

Project_codes

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```
# -----  
# Helper Functions  
# -----  
  
### Smooth ES Curve for Martingale residuals  
smoothSEcurve <- function(yy, xx) {  
  xx.list <- min(xx) + ((0:100)/100)*(max(xx) - min(xx))  
  yy.xx <- predict(loess(yy ~ xx), se=T, newdata=data.frame(xx=xx.list))  
  quantile.t = qt(0.975, yy.xx$df)  
  lines(yy.xx$fit ~ xx.list, lwd=2)  
  lines(yy.xx$fit - quantile.t*yy.xx$se.fit ~ xx.list, lty=2)  
  lines(yy.xx$fit + quantile.t*yy.xx$se.fit ~ xx.list, lty=2)  
}  
  
# ---- Extractor Functions ----  
extract_metrics_cox <- function(model) {  
  ll <- logLik(model)  
  data.frame(  
    Log_Likelihood = as.numeric(ll),  
    Degrees_of_Freedom = attr(ll, "df"),  
    AIC = AIC(model),  
    Concordance = summary(model)$concordance[1]  
  )  
}  
  
extract_metrics_aft <- function(model) {  
  ll <- logLik(model)  
  data.frame(  
    Log_Likelihood = as.numeric(ll),  
    Degrees_of_Freedom = attr(ll, "df"),  
    AIC = AIC(model),  
    Concordance = NA  
  )  
}  
  
# Compute vertical lines for mean and median survival  
get_stats <- function(fit, label) {  
  tbl <- summary(fit)$table  
  if (is.matrix(tbl)) {  
    # Multi-group (e.g., ~ drug)  
    data.frame(  
      group = rownames(tbl),
```

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    rmean = tbl[, "rmean"],
    median = tbl[, "median"]
  )
} else {
  # Single group (e.g., ~1)
  data.frame(
    group = label,
    rmean = tbl["rmean"],
    median = tbl["median"]
  )
}
}

```

```

# -----
# Data Preprocessing
# -----
attach(aids.id)
attach(aids)
myseed = set.seed(1995)
myid = sample(aids.id$patient, 400)
myaids.id = subset(aids.id, patient %in% myid)
myaids = subset(aids, patient %in% myid)
glimpse(myaids.id)

```

```

## Rows: 400
## Columns: 12
## $ patient <fct> 1, 2, 3, 4, 6, 8, 10, 11, 12, 14, 15, 16, 17, 18, 19, 23, 24, ~
## $ Time <dbl> 16.97, 19.00, 18.53, 12.70, 1.90, 9.57, 16.43, 2.40, 18.10, 2.~
## $ death <int> 0, 0, 1, 0, 1, 1, 0, 1, 0, 1, 0, 1, 0, 0, 1, 1, 0, 1, 0, 0, 0,~
## $ CD4 <dbl> 10.677078, 6.324555, 3.464102, 3.872983, 4.582576, 3.464102, 1~
## $ obstime <int> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,~
## $ drug <fct> ddC, ddI, ddI, ddC, ddC, ddI, ddI, ddC, ddI, ddI, ddI, ddC, dd~
## $ gender <fct> male, male, female, male, female, female, male, male, male, ma~
## $ prevOI <fct> AIDS, noAIDS, AIDS, AIDS, AIDS, noAIDS, AIDS, AIDS, noAIDS, no~
## $ AZT <fct> intolerance, intolerance, intolerance, failure, failure, intol~
## $ start <int> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,~
## $ stop <dbl> 6.00, 6.00, 2.00, 2.00, 1.90, 2.00, 2.00, 2.40, 2.00, 2.00, 2.~
## $ event <dbl> 0, 0, 0, 0, 1, 0, 0, 1, 0, 0, 0, 0, 0, 0, 1, 1, 0, 1, 0, 0, 0,~
glimpse(myaids)

```

```

## Rows: 1,211
## Columns: 12
## $ patient <fct> 1, 1, 1, 2, 2, 2, 2, 3, 3, 3, 4, 4, 4, 4, 6, 8, 8, 8, 10, 10, ~
## $ Time <dbl> 16.97, 16.97, 16.97, 19.00, 19.00, 19.00, 19.00, 18.53, 18.53,~
## $ death <int> 0, 0, 0, 0, 0, 0, 0, 1, 1, 1, 0, 0, 0, 0, 1, 1, 1, 1, 0, 0, 0,~
## $ CD4 <dbl> 10.677078, 8.426150, 9.433981, 6.324555, 8.124038, 4.582576, 5~
## $ obstime <int> 0, 6, 12, 0, 6, 12, 18, 0, 2, 6, 0, 2, 6, 12, 0, 0, 2, 6, 0, 2~
## $ drug <fct> ddC, ddC, ddC, ddI, ddI, ddI, ddI, ddI, ddI, ddI, ddC, ddC, dd~
## $ gender <fct> male, male, male, male, male, male, male, female, female, fema~
## $ prevOI <fct> AIDS, AIDS, AIDS, noAIDS, noAIDS, noAIDS, noAIDS, AIDS, AIDS, ~
## $ AZT <fct> intolerance, intolerance, intolerance, intolerance, intoleranc~
## $ start <int> 0, 6, 12, 0, 6, 12, 18, 0, 2, 6, 0, 2, 6, 12, 0, 0, 2, 6, 0, 2~
## $ stop <dbl> 6.00, 12.00, 16.97, 6.00, 12.00, 18.00, 19.00, 2.00, 6.00, 18.~
## $ event <dbl> 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 0, 1, 0, 0, 1, 0, 0, 0,~

```

```

# -----
# Kaplan-Meier Model
# -----

# No assumption null model
km_fit <- survfit(Surv(Time, death) ~ 1, data = myaids.id, conf.type = "log-log")
summary(km_fit)$table

##      records      n.max      n.start      events      rmean      se(rmean)
## 400.0000000 400.0000000 400.0000000 162.0000000 15.7664366  0.3558219
##      median      0.95LCL      0.95UCL
##      NA 17.2700000      NA

# Model stratified with treatment group
km_fit_drug <- survfit(Surv(Time, death) ~ drug, data = myaids.id, conf.type = "log-log")
summary(km_fit_drug)$table

##      records n.max n.start events      rmean se(rmean) median 0.95LCL 0.95UCL
## drug=ddC    199  199   199    73 16.14124 0.5056964     NA   17.27     NA
## drug=ddI    201  201   201    89 15.38718 0.4991256   18.53   14.13     NA

# -----
# Time independent Cox model
# -----

## Model Selection

### Null Model
cox_ti_null <- coxph(Surv(Time, death) ~ 1, data = myaids.id)
summary(cox_ti_null)

## Call:  coxph(formula = Surv(Time, death) ~ 1, data = myaids.id)
##
## Null model
##   log likelihood= -911.3012
##     n= 400
paste0("AIC of Null Model: ", AIC(cox_ti_null))

## [1] "AIC of Null Model: 1822.60235408444"

### Full model with Univariate
cox_full_ti_uni <- coxph(Surv(Time, death) ~ CD4 + drug + gender + prevOI + AZT, data = myaids.id)
summary(cox_full_ti_uni)

## Call:
## coxph(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##      AZT, data = myaids.id)
##
## n= 400, number of events= 162
##
##      coef exp(coef) se(coef)      z Pr(>|z|)
## CD4      -0.13200   0.87634  0.02538 -5.201 1.98e-07 ***
## drugddI    0.27572   1.31748  0.15886  1.736  0.08264 .
## gendermale -0.45685   0.63328  0.25335 -1.803  0.07136 .
## prevOIAIDS 0.79223   2.20831  0.25483  3.109  0.00188 **
## AZTfailure 0.23853   1.26939  0.17513  1.362  0.17318

