-rank test to determine whether the survival experiences differ between the different weight categories. The results of this test can be found above in *Table 8.* The null hypothesis is that the probability of a participant maintaining their balance beyond time t seconds is the same regardless of weight category for any time t. Based on the high test statistic for this test of 34.1, and very small p-value of <.0001, we reject this null hypothesis at any reasonable level of significance. There is very strong evidence to conclude that the survival experiences for the different weight categories differ significantly for at least some time t.

Regression Analysis

In order to examine the relationship between the hazard of losing balance and the variables age, gender, BMI, weight and height, we fit Cox regression models to the data. After iterating through multiple models, our final Cox regression model includes age and the interaction between gender and BMI, and excludes weight and height.

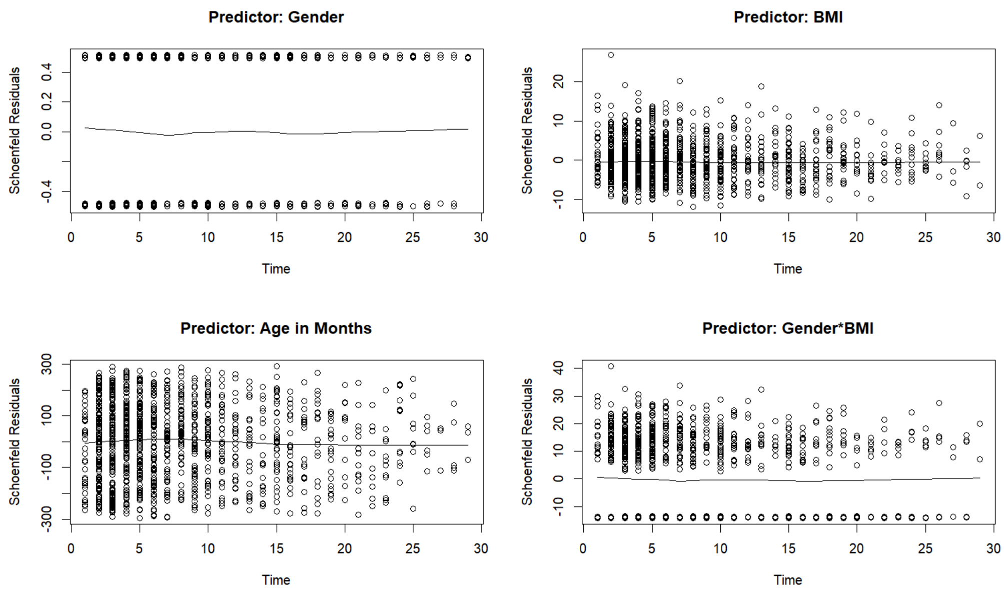
Table 9: Final Model Parameter Estimates and Significance

Predictor	**Parameter Estimate ($\hat{\beta}$)**	$e^{\hat{\beta}}$	**Standard Error**	**Wald Test P-Value**	**95% Confidence Interval for e^{β}**	
					Lower Bound	***Upper Bound***
Gender (Female)	-1.093	0.334	0.348	0.00169	0.1695	0.6631
BMI	-0.0531	0.948	0.0104	3.24e-07	0.9291	0.9678
Age (Months)	0.00388	1.004	0.000197	2e-16	1.0035	1.0043
Gender * BMI	0.0425	1.043	0.0125	0.000649	1.0182	1.0692

At a significance level of 0.01, based on the extremely small p-values from Wald tests performed on each of the individual predictors, we can conclude that each of these predictors are significantly associated with the hazard of losing balance, after adjusting for the remaining predictors. Furthermore, based on the small p-value for the likelihood ratio test, we can conclude that age and the interaction between gender and BMI are jointly significantly associated with the hazard of losing balance.

In order to use Cox regression, the data must conform to the proportional hazards assumption. We examined LOWESS curves fit to the Schoenfeld residuals as a factor of time, as well as performing a formal Schoenfeld residuals test, in order to determine if the assumption is fulfilled.

Figure 13: Schoenfeld Residuals for Cox Regression Predictors as a Factor of Time



At a significance level of 0.01, none of the Schoenfeld residual tests on the predictors yielded a p-value less than or equal to 0.01. Based on both observing flat horizontal LOWESS curves for the Schoenfeld residuals as a function of time for each predictor, as well as the high p-values for the Schoenfeld residuals test test, we can conclude that the proportional hazards assumption has not been violated for any of the predictors included in this model. It is therefore appropriate to use Cox regression to analyze the joint relationship between each of these predictors and the risk of losing balance during the balance test. No outlying values were removed from the analysis.