```

```
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##           exp(coef) exp(-coef) lower .95 upper .95
## CD4      0.8763     1.1411     0.8338     0.921
## drugddI   1.3175     0.7590     0.9650     1.799
## gendermale 0.6333     1.5791     0.3854     1.041
## prevOIAIDS 2.2083     0.4528     1.3401     3.639
## AZTfailure 1.2694     0.7878     0.9006     1.789
##
## Concordance= 0.716 (se = 0.02 )
## Likelihood ratio test= 93.46 on 5 df,  p=<2e-16
## Wald test              = 71.18 on 5 df,  p=6e-14
## Score (logrank) test = 81.36 on 5 df,  p=4e-16
paste0("AIC of Main Effects (Univariate) Model: ", AIC(cox_full_ti_uni))

## [1] "AIC of Main Effects (Univariate) Model: 1739.14143463543"
### Functional form of CD4 using Martingale model

#### Raw CD4 martingale
mart_full_ti <- resid(cox_full_ti_uni, type = "martingale")

#### Log-transformed CD4
myaids_log <- myaids.id %>%
  mutate(CD4_log = log(CD4 + 1)) # add small constant to avoid log(0)
cox_ti_log <- coxph(Surv(Time, death) ~ CD4_log + drug + gender + prevOI + AZT, data = myaids_log)
summary(cox_ti_log)

## Call:
## coxph(formula = Surv(Time, death) ~ CD4_log + drug + gender +
##       prevOI + AZT, data = myaids_log)
##
##      n= 400, number of events= 162
##
##           coef exp(coef) se(coef)      z Pr(>|z|)
## CD4_log      -0.7859   0.4557  0.1364 -5.763 8.25e-09 ***
## drugddI       0.2788   1.3216  0.1588  1.756 0.079056 .
## gendermale    -0.4548   0.6346  0.2533 -1.796 0.072556 .
## prevOIAIDS    0.8929   2.4423  0.2521  3.542 0.000397 ***
## AZTfailure    0.2013   1.2230  0.1756  1.146 0.251734
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##           exp(coef) exp(-coef) lower .95 upper .95
## CD4_log      0.4557     2.1944     0.3488     0.5953
## drugddI       1.3216     0.7567     0.9682     1.8040
## gendermale    0.6346     1.5759     0.3862     1.0425
## prevOIAIDS    2.4423     0.4094     1.4901     4.0031
## AZTfailure    1.2230     0.8177     0.8668     1.7255
##
## Concordance= 0.716 (se = 0.02 )
## Likelihood ratio test= 92.89 on 5 df,  p=<2e-16
## Wald test              = 82.4 on 5 df,  p=3e-16
```

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## Score (logrank) test = 90.53 on 5 df, p=<2e-16
#### Log CD4 martingale
mart_ti_log <- resid(cox_ti_log, type = "martingale")

aic_ti_linear <- round(AIC(cox_full_ti_uni),2)
aic_ti_log <- round(AIC(cox_ti_log),2)

### Full model with Univariate - Step
cox_full_ti_uni_step <- step(cox_full_ti_uni,
                             scope = list(upper = ~ CD4 + drug + gender + prevOI + AZT), trace = 0)
summary(cox_full_ti_uni_step)

## Call:
## coxph(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI,
##       data = myaids.id)
##
## n= 400, number of events= 162
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## CD4          -0.13354   0.87499  0.02552 -5.232 1.68e-07 ***
## drugddI       0.25589   1.29161  0.15813  1.618  0.106
## gendermale  -0.41173   0.66250  0.25089 -1.641  0.101
## prevOIAIDS   0.91954   2.50813  0.23539  3.906 9.37e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## CD4              0.8750      1.1429   0.8323   0.9199
## drugddI          1.2916      0.7742   0.9474   1.7609
## gendermale       0.6625      1.5094   0.4052   1.0833
## prevOIAIDS       2.5081      0.3987   1.5812   3.9784
##
## Concordance= 0.712 (se = 0.02 )
## Likelihood ratio test= 91.58 on 4 df, p=<2e-16
## Wald test            = 68.73 on 4 df, p=4e-14
## Score (logrank) test = 78.8 on 4 df, p=3e-16

paste0("AIC of Main Effects (Univariate) Model with Stepwise Selection: ", AIC(cox_full_ti_uni_step))

## [1] "AIC of Main Effects (Univariate) Model with Stepwise Selection: 1739.02126418427"
#### Full model with Interactions
cox_full_ti_int <- coxph(Surv(Time, death) ~ (CD4 + drug + gender + prevOI + AZT)^5, data = myaids.id)
summary(cox_full_ti_int)