In order to investigate how the effect of gender on the hazard of losing balance may change depending on BMI due to the interaction between gender and BMI, we examined the hazard ratio for each of the scenarios seen in Table X below.

Table 10: Estimated Hazard Ratios between Genders, for Different BMI values, Adjusting for Age

Hazard Ratio (HR) Description	**Estimated HR**	**95% Confidence Interval for HR**	
		Lower Bound	***Upper Bound***
Male with Sample Minimum BMI (15.8) vs. Female with Sample Minimum BMI, Adjusting for Age	1.524	0.840	2.765
Male with Sample Average BMI (28.139) vs. Female with Sample	0.902	0.451	1.795

Average BMI, Adjusting for Age			
Male with Sample Maximum BMI (54.65) vs. Female with Sample Maximum BMI, Adjusting for Age	0.292	0.0915	0.934

The risk of losing balance is estimated to be 52% higher for male balance test participants with sample minimum BMI (15.80) compared to female balance test participants of sample minimum BMI, after adjusting for age. Furthermore, we are 95% confident that the risk of losing balance for male balance test participants of sample minimum BMI is between 16% lower to 176% higher than the risk of losing balance for female balance test participants of sample minimum BMI, after adjusting for age.

The risk of losing balance is estimated to be 10% lower for male balance test participants with sample average BMI (28.14) compared to female balance test participants of sample average BMI, after adjusting for age. Furthermore, we are 95% confident that the risk of losing balance for male balance test participants of sample average BMI is between 55% lower to 79% higher than the risk of losing balance for female balance test participants of sample average BMI, after adjusting for age.

The risk of losing balance is estimated to be 71% lower for male balance test participants with sample maximum BMI (54.65) compared to female balance test participants of sample maximum BMI, after adjusting for age. Furthermore, we are 95% confident that the risk of losing balance for male balance test participants of sample maximum BMI is between 7% to 91% lower than the risk of losing balance for female balance test participants of sample maximum BMI, after adjusting for age.

Between all three comparisons of gender (at sample minimum BMI, average BMI, and maximum BMI), we can see how the relationship between the hazard of losing balance and gender changes depending on BMI in this model. For the sample minimum BMI, the risk of losing balance is estimated to be higher for male participants than female participants while for the sample maximum BMI, the risk of losing balance is estimated to be lower for male participants than female participants, after adjusting for age. Because we observe that after adjusting for age, the 95% confidence intervals for the true hazard ratio between male and female participants at sample minimum BMI and sample average BMI both capture the value of 1 while the 95% confidence interval for the true hazard ratio between male and female participants at sample maximum BMI does not, there is evidence for a difference in true hazard ratio between genders at higher BMI but not lower BMI, after adjusting for age.

We additionally investigated how the relationship between BMI and the hazard of losing balance differed by gender.

Table 11: Estimated Hazard Ratio for 5 Unit Increase in BMI, by Gender, Adjusting for Age

Hazard Ratio (HR) Description	**Estimated HR**	**95% Confidence Interval for HR**	
		Lower Bound	***Upper Bound***

5 Unit Increase in BMI, Male, Adjusting for Age	0.767	0.692	0.849
5 Unit Increase in BMI, Female, Adjusting for Age	0.948	0.839	1.072

The risk of losing balance is estimated to decrease by 23% for every 5 unit increase in BMI in male balance test subjects, after adjusting for age. Furthermore, we are 95% confident that the risk of losing balance decreases by between 15% to 31% for every 5 unit increase in BMI in male balance test subjects, after adjusting for age.

The risk of losing balance is estimated to decrease by 5% for every 5 unit increase in BMI in female balance test subjects, after adjusting for age. Furthermore, we are 95% confident that the risk of losing balance is between 16% lower to 7% higher for every 5 unit increase in BMI in male balance test subjects, after adjusting for age.

Between both hazard ratio analyses, male and female, for a 5 unit BMI increase, we can see that for both genders, a 5 unit increase in BMI corresponds to an estimated decrease in risk of losing balance at any time during the balance test. However, the 95% confidence interval for a 5 unit increase in BMI for female participants captures the value 1, which corresponds to a percent difference of 0% and indicates a lack of evidence that BMI is associated with the hazard of losing balance for female participants. On the other hand, the 95% confidence interval for a 5 unit increase in BMI for male participants does not capture the value 1, indicating evidence that BMI is associated with the hazard of losing balance for male participants.

Conclusion

Based on our survival analysis using parametric, nonparametric, and regression methods, we identified significant trends and patterns in time until losing balance during the fourth trial of the NHANES balance test. In general, for the population of healthy and unimpaired U.S. adults ages 40 and over, the greatest estimated risk of losing balance during the balance test occurs within the first five seconds. Survival times for the balance test may be best described by a three-parameter lognormal distribution. These findings imply that adults with poor balance might be quickly distinguished by an extremely short survival time.

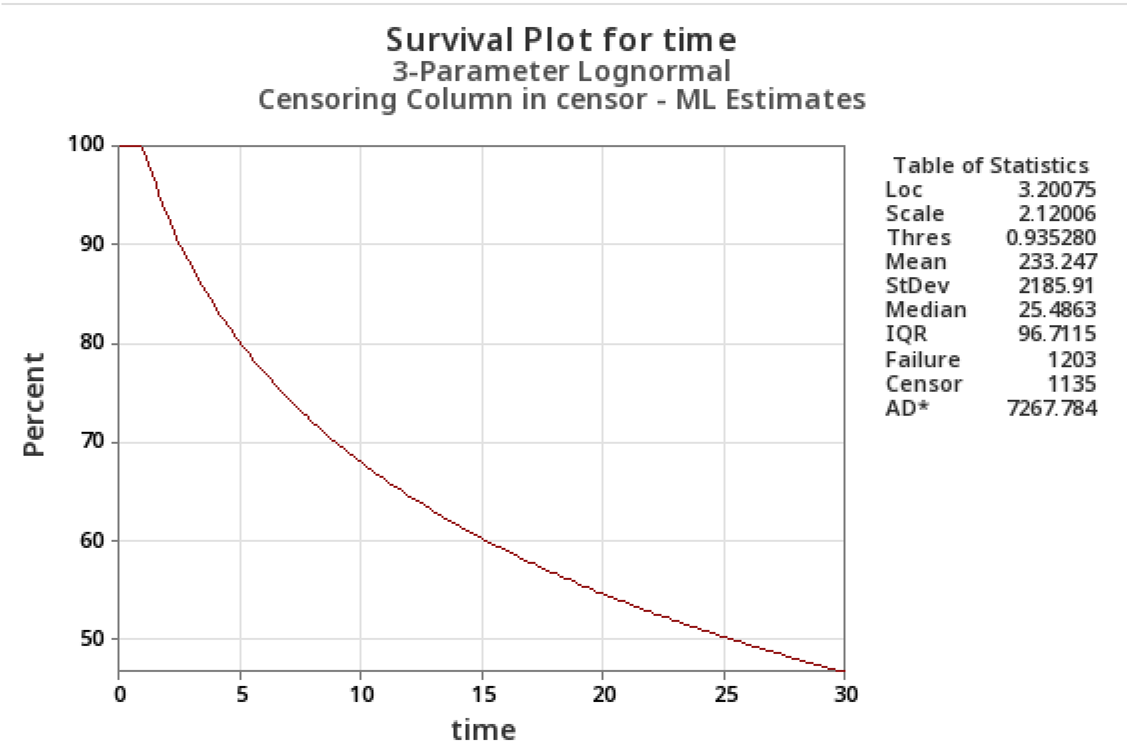
Furthermore, we identified differences in balance test survival experiences for varying populations based on gender, height, weight, age in months, and BMI. Specifically, in our parametric and nonparametric survival analyses, we found that survival experiences differ considerably between BMI classes. For any time t, individuals classified as obese or overweight were estimated to be at lower risk for losing balance and had a higher estimated probability of remaining balanced past that time, compared to healthy or underweight individuals. Applying a Cox regression analysis with a model involving age and an interaction between gender and BMI revealed that this relationship between risk of losing balance and BMI depends on gender, with more significant differences in estimated risk of losing balance between high and low BMI occurring for male participants than female participants, after controlling for age.