## Call:
## coxph(formula = Surv(Time, death) ~ (CD4 + drug + gender + prevOI +
##       AZT)^5, data = myaids.id)
##
## n= 400, number of events= 162
##
##              coef      exp(coef)
## CD4          2.086e+01  1.143e+09
## drugddI      3.594e+02  1.245e+156
## gendermale   3.579e+02  2.807e+155

```

## prevOIAIDS	3.604e+02	3.296e+156		
## AZTfailure	-1.653e+01	6.612e-08		
## CD4:drugddI	-2.094e+01	8.068e-10		
## CD4:gendermale	-2.099e+01	7.667e-10		
## CD4:prevOIAIDS	-2.110e+01	6.879e-10		
## CD4:AZTfailure	6.822e-01	1.978e+00		
## drugddI:gendermale	-3.584e+02	2.205e-156		
## drugddI:prevOIAIDS	-3.583e+02	2.538e-156		
## drugddI:AZTfailure	-1.443e+00	2.363e-01		
## gendermale:prevOIAIDS	-3.589e+02	1.291e-156		
## gendermale:AZTfailure	2.883e+00	1.788e+01		
## prevOIAIDS:AZTfailure	1.423e+01	1.515e+06		
## CD4:drugddI:gendermale	2.097e+01	1.277e+09		
## CD4:drugddI:prevOIAIDS	2.038e+01	7.126e+08		
## CD4:drugddI:AZTfailure	1.177e+00	3.245e+00		
## CD4:gendermale:prevOIAIDS	2.112e+01	1.494e+09		
## CD4:gendermale:AZTfailure	-7.747e-01	4.608e-01		
## CD4:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## drugddI:gendermale:prevOIAIDS	3.576e+02	1.951e+155		
## drugddI:gendermale:AZTfailure	1.263e+00	3.535e+00		
## drugddI:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## gendermale:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## CD4:drugddI:gendermale:prevOIAIDS	-2.045e+01	1.313e-09		
## CD4:drugddI:gendermale:AZTfailure	-1.142e+00	3.193e-01		
## CD4:drugddI:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## CD4:gendermale:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## drugddI:gendermale:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure	0.000e+00	1.000e+00		
##	se(coef)	z	Pr(> z)	
## CD4	2.297e-02	908.113	< 2e-16	***
## drugddI	1.581e-01	2272.696	< 2e-16	***
## gendermale	2.566e-01	1394.932	< 2e-16	***
## prevOIAIDS	2.220e-01	1623.074	< 2e-16	***
## AZTfailure	1.578e-01	-104.749	< 2e-16	***
## CD4:drugddI	2.153e-02	-972.676	< 2e-16	***
## CD4:gendermale	2.300e-02	-912.616	< 2e-16	***
## CD4:prevOIAIDS	2.711e-02	-778.345	< 2e-16	***
## CD4:AZTfailure	2.844e-02	23.991	< 2e-16	***
## drugddI:gendermale	1.576e-01	-2274.047	< 2e-16	***
## drugddI:prevOIAIDS	1.588e-01	-2255.657	< 2e-16	***
## drugddI:AZTfailure	1.818e-01	-7.938	2.06e-15	***
## gendermale:prevOIAIDS	1.868e-01	-1921.104	< 2e-16	***
## gendermale:AZTfailure	1.579e-01	18.265	< 2e-16	***
## prevOIAIDS:AZTfailure	1.578e-01	90.171	< 2e-16	***
## CD4:drugddI:gendermale	2.222e-02	943.536	< 2e-16	***
## CD4:drugddI:prevOIAIDS	2.908e-02	700.859	< 2e-16	***
## CD4:drugddI:AZTfailure	3.588e-02	32.813	< 2e-16	***
## CD4:gendermale:prevOIAIDS	2.645e-02	798.737	< 2e-16	***
## CD4:gendermale:AZTfailure	2.910e-02	-26.617	< 2e-16	***
## CD4:prevOIAIDS:AZTfailure	2.844e-02	0.000	1	
## drugddI:gendermale:prevOIAIDS	1.606e-01	2226.981	< 2e-16	***
## drugddI:gendermale:AZTfailure	1.856e-01	6.802	1.03e-11	***
## drugddI:prevOIAIDS:AZTfailure	1.818e-01	0.000	1	
## gendermale:prevOIAIDS:AZTfailure	1.579e-01	0.000	1	

```

## CD4:drugddI:gendermale:prevOIAIDS          2.924e-02  -699.517  < 2e-16 ***
## CD4:drugddI:gendermale:AZTfailure           3.641e-02   -31.356  < 2e-16 ***
## CD4:drugddI:prevOIAIDS:AZTfailure           3.588e-02    0.000      1
## CD4:gendermale:prevOIAIDS:AZTfailure         2.910e-02    0.000      1
## drugddI:gendermale:prevOIAIDS:AZTfailure     1.856e-01    0.000      1
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure 3.641e-02    0.000      1
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##
##              exp(coef) exp(-coef) lower .95
## CD4          1.143e+09  8.748e-10  1.093e+09
## drugddI      1.245e+156 8.030e-157 9.134e+155
## gendermale   2.807e+155 3.563e-156 1.698e+155
## prevOIAIDS   3.296e+156 3.034e-157 2.133e+156
## AZTfailure    6.612e-08  1.512e+07  4.853e-08
## CD4:drugddI   8.068e-10  1.240e+09  7.734e-10
## CD4:gendermale 7.667e-10  1.304e+09  7.329e-10
## CD4:prevOIAIDS 6.879e-10  1.454e+09  6.523e-10
## CD4:AZTfailure 1.978e+00  5.055e-01  1.871e+00
## drugddI:gendermale 2.205e-156 4.534e+155 1.619e-156
## drugddI:prevOIAIDS 2.538e-156 3.941e+155 1.859e-156
## drugddI:AZTfailure 2.363e-01  4.233e+00  1.654e-01
## gendermale:prevOIAIDS 1.291e-156 7.743e+155 8.955e-157
## gendermale:AZTfailure 1.788e+01  5.594e-02  1.312e+01
## prevOIAIDS:AZTfailure 1.515e+06  6.600e-07  1.112e+06
## CD4:drugddI:gendermale 1.277e+09  7.830e-10  1.223e+09
## CD4:drugddI:prevOIAIDS 7.126e+08  1.403e-09  6.731e+08
## CD4:drugddI:AZTfailure 3.245e+00  3.081e-01  3.025e+00
## CD4:gendermale:prevOIAIDS 1.494e+09  6.695e-10  1.418e+09
## CD4:gendermale:AZTfailure 4.608e-01  2.170e+00  4.353e-01
## CD4:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  9.458e-01
## drugddI:gendermale:prevOIAIDS 1.951e+155 5.125e-156 1.424e+155
## drugddI:gendermale:AZTfailure 3.535e+00  2.829e-01  2.457e+00
## drugddI:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  7.003e-01
## gendermale:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  7.339e-01
## CD4:drugddI:gendermale:prevOIAIDS 1.313e-09  7.614e+08  1.240e-09
## CD4:drugddI:gendermale:AZTfailure 3.193e-01  3.132e+00  2.973e-01
## CD4:drugddI:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  9.321e-01
## CD4:gendermale:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  9.446e-01
## drugddI:gendermale:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  6.950e-01
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure 1.000e+00  1.000e+00  9.311e-01
##
##              upper .95
## CD4          1.196e+09
## drugddI      1.698e+156
## gendermale   4.642e+155
## prevOIAIDS   5.094e+156
## AZTfailure    9.009e-08
## CD4:drugddI   8.415e-10
## CD4:gendermale 8.021e-10
## CD4:prevOIAIDS 7.255e-10
## CD4:AZTfailure 2.092e+00
## drugddI:gendermale 3.004e-156
## drugddI:prevOIAIDS 3.464e-156
## drugddI:AZTfailure 3.374e-01

```