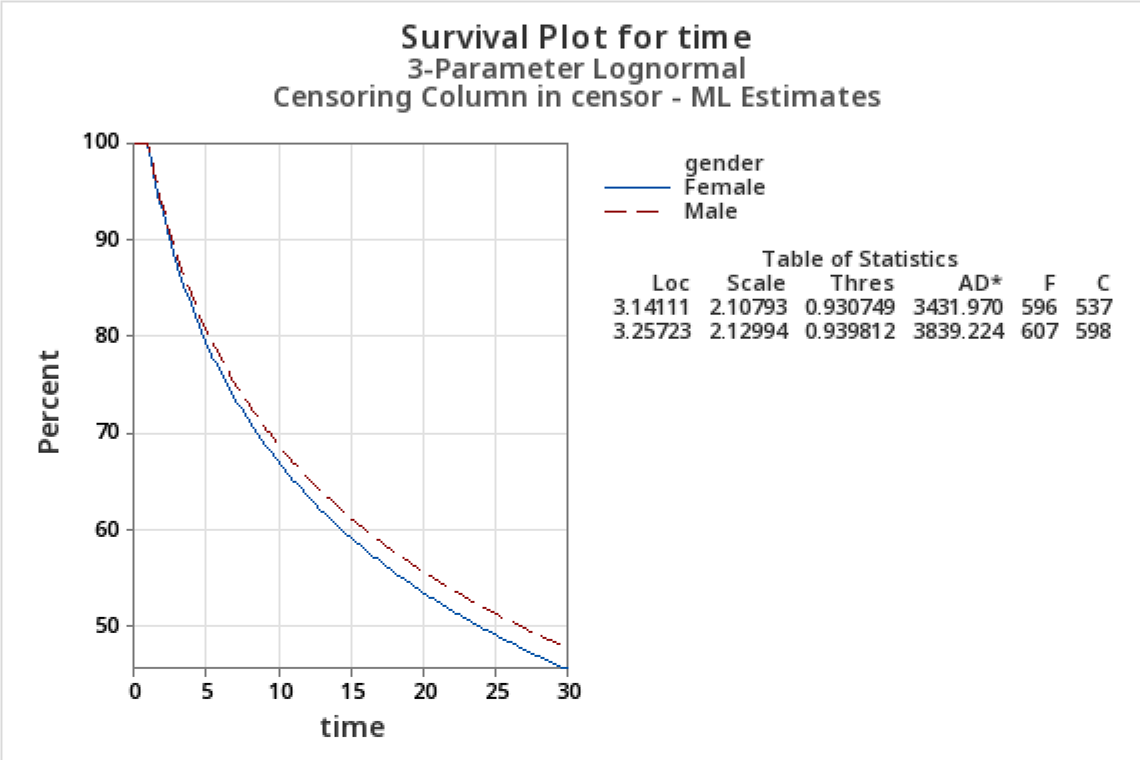
While there may not be significantly different survival experiences between male and female gendered participants, after controlling for age, the relationship between risk of losing balance significantly depends on gender.

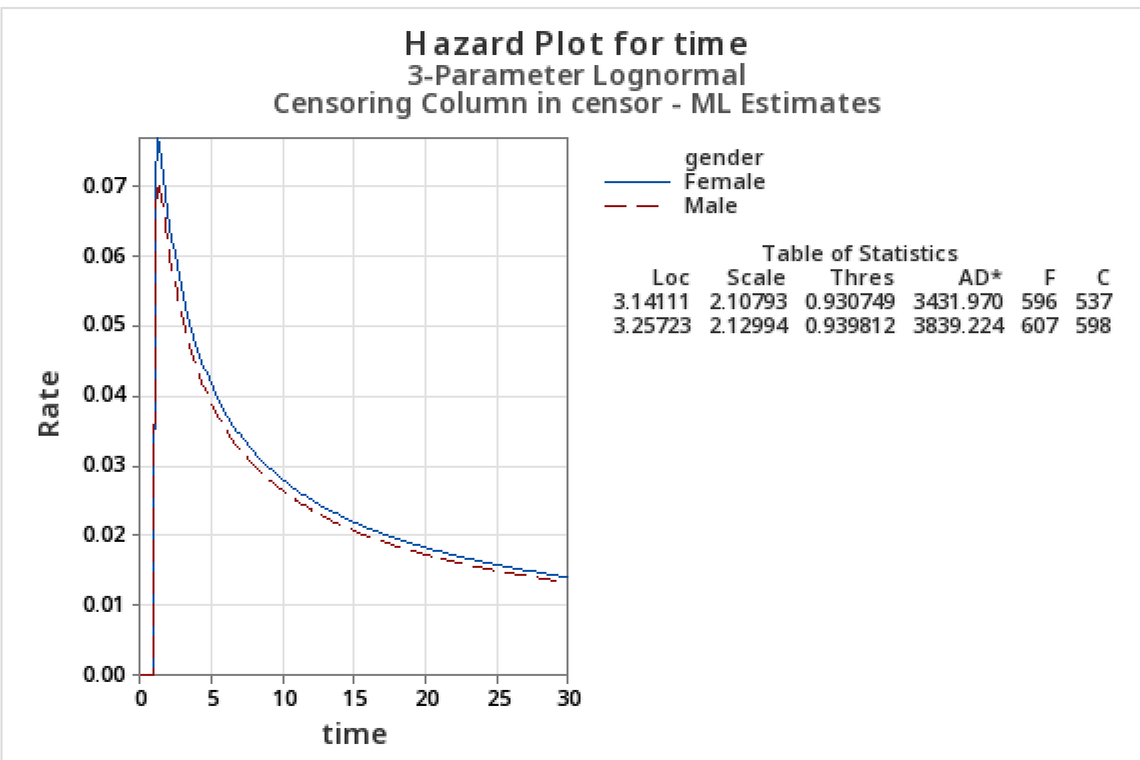
Overall, this survival analysis revealed that BMI is a significant factor in survival experience for individuals undergoing balance tests. As a result, it is important to keep BMI under consideration when evaluating an individual for balance disorders. Because adults with higher BMI are estimated to have a higher probability of remaining balanced beyond any given time compared to adults with lower BMI, it may be more difficult to diagnose balance disorders and conditions where loss of balance is an important symptom for individuals with higher BMI.