```

## gendermale:prevOIAIDS 1.863e-156
## gendermale:AZTfailure 2.436e+01
## prevOIAIDS:AZTfailure 2.064e+06
## CD4:drugddI:gendermale 1.334e+09
## CD4:drugddI:prevOIAIDS 7.544e+08
## CD4:drugddI:AZTfailure 3.482e+00
## CD4:gendermale:prevOIAIDS 1.573e+09
## CD4:gendermale:AZTfailure 4.879e-01
## CD4:prevOIAIDS:AZTfailure 1.057e+00
## drugddI:gendermale:prevOIAIDS 2.673e+155
## drugddI:gendermale:AZTfailure 5.086e+00
## drugddI:prevOIAIDS:AZTfailure 1.428e+00
## gendermale:prevOIAIDS:AZTfailure 1.363e+00
## CD4:drugddI:gendermale:prevOIAIDS 1.391e-09
## CD4:drugddI:gendermale:AZTfailure 3.429e-01
## CD4:drugddI:prevOIAIDS:AZTfailure 1.073e+00
## CD4:gendermale:prevOIAIDS:AZTfailure 1.059e+00
## drugddI:gendermale:prevOIAIDS:AZTfailure 1.439e+00
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure 1.074e+00
##
## Concordance= 0.736 (se = 0.019 )
## Likelihood ratio test= 132.4 on 31 df, p=2e-14
## Wald test = 34395827 on 31 df, p=<2e-16
## Score (logrank) test = 309.4 on 31 df, p=<2e-16
paste0("AIC of Interactions Model: ", AIC(cox_full_ti_int))

## [1] "AIC of Interactions Model: 1752.21545241238"

### Full model with Interactions - Step
cox_full_ti_int_step <- step(cox_full_ti_int,
                             scope = list(upper = ~ (CD4 + drug + gender + prevOI + AZT)^5), trace = 0)
summary(cox_full_ti_int_step)

## Call:
## coxph(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
## AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
## drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
## CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
## drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id)
##
## n= 400, number of events= 162
##
##               coef exp(coef) se(coef)      z
## CD4           5.679e-01  1.765e+00  3.500e-01  1.622
## drugddI       1.061e+01  4.052e+04  5.695e+00  1.863
## gendermale    8.893e+00  7.282e+03  5.941e+00  1.497
## prevOIAIDS    1.155e+01  1.037e+05  5.547e+00  2.082
## AZTfailure    -2.178e+00  1.133e-01  1.531e+00 -1.422
## CD4:drugddI   -6.384e-01  5.281e-01  3.341e-01 -1.911
## CD4:gendermale -6.641e-01  5.147e-01  3.585e-01 -1.852
## CD4:prevOIAIDS -7.793e-01  4.587e-01  3.044e-01 -2.560
## CD4:AZTfailure  6.538e-01  1.923e+00  2.874e-01  2.275
## drugddI:gendermale -9.225e+00  9.853e-05  5.751e+00 -1.604
## drugddI:prevOIAIDS -9.217e+00  9.931e-05  4.902e+00 -1.880

```



```

## drugddI:AZTfailure -1.686e+00 1.853e-01 2.189e+00 -0.770
## gendermale:prevOIAIDS -9.700e+00 6.130e-05 5.590e+00 -1.735
## gendermale:AZTfailure 2.663e+00 1.433e+01 1.605e+00 1.659
## CD4:drugddI:gendermale 6.263e-01 1.871e+00 3.432e-01 1.825
## CD4:drugddI:AZTfailure 1.262e+00 3.534e+00 5.222e-01 2.417
## CD4:gendermale:prevOIAIDS 7.562e-01 2.130e+00 3.133e-01 2.414
## CD4:gendermale:AZTfailure -7.297e-01 4.821e-01 3.013e-01 -2.422
## drugddI:gendermale:prevOIAIDS 8.012e+00 3.016e+03 4.943e+00 1.621
## drugddI:gendermale:AZTfailure 1.648e+00 5.199e+00 2.279e+00 0.723
## CD4:drugddI:gendermale:AZTfailure -1.253e+00 2.856e-01 5.354e-01 -2.341
## Pr(>|z|)
## CD4 0.1047
## drugddI 0.0625 .
## gendermale 0.1344
## prevOIAIDS 0.0373 *
## AZTfailure 0.1549
## CD4:drugddI 0.0560 .
## CD4:gendermale 0.0640 .
## CD4:prevOIAIDS 0.0105 *
## CD4:AZTfailure 0.0229 *
## drugddI:gendermale 0.1087
## drugddI:prevOIAIDS 0.0601 .
## drugddI:AZTfailure 0.4413
## gendermale:prevOIAIDS 0.0827 .
## gendermale:AZTfailure 0.0972 .
## CD4:drugddI:gendermale 0.0680 .
## CD4:drugddI:AZTfailure 0.0156 *
## CD4:gendermale:prevOIAIDS 0.0158 *
## CD4:gendermale:AZTfailure 0.0155 *
## drugddI:gendermale:prevOIAIDS 0.1051
## drugddI:gendermale:AZTfailure 0.4696
## CD4:drugddI:gendermale:AZTfailure 0.0193 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## exp(coef) exp(-coef) lower .95 upper .95
## CD4 1.765e+00 5.667e-01 8.886e-01 3.504e+00
## drugddI 4.052e+04 2.468e-05 5.759e-01 2.851e+09
## gendermale 7.282e+03 1.373e-04 6.392e-02 8.295e+08
## prevOIAIDS 1.037e+05 9.640e-06 1.969e+00 5.466e+09
## AZTfailure 1.133e-01 8.829e+00 5.632e-03 2.278e+00
## CD4:drugddI 5.281e-01 1.894e+00 2.744e-01 1.017e+00
## CD4:gendermale 5.147e-01 1.943e+00 2.549e-01 1.039e+00
## CD4:prevOIAIDS 4.587e-01 2.180e+00 2.526e-01 8.331e-01
## CD4:AZTfailure 1.923e+00 5.200e-01 1.095e+00 3.377e+00
## drugddI:gendermale 9.853e-05 1.015e+04 1.255e-09 7.735e+00
## drugddI:prevOIAIDS 9.931e-05 1.007e+04 6.672e-09 1.478e+00
## drugddI:AZTfailure 1.853e-01 5.396e+00 2.537e-03 1.354e+01
## gendermale:prevOIAIDS 6.130e-05 1.631e+04 1.070e-09 3.513e+00
## gendermale:AZTfailure 1.433e+01 6.976e-02 6.165e-01 3.333e+02
## CD4:drugddI:gendermale 1.871e+00 5.346e-01 9.547e-01 3.665e+00
## CD4:drugddI:AZTfailure 3.534e+00 2.829e-01 1.270e+00 9.836e+00
## CD4:gendermale:prevOIAIDS 2.130e+00 4.695e-01 1.153e+00 3.936e+00
## CD4:gendermale:AZTfailure 4.821e-01 2.074e+00 2.671e-01 8.701e-01

```

```
## drugddI:gendermale:prevOIAIDS      3.016e+03  3.316e-04  1.870e-01  4.863e+07
## drugddI:gendermale:AZTfailure      5.199e+00  1.923e-01  5.965e-02  4.531e+02
## CD4:drugddI:gendermale:AZTfailure  2.856e-01  3.502e+00  1.000e-01  8.156e-01
##
## Concordance= 0.737 (se = 0.019 )
## Likelihood ratio test= 129.7 on 21 df,  p=<2e-16
## Wald test              = 114.8 on 21 df,  p=6e-15
## Score (logrank) test = 301.6 on 21 df,  p=<2e-16
paste0("AIC of Interactions Model with Stepwise Selection: ", AIC(cox_full_ti_int_step))
```