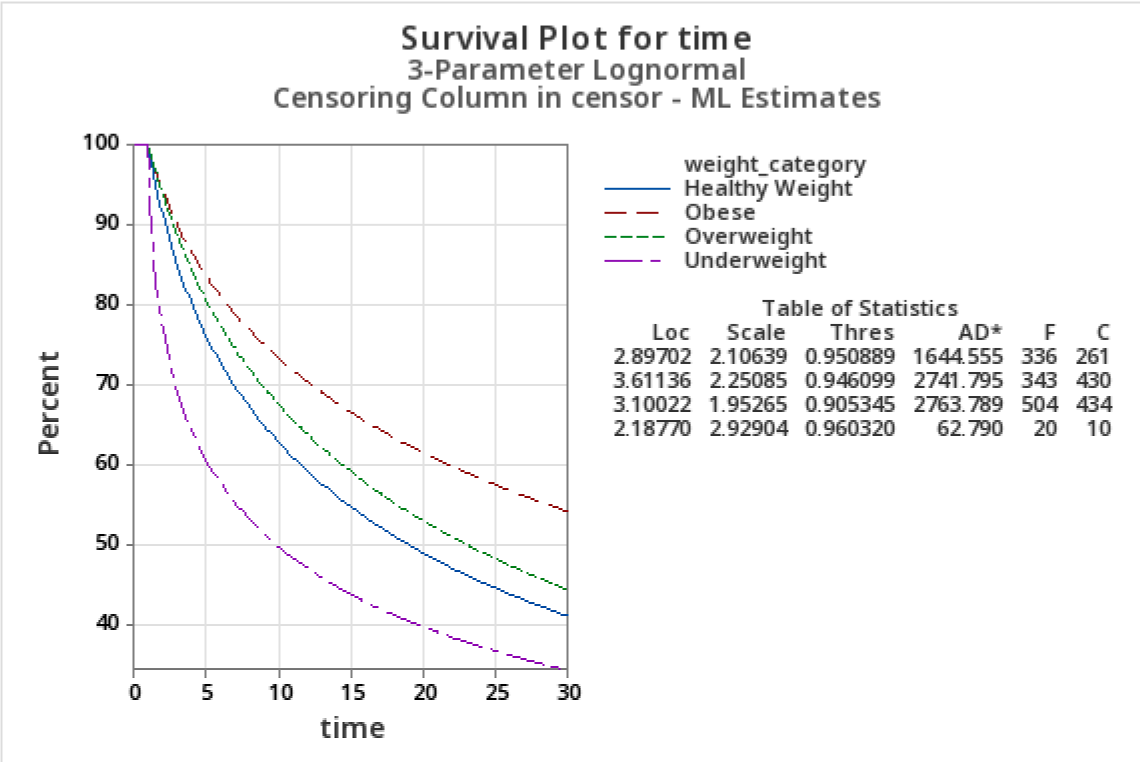
Appendix

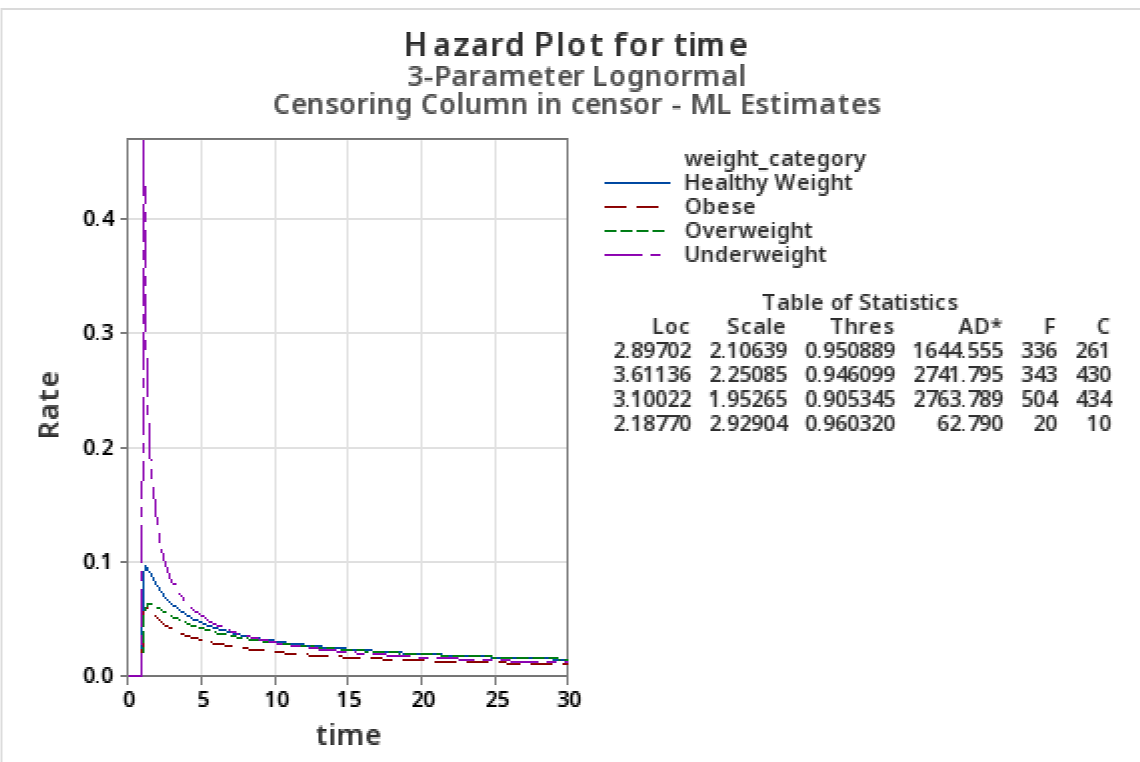
Parametric Analysis Minitab Output




Survival Plot for time
3-Parameter Lognormal
Censoring Column in censor - ML Estimates
Percent
time
gender
Female
Male
Table of Statistics
Loc Scale Thres AD* F C
3.14111 2.10793 0.930749 3431.970 596 537
3.25723 2.12994 0.939812 3839.224 607 598


Hazard Plot for time
3-Parameter Lognormal
Censoring Column in censor - ML Estimates
Rate
time
gender
Female
Male
Table of Statistics
Loc Scale Thres AD* F C
3.14111 2.10793 0.930749 3431.970 596 537
3.25723 2.12994 0.939812 3839.224 607 598





Cox Regression Code

```
# Setup
```

```
library(survival)
library(tidyverse)

balance <- read.csv("balance_test.csv")
balance

cr.obj <- coxph(Surv(time, censor)~as.factor(gender)*bmi+age_months,
                data = balance)
summary(cr.obj)

# Schoenfeld Residuals Analysis
schoen <- residuals(cr.obj, type="schoenfeld")

balance2 <- balance %>%
  select(time, censor, gender, bmi, age_months) %>%
  drop_na()

comp.times <-  balance2 %>%
  filter(censor != 0) %>%
  pull(time)

par(mfrow=c(2,2))

## Schoenfeld Residuals vs Gender
plot(comp.times, schoen[,1], xlab="Time",
     ylab="Schoenfeld Residuals", main="Predictor: Gender")
smooth.sres <- lowess(comp.times, schoen[,1])
lines(smooth.sres$x, smooth.sres$y, lty=1)

## Schoenfeld Residuals vs BMI
plot(comp.times, schoen[,2], xlab="Time",
     ylab="Schoenfeld Residuals", main="Predictor: BMI")
smooth.sres <- lowess(comp.times, schoen[,2])
lines(smooth.sres$x, smooth.sres$y, lty=1)

## Schoenfeld Residuals vs Age in Months
plot(comp.times, schoen[,3], xlab="Time",
     ylab="Schoenfeld Residuals", main="Predictor: Age in Months")
smooth.sres <- lowess(comp.times, schoen[,3])
lines(smooth.sres$x, smooth.sres$y, lty=1)

## Schoenfeld Residuals vs Gender x BMI
plot(comp.times, schoen[,4], xlab="Time",
     ylab="Schoenfeld Residuals", main="Predictor: Gender*BMI")
smooth.sres <- lowess(comp.times, schoen[,4])
```

```
lines(smooth.sres$x, smooth.sres$y, lty=1)

## Schoenfeld Residuals Test
cox.zph(cr.obj, transform="log")

# Hazard Ratios
min_age <- min(balance2$age_months)
mean_age <- mean(balance2$age_months)
max_age <- max(balance2$age_months)

## Function to calculate estimated hazard ratio
haz.ratio <- function(cr.obj, v1, v2) {
  coefs <- cr.obj$coefficients
  hr <- exp(sum(coefs * v1)) / exp(sum(coefs * v2))
  return(hr)
}

## Function to calculate hazard ratio confidence interval
## Verified correctness by comparing with summary(cr.obj) output
hr.ci <- function(cr.obj, v1, v2) {
  v <- v1 - v2
  varcov <- cr.obj$var
  varcov[lower.tri(varcov)] <- 0 # Make sure we don't repeat
covariances
  var <- sum(v[1] * v * varcov[1,]) +
    sum(v[2] * v * varcov[2,]) +
    sum(v[3] * v * varcov[3,]) +
    sum(v[4] * v * varcov[4,])
  se <- sqrt(var)
  loghr <- log(haz.ratio(cr.obj, v1, v2))
  return(exp(loghr + c(-1.96, 1.96)*se))
}

## HR Comparing Gender, Min BMI
haz.ratio(cr.obj,
          c(0, min_bmi, mean_age, 0*min_bmi),
          c(1, min_bmi, mean_age, 1*min_bmi))
hr.ci(cr.obj,
      c(0, min_bmi, mean_age, 0*min_bmi),
      c(1, min_bmi, mean_age, 1*min_bmi))

## HR Comparing Gender, Average BMI
haz.ratio(cr.obj,
          c(0, mean_bmi, mean_age, 0*mean_bmi),
          c(1, mean_bmi, mean_age, 1*mean_bmi))
```

```
hr.ci(cr.obj,
      c(0, mean_bmi, mean_age, 0*mean_bmi),
      c(1, mean_bmi, mean_age, 1*mean_bmi))

## HR Comparing Gender, Max BMI
haz.ratio(cr.obj,
          c(0, max_bmi, mean_age, 0*max_bmi),
          c(1, max_bmi, mean_age, 1*max_bmi))
hr.ci(cr.obj,
      c(0, max_bmi, mean_age, 0*max_bmi),
      c(1, max_bmi, mean_age, 1*max_bmi))

## HR for 5 Unit Increase in BMI, Male
haz.ratio(cr.obj,
          c(0, 5, mean_age, 0*5),
          c(0, 0, mean_age, 0*0))
hr.ci(cr.obj,
      c(0, 5, mean_age, 0*5),
      c(0, 0, mean_age, 0*0))

## HR for 5 Unit Increase in BMI, Female
haz.ratio(cr.obj,
          c(1, 5, mean_age, 1*5),
          c(1, 0, mean_age, 1*0))
hr.ci(cr.obj,
      c(1, 5, mean_age, 1*5),
      c(1, 0, mean_age, 1*0))
```

Cox Regression Final Model Summary

```
Call:
coxph(formula = Surv(time, censor) ~ as.factor(gender) * bmi +
    age_months, data = balance)

  n= 2338, number of events= 1203
   (95 observations deleted due to missingness)

                             coef  exp(coef)   se(coef)      z
Pr(>|z|)
as.factor(gender)2     -1.0929764  0.3352173  0.3480523 -3.140
0.001688 **
bmi                    -0.0531210  0.9482653  0.0103980 -5.109
3.24e-07 ***
age_months              0.0038782  1.0038857  0.0001967 19.712  <
2e-16 ***
```

```
as.factor(gender)2:bmi  0.0425052  1.0434215  0.0124639  3.410
0.000649 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

                       exp(coef) exp(-coef) lower .95 upper .95
as.factor(gender)2        0.3352     2.9831    0.1695    0.6631
bmi                       0.9483     1.0546    0.9291    0.9678
age_months                1.0039     0.9961    1.0035    1.0043
as.factor(gender)2:bmi    1.0434     0.9584    1.0182    1.0692

Concordance= 0.67  (se = 0.008 )
Likelihood ratio test= 425.1  on 4 df,   p=<2e-16
Wald test            = 428.6  on 4 df,   p=<2e-16
Score (logrank) test = 452.8  on 4 df,   p=<2e-16
```