```
## [1] "AIC of Interactions Model with Stepwise Selection: 1734.89585749095"
```

```
### Final Time Independent Cox Model
```

```
cox_ti_final <- coxph(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
  AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
  drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
  CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
  drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id)
summary(cox_ti_final)
```

```
## Call:
```

```
## coxph(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##     AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
##     drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
##     CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
##     drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id)
##
```

```
## n= 400, number of events= 162
```

```
##
##               coef exp(coef) se(coef)      z
## CD4           5.679e-01  1.765e+00  3.500e-01  1.622
## drugddI       1.061e+01  4.052e+04  5.695e+00  1.863
## gendermale     8.893e+00  7.282e+03  5.941e+00  1.497
## prevOIAIDS     1.155e+01  1.037e+05  5.547e+00  2.082
## AZTfailure     -2.178e+00  1.133e-01  1.531e+00 -1.422
## CD4:drugddI    -6.384e-01  5.281e-01  3.341e-01 -1.911
## CD4:gendermale -6.641e-01  5.147e-01  3.585e-01 -1.852
## CD4:prevOIAIDS -7.793e-01  4.587e-01  3.044e-01 -2.560
## CD4:AZTfailure  6.538e-01  1.923e+00  2.874e-01  2.275
## drugddI:gendermale -9.225e+00  9.853e-05  5.751e+00 -1.604
## drugddI:prevOIAIDS -9.217e+00  9.931e-05  4.902e+00 -1.880
## drugddI:AZTfailure -1.686e+00  1.853e-01  2.189e+00 -0.770
## gendermale:prevOIAIDS -9.700e+00  6.130e-05  5.590e+00 -1.735
## gendermale:AZTfailure  2.663e+00  1.433e+01  1.605e+00  1.659
## CD4:drugddI:gendermale  6.263e-01  1.871e+00  3.432e-01  1.825
## CD4:drugddI:AZTfailure  1.262e+00  3.534e+00  5.222e-01  2.417
## CD4:gendermale:prevOIAIDS  7.562e-01  2.130e+00  3.133e-01  2.414
## CD4:gendermale:AZTfailure -7.297e-01  4.821e-01  3.013e-01 -2.422
## drugddI:gendermale:prevOIAIDS  8.012e+00  3.016e+03  4.943e+00  1.621
## drugddI:gendermale:AZTfailure  1.648e+00  5.199e+00  2.279e+00  0.723
## CD4:drugddI:gendermale:AZTfailure -1.253e+00  2.856e-01  5.354e-01 -2.341
##
## Pr(>|z|)
## CD4           0.1047
## drugddI       0.0625 .
```

```

## gendermale 0.1344
## prevOIAIDS 0.0373 *
## AZTfailure 0.1549
## CD4:drugddI 0.0560 .
## CD4:gendermale 0.0640 .
## CD4:prevOIAIDS 0.0105 *
## CD4:AZTfailure 0.0229 *
## drugddI:gendermale 0.1087
## drugddI:prevOIAIDS 0.0601 .
## drugddI:AZTfailure 0.4413
## gendermale:prevOIAIDS 0.0827 .
## gendermale:AZTfailure 0.0972 .
## CD4:drugddI:gendermale 0.0680 .
## CD4:drugddI:AZTfailure 0.0156 *
## CD4:gendermale:prevOIAIDS 0.0158 *
## CD4:gendermale:AZTfailure 0.0155 *
## drugddI:gendermale:prevOIAIDS 0.1051
## drugddI:gendermale:AZTfailure 0.4696
## CD4:drugddI:gendermale:AZTfailure 0.0193 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##
## exp(coef) exp(-coef) lower .95 upper .95
## CD4 1.765e+00 5.667e-01 8.886e-01 3.504e+00
## drugddI 4.052e+04 2.468e-05 5.759e-01 2.851e+09
## gendermale 7.282e+03 1.373e-04 6.392e-02 8.295e+08
## prevOIAIDS 1.037e+05 9.640e-06 1.969e+00 5.466e+09
## AZTfailure 1.133e-01 8.829e+00 5.632e-03 2.278e+00
## CD4:drugddI 5.281e-01 1.894e+00 2.744e-01 1.017e+00
## CD4:gendermale 5.147e-01 1.943e+00 2.549e-01 1.039e+00
## CD4:prevOIAIDS 4.587e-01 2.180e+00 2.526e-01 8.331e-01
## CD4:AZTfailure 1.923e+00 5.200e-01 1.095e+00 3.377e+00
## drugddI:gendermale 9.853e-05 1.015e+04 1.255e-09 7.735e+00
## drugddI:prevOIAIDS 9.931e-05 1.007e+04 6.672e-09 1.478e+00
## drugddI:AZTfailure 1.853e-01 5.396e+00 2.537e-03 1.354e+01
## gendermale:prevOIAIDS 6.130e-05 1.631e+04 1.070e-09 3.513e+00
## gendermale:AZTfailure 1.433e+01 6.976e-02 6.165e-01 3.333e+02
## CD4:drugddI:gendermale 1.871e+00 5.346e-01 9.547e-01 3.665e+00
## CD4:drugddI:AZTfailure 3.534e+00 2.829e-01 1.270e+00 9.836e+00
## CD4:gendermale:prevOIAIDS 2.130e+00 4.695e-01 1.153e+00 3.936e+00
## CD4:gendermale:AZTfailure 4.821e-01 2.074e+00 2.671e-01 8.701e-01
## drugddI:gendermale:prevOIAIDS 3.016e+03 3.316e-04 1.870e-01 4.863e+07
## drugddI:gendermale:AZTfailure 5.199e+00 1.923e-01 5.965e-02 4.531e+02
## CD4:drugddI:gendermale:AZTfailure 2.856e-01 3.502e+00 1.000e-01 8.156e-01
##
## Concordance= 0.737 (se = 0.019 )
## Likelihood ratio test= 129.7 on 21 df, p=<2e-16
## Wald test = 114.8 on 21 df, p=6e-15
## Score (logrank) test = 301.6 on 21 df, p=<2e-16
paste0("AIC Final Selected Model: ", AIC(cox_ti_final))

## [1] "AIC Final Selected Model: 1734.89585749095"

```

```

# -----
# Time dependent Cox model
# -----
# Create survival object with start-stop format
surv_td <- Surv(time = myaids$start, time2 = myaids$stop, event = myaids$event)

### Null Model
cox_td_null <- coxph(surv_td ~ 1, data = myaids)
summary(cox_td_null)

## Call: coxph(formula = surv_td ~ 1, data = myaids)
##
## Null model
##   log likelihood= -911.3012
##   n= 1211
paste0("AIC of Null Model: ", AIC(cox_td_null))

## [1] "AIC of Null Model: 1822.60235408444"

### Full model with Univariate
cox_full_td_uni <- coxph(surv_td ~ CD4 + drug + gender + prevOI + AZT, data = myaids)
summary(cox_full_td_uni)

## Call:
## coxph(formula = surv_td ~ CD4 + drug + gender + prevOI + AZT,
##       data = myaids)
##
##   n= 1211, number of events= 162
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## CD4           -0.15180   0.85916  0.02774 -5.473 4.43e-08 ***
## drugddI        0.32778   1.38788  0.15918  2.059  0.0395 *
## gendermale    -0.55332   0.57503  0.25305 -2.187  0.0288 *
## prevOIAIDS    0.79932   2.22403  0.25182  3.174  0.0015 **
## AZTfailure    0.20847   1.23179  0.17550  1.188  0.2349
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## CD4               0.8592     1.1639     0.8137     0.9072
## drugddI            1.3879     0.7205     1.0159     1.8960
## gendermale         0.5750     1.7390     0.3502     0.9443
## prevOIAIDS         2.2240     0.4496     1.3577     3.6433
## AZTfailure         1.2318     0.8118     0.8733     1.7375
##
## Concordance= 0.719 (se = 0.019 )
## Likelihood ratio test= 99.09 on 5 df,  p=<2e-16
## Wald test               = 69.93 on 5 df,  p=1e-13
## Score (logrank) test = 80.75 on 5 df,  p=6e-16
paste0("AIC of Main Effects (Univariate) Model: ", AIC(cox_full_td_uni))

## [1] "AIC of Main Effects (Univariate) Model: 1733.51489997613"

```

```

### Functional form of CD4 using Martingale model

#### Raw CD4 martingale
mart_td <- resid(cox_full_td_uni, type = "martingale")

#### Log CD4 martingale
myaids_log <- myaids %>% mutate(CD4_log = log(CD4 + 1))
cox_td_log <- coxph(surv_td ~ CD4_log + drug + gender + prevOI + AZT, data = myaids_log)
mart_td_log <- resid(cox_td_log, type = "martingale")

#### AIC Comparison
aic_td_linear <- round(AIC(cox_full_td_uni), 2)
aic_td_log <- round(AIC(cox_td_log), 2)

### Full model with Univariate - Step
cox_full_td_uni_step <- step(cox_full_td_uni,
                             scope = list(upper = ~ CD4 + drug + gender + prevOI + AZT), trace = 0)
summary(cox_full_td_uni_step)

## Call:
## coxph(formula = surv_td ~ CD4 + drug + gender + prevOI, data = myaids)
##
## n= 1211, number of events= 162
##
##              coef exp(coef) se(coef)      z Pr(>|z|)
## CD4          -0.15330   0.85787  0.02775 -5.524 3.32e-08 ***
## drugddI       0.31154   1.36552  0.15851  1.965  0.0494 *
## gendermale   -0.51525   0.59735  0.25080 -2.054  0.0399 *
## prevOIAIDS   0.91278   2.49124  0.23122  3.948 7.89e-05 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##              exp(coef) exp(-coef) lower .95 upper .95
## CD4              0.8579      1.1657   0.8125   0.9058
## drugddI          1.3655      0.7323   1.0009   1.8630
## gendermale       0.5973      1.6741   0.3654   0.9766
## prevOIAIDS       2.4912      0.4014   1.5834   3.9195
##
## Concordance= 0.715 (se = 0.019 )
## Likelihood ratio test= 97.66 on 4 df,  p=<2e-16
## Wald test              = 68.15 on 4 df,  p=6e-14
## Score (logrank) test = 78.73 on 4 df,  p=3e-16

paste0("AIC of Main Effects (Univariate) Model with Stepwise Selection: ", AIC(cox_full_td_uni_step))

## [1] "AIC of Main Effects (Univariate) Model with Stepwise Selection: 1732.94301975638"

#### Full model with Interactions
cox_full_td_int <- coxph(surv_td ~ (CD4 + drug + gender + prevOI + AZT)^5, data = myaids)
summary(cox_full_td_int)

## Call:
## coxph(formula = surv_td ~ (CD4 + drug + gender + prevOI + AZT)^5,
##       data = myaids)

```

```

##
##   n= 1211, number of events= 162
##
##
##               coef   exp(coef)   se(coef)
## CD4           -2.382e-01  7.881e-01  3.685e-01
## drugddI        2.702e-01  1.310e+00  2.720e+00
## gendermale     -2.134e+00  1.184e-01  2.671e+00
## prevOIAIDS      1.393e+00  4.027e+00  2.814e+00
## AZTfailure     -1.569e+01  1.541e-07  4.374e+03
## CD4:drugddI     1.467e-01  1.158e+00  3.834e-01
## CD4:gendermale  2.142e-01  1.239e+00  3.783e-01
## CD4:prevOIAIDS -1.416e-01  8.680e-01  5.212e-01
## CD4:AZTfailure  9.002e-01  2.460e+00  1.279e+03
## drugddI:gendermale 1.567e+00  4.795e+00  2.885e+00
## drugddI:prevOIAIDS -4.069e-02  9.601e-01  3.146e+00
## drugddI:AZTfailure -8.523e-01  4.265e-01  2.593e+00
## gendermale:prevOIAIDS 1.177e+00  3.245e+00  2.959e+00
## gendermale:AZTfailure 2.684e+00  1.464e+01  1.678e+00
## prevOIAIDS:AZTfailure 1.336e+01  6.369e+05  4.374e+03
## CD4:drugddI:gendermale -2.317e-01  7.932e-01  3.968e-01
## CD4:drugddI:prevOIAIDS -2.289e-01  7.954e-01  5.971e-01
## CD4:drugddI:AZTfailure 6.274e-01  1.873e+00  6.599e-01
## CD4:gendermale:prevOIAIDS -2.964e-02  9.708e-01  5.355e-01
## CD4:gendermale:AZTfailure -8.602e-01  4.231e-01  4.389e-01
## CD4:prevOIAIDS:AZTfailure -1.196e-01  8.873e-01  1.279e+03
## drugddI:gendermale:prevOIAIDS -1.763e+00  1.715e-01  3.330e+00
## drugddI:gendermale:AZTfailure 6.974e-01  2.008e+00  2.675e+00
## drugddI:prevOIAIDS:AZTfailure NA NA 0.000e+00
## gendermale:prevOIAIDS:AZTfailure NA NA 0.000e+00
## CD4:drugddI:gendermale:prevOIAIDS 3.534e-01  1.424e+00  6.168e-01
## CD4:drugddI:gendermale:AZTfailure -5.683e-01  5.665e-01  6.784e-01
## CD4:drugddI:prevOIAIDS:AZTfailure NA NA 0.000e+00
## CD4:gendermale:prevOIAIDS:AZTfailure NA NA 0.000e+00
## drugddI:gendermale:prevOIAIDS:AZTfailure NA NA 0.000e+00
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure NA NA 0.000e+00
##
##               z Pr(>|z|)
## CD4           -0.646   0.518
## drugddI        0.099   0.921
## gendermale     -0.799   0.424
## prevOIAIDS      0.495   0.621
## AZTfailure     -0.004   0.997
## CD4:drugddI     0.383   0.702
## CD4:gendermale  0.566   0.571
## CD4:prevOIAIDS -0.272   0.786
## CD4:AZTfailure  0.001   0.999
## drugddI:gendermale 0.543   0.587
## drugddI:prevOIAIDS -0.013   0.990
## drugddI:AZTfailure -0.329   0.742
## gendermale:prevOIAIDS 0.398   0.691
## gendermale:AZTfailure 1.599   0.110
## prevOIAIDS:AZTfailure 0.003   0.998
## CD4:drugddI:gendermale -0.584   0.559
## CD4:drugddI:prevOIAIDS -0.383   0.701
## CD4:drugddI:AZTfailure 0.951   0.342

```

```

## CD4:gendermale:prevOIAIDS -0.055 0.956
## CD4:gendermale:AZTfailure -1.960 0.050 .
## CD4:prevOIAIDS:AZTfailure 0.000 1.000
## drugddI:gendermale:prevOIAIDS -0.530 0.596
## drugddI:gendermale:AZTfailure 0.261 0.794
## drugddI:prevOIAIDS:AZTfailure NA NA
## gendermale:prevOIAIDS:AZTfailure NA NA
## CD4:drugddI:gendermale:prevOIAIDS 0.573 0.567
## CD4:drugddI:gendermale:AZTfailure -0.838 0.402
## CD4:drugddI:prevOIAIDS:AZTfailure NA NA
## CD4:gendermale:prevOIAIDS:AZTfailure NA NA
## drugddI:gendermale:prevOIAIDS:AZTfailure NA NA
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure NA NA
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##
## exp(coef) exp(-coef) lower .95
## CD4 7.881e-01 1.269e+00 0.3827731
## drugddI 1.310e+00 7.632e-01 0.0063436
## gendermale 1.184e-01 8.448e+00 0.0006304
## prevOIAIDS 4.027e+00 2.483e-01 0.0162090
## AZTfailure 1.541e-07 6.491e+06 0.0000000
## CD4:drugddI 1.158e+00 8.635e-01 0.5461706
## CD4:gendermale 1.239e+00 8.072e-01 0.5901607
## CD4:prevOIAIDS 8.680e-01 1.152e+00 0.3125264
## CD4:AZTfailure 2.460e+00 4.065e-01 0.0000000
## drugddI:gendermale 4.795e+00 2.086e-01 0.0167997
## drugddI:prevOIAIDS 9.601e-01 1.042e+00 0.0020145
## drugddI:AZTfailure 4.265e-01 2.345e+00 0.0026456
## gendermale:prevOIAIDS 3.245e+00 3.082e-01 0.0098276
## gendermale:AZTfailure 1.464e+01 6.832e-02 0.5455070
## prevOIAIDS:AZTfailure 6.369e+05 1.570e-06 0.0000000
## CD4:drugddI:gendermale 7.932e-01 1.261e+00 0.3644734
## CD4:drugddI:prevOIAIDS 7.954e-01 1.257e+00 0.2468233
## CD4:drugddI:AZTfailure 1.873e+00 5.340e-01 0.5137888
## CD4:gendermale:prevOIAIDS 9.708e-01 1.030e+00 0.3398486
## CD4:gendermale:AZTfailure 4.231e-01 2.364e+00 0.1789775
## CD4:prevOIAIDS:AZTfailure 8.873e-01 1.127e+00 0.0000000
## drugddI:gendermale:prevOIAIDS 1.715e-01 5.832e+00 0.0002511
## drugddI:gendermale:AZTfailure 2.008e+00 4.979e-01 0.0106045
## drugddI:prevOIAIDS:AZTfailure NA NA NA
## gendermale:prevOIAIDS:AZTfailure NA NA NA
## CD4:drugddI:gendermale:prevOIAIDS 1.424e+00 7.023e-01 0.4250626
## CD4:drugddI:gendermale:AZTfailure 5.665e-01 1.765e+00 0.1498708
## CD4:drugddI:prevOIAIDS:AZTfailure NA NA NA
## CD4:gendermale:prevOIAIDS:AZTfailure NA NA NA
## drugddI:gendermale:prevOIAIDS:AZTfailure NA NA NA
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure NA NA NA
##
## upper .95
## CD4 1.623
## drugddI 270.639
## gendermale 22.230
## prevOIAIDS 1000.360
## AZTfailure Inf

```

```
## CD4:drugddI 2.455
## CD4:gendermale 2.601
## CD4:prevOIAIDS 2.411
## CD4:AZTfailure Inf
## drugddI:gendermale 1368.357
## drugddI:prevOIAIDS 457.607
## drugddI:AZTfailure 68.740
## gendermale:prevOIAIDS 1071.315
## gendermale:AZTfailure 392.763
## prevOIAIDS:AZTfailure Inf
## CD4:drugddI:gendermale 1.726
## CD4:drugddI:prevOIAIDS 2.563
## CD4:drugddI:AZTfailure 6.826
## CD4:gendermale:prevOIAIDS 2.773
## CD4:gendermale:AZTfailure 1.000
## CD4:prevOIAIDS:AZTfailure Inf
## drugddI:gendermale:prevOIAIDS 117.073
## drugddI:gendermale:AZTfailure 380.395
## drugddI:prevOIAIDS:AZTfailure NA
## gendermale:prevOIAIDS:AZTfailure NA
## CD4:drugddI:gendermale:prevOIAIDS 4.770
## CD4:drugddI:gendermale:AZTfailure 2.141
## CD4:drugddI:prevOIAIDS:AZTfailure NA
## CD4:gendermale:prevOIAIDS:AZTfailure NA
## drugddI:gendermale:prevOIAIDS:AZTfailure NA
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure NA
```

```
##
## Concordance= 0.74 (se = 0.018 )
## Likelihood ratio test= 126.9 on 25 df, p=1e-15
## Wald test = 106.1 on 25 df, p=6e-12
## Score (logrank) test = 178.4 on 25 df, p=<2e-16
```

```
paste0("AIC of Interactions Model: ", AIC(cox_full_td_int))
```

```
## [1] "AIC of Interactions Model: 1745.68990671712"
```

```
### Stepwise on Interaction Model
```

```
cox_full_td_int_step <- step(cox_full_td_int,
                             scope = list(upper = ~ (CD4 + drug + gender + prevOI + AZT)^5), trace = 0)
summary(cox_full_td_int_step)
```

```
## Call:
```

```
## coxph(formula = surv_td ~ CD4 + drug + gender + prevOI + AZT +
##       CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:AZT +
##       CD4:gender:AZT, data = myaids)
```

```
##
```

```
## n= 1211, number of events= 162
```

```
##
```

	coef	exp(coef)	se(coef)	z	Pr(> z)
## CD4	-0.12217	0.88500	0.09604	-1.272	0.203326
## drugddI	1.24317	3.46658	0.47353	2.625	0.008656 **
## gendermale	-0.53340	0.58661	0.56688	-0.941	0.346732
## prevOIAIDS	2.04388	7.72050	0.56162	3.639	0.000273 ***
## AZTfailure	-1.56505	0.20908	0.99618	-1.571	0.116171
## CD4:gendermale	0.03784	1.03856	0.09722	0.389	0.697135


```

## CD4:prevOIAIDS          -0.10887    0.89685    0.07121 -1.529 0.126307
## CD4:AZTfailure          0.63024    1.87807    0.19887    3.169 0.001529 **
## drugddI:prevOIAIDS      -1.01782    0.36138    0.50448 -2.018 0.043635 *
## gendermale:AZTfailure    1.80718    6.09322    1.01972    1.772 0.076356 .
## CD4:gendermale:AZTfailure -0.65813    0.51782    0.20219 -3.255 0.001134 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## CD4              0.8850      1.1299    0.73315    1.0683
## drugddI          3.4666      0.2885    1.37036    8.7694
## gendermale        0.5866      1.7047    0.19312    1.7819
## prevOIAIDS        7.7205      0.1295    2.56799   23.2112
## AZTfailure         0.2091      4.7829    0.02967    1.4732
## CD4:gendermale     1.0386      0.9629    0.85838    1.2566
## CD4:prevOIAIDS     0.8968      1.1150    0.78001    1.0312
## CD4:AZTfailure     1.8781      0.5325    1.27184    2.7733
## drugddI:prevOIAIDS 0.3614      2.7672    0.13445    0.9714
## gendermale:AZTfailure 6.0932      0.1641    0.82577   44.9606
## CD4:gendermale:AZTfailure 0.5178      1.9312    0.34839    0.7696
##
## Concordance= 0.733 (se = 0.019 )
## Likelihood ratio test= 119.3 on 11 df,  p=<2e-16
## Wald test              = 95.24 on 11 df,  p=2e-15
## Score (logrank) test = 132.9 on 11 df,  p=<2e-16

paste0("AIC of Interactions Model with Stepwise Selection: ", AIC(cox_full_td_int_step))

## [1] "AIC of Interactions Model with Stepwise Selection: 1725.31023538143"

### Final Time dependent Cox Model
cox_td_final <- coxph(surv_td ~ CD4 + drug + gender + prevOI + AZT +
  CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:AZT +
  CD4:gender:AZT, data = myaids)
summary(cox_td_final)

## Call:
## coxph(formula = surv_td ~ CD4 + drug + gender + prevOI + AZT +
##       CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:AZT +
##       CD4:gender:AZT, data = myaids)
##
##      n= 1211, number of events= 162
##
##               coef exp(coef) se(coef)      z Pr(>|z|)
## CD4             -0.12217    0.88500  0.09604 -1.272 0.203326
## drugddI          1.24317    3.46658  0.47353  2.625 0.008656 **
## gendermale       -0.53340    0.58661  0.56688 -0.941 0.346732
## prevOIAIDS        2.04388    7.72050  0.56162  3.639 0.000273 ***
## AZTfailure        -1.56505    0.20908  0.99618 -1.571 0.116171
## CD4:gendermale     0.03784    1.03856  0.09722  0.389 0.697135
## CD4:prevOIAIDS     -0.10887    0.89685  0.07121 -1.529 0.126307
## CD4:AZTfailure     0.63024    1.87807  0.19887    3.169 0.001529 **
## drugddI:prevOIAIDS -1.01782    0.36138  0.50448 -2.018 0.043635 *
## gendermale:AZTfailure 1.80718    6.09322  1.01972    1.772 0.076356 .
## CD4:gendermale:AZTfailure -0.65813    0.51782  0.20219 -3.255 0.001134 **

```

```
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##               exp(coef) exp(-coef) lower .95 upper .95
## CD4           0.8850    1.1299    0.73315    1.0683
## drugddI       3.4666    0.2885    1.37036    8.7694
## gendermale    0.5866    1.7047    0.19312    1.7819
## prevOIAIDS    7.7205    0.1295    2.56799   23.2112
## AZTfailure    0.2091    4.7829    0.02967    1.4732
## CD4:gendermale 1.0386    0.9629    0.85838    1.2566
## CD4:prevOIAIDS 0.8968    1.1150    0.78001    1.0312
## CD4:AZTfailure 1.8781    0.5325    1.27184    2.7733
## drugddI:prevOIAIDS 0.3614    2.7672    0.13445    0.9714
## gendermale:AZTfailure 6.0932    0.1641    0.82577   44.9606
## CD4:gendermale:AZTfailure 0.5178    1.9312    0.34839    0.7696
##
## Concordance= 0.733 (se = 0.019 )
## Likelihood ratio test= 119.3 on 11 df,  p=<2e-16
## Wald test              = 95.24 on 11 df,  p=2e-15
## Score (logrank) test = 132.9 on 11 df,  p=<2e-16
paste0("AIC Final Selected Model: ", AIC(cox_td_final))

## [1] "AIC Final Selected Model: 1725.31023538143"
# -----
# Accelerated Failure Time (AFT) model
# -----

# -----
# Weibull Distribution
# -----

### Null model
weibull_ti_null <- survreg(Surv(Time, death) ~ 1, data = myaids.id, dist = "weibull")
summary(weibull_ti_null)

##
## Call:
## survreg(formula = Surv(Time, death) ~ 1, data = myaids.id, dist = "weibull")
##               Value Std. Error      z      p
## (Intercept)  3.2448    0.0717 45.26 <2e-16
## Log(scale)  -0.2945    0.0726 -4.06 5e-05
##
## Scale= 0.745
##
## Weibull distribution
## Loglik(model)= -712.9  Loglik(intercept only)= -712.9
## Number of Newton-Raphson Iterations: 5
## n= 400
paste0("AIC of Null Model: ", AIC(weibull_ti_null))

## [1] "AIC of Null Model: 1429.84810629383"
```

```

### Full model with Univariates
weibull_full_ti_uni <- survreg(Surv(Time, death) ~ CD4 + drug + gender + prevOI + AZT, data = myaids.id)
summary(weibull_full_ti_uni)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##      AZT, data = myaids.id, dist = "weibull")
##              Value Std. Error      z      p
## (Intercept)  2.9119      0.2440 11.93 < 2e-16
## CD4          0.0916      0.0182  5.03 4.9e-07
## drugddI     -0.1889      0.1102 -1.71  0.086
## gendermale   0.3286      0.1756  1.87  0.061
## prevOIAIDS  -0.5510      0.1784 -3.09  0.002
## AZTfailure   -0.1627      0.1212 -1.34  0.179
## Log(scale)  -0.3715      0.0705 -5.27 1.3e-07
##
## Scale= 0.69
##
## Weibull distribution
## Loglik(model)= -665.5   Loglik(intercept only)= -712.9
## Chisq= 94.83 on 5 degrees of freedom