Schoenfeld Residuals Test Output

```
                      chisq df    p
as.factor(gender)     0.0568  1 0.81
bmi                   1.8705  1 0.17
age_months            0.3432  1 0.56
as.factor(gender):bmi 0.1070  1 0.74
GLOBAL                4.2982  4 0.37
```

Non-parametric Analysis Code

```
# Non-parametric Estimates
# Creating Weight Category Variable
balance_test$weight_category <- ifelse(balance_test$bmi < 18.5,
"Underweight",
                                       ifelse(balance_test$bmi >=
18.5 & balance_test$bmi < 24.9, "Healthy Weight",
                                              ifelse(balance_test$bmi
>= 25 & balance_test$bmi < 29.9, "Overweight",
                                                     "Obese")))
# Overall
KM.obj <- survfit(Surv(time,censor)~1,  conf.type = "none",
data=balance_test)
# KM overall survival curve
plot(KM.obj, xlab = "Seconds", ylab = "Survival Probability",
     main = "KM Curve overall")
# KM hazard overall
plot.haz(KM.obj)
# KM estimates overall
```

```
summary(KM.obj)
mean(balance_test$time)

# By Gender (male = 1, female = 2)
KM.obj.Gender <- survfit(Surv(time, censor) ~ gender, data =
balance_test)
# KM Survival Curve Gender
plot(KM.obj.Gender, xlab = "Seconds", ylab = "Survival Probability",
     main = "KM Curve by Gender", lty = 1:2)
legend(1,.3,c("Males", "Females"),lty=1:2)
# Side by side KM hazard by gender
Males <- subset(balance_test, gender == 1)
KM.obj.Males <- survfit(Surv(time, censor) ~ gender, data = Males)
mean(Males$time)
par(mfrow=c(1,2))
plot.hazNew(KM.obj.Males, title = "Males", ylimits = c(0, .09))
Females <- subset(balance_test, gender == 2)
KM.obj.Females <- survfit(Surv(time, censor) ~ gender, data =
Females)
mean(Females$time)
plot.hazNew(KM.obj.Females, title = "Females", ylimits = c(0, .09))
# KM estimates by Gender
summary(KM.obj.Gender)
# Log-rank Gender
survdiff(Surv(time, censor) ~ gender, data = balance_test)

# By BMI category
KM.obj.BMI <- survfit(Surv(time, censor) ~ weight_category, data =
balance_test)
# KM Survival curve by BMI category
plot(KM.obj.BMI, xlab = "Seconds", ylab = "Survival Probability",
     main = "KM Curve by Weight Category", lty = 1:4)
legend(-1,.4,c("Healthy Weight","Obese" , "Overweight",
"Underweight"),lty=1:4)
# Side by Side KM hazard by BMI category
par(mfrow=c(2,2))
Underweight <- subset(balance_test, weight_category == "Underweight")
KM.obj.Underweight <- survfit(Surv(time, censor) ~ weight_category,
data = Underweight)
mean(Underweight$time)
HealthyWeight <- subset(balance_test, weight_category == "Healthy
Weight")
KM.obj.Healthy <- survfit(Surv(time, censor) ~ weight_category, data
= HealthyWeight)
mean(HealthyWeight$time)
```

```
Obese <- subset(balance_test, weight_category == "Obese")
KM.obj.Obese <- survfit(Surv(time, censor) ~ weight_category, data =
Obese)
mean(Obese$time)
Overweight <- subset(balance_test, weight_category == "Overweight")
KM.obj.Overweight <- survfit(Surv(time, censor) ~ weight_category,
data = Overweight)
mean(Overweight$time)
plot.hazNew(KM.obj.Underweight, title = "Underweight", ylimits = c(0,
.14))
plot.hazNew(KM.obj.Healthy, title = "Healthy Weight", ylimits = c(0,
.14))
plot.hazNew(KM.obj.Overweight, title = "Overweight", ylimits = c(0,
.14))
plot.hazNew(KM.obj.Obese, title = "Obese", ylimits = c(0, .14))
# KM estimates by BMI cateogory
summary(KM.obj.BMI)
# Log-rank BMI category
survdiff(Surv(time, censor) ~ weight_category, data = balance_test)
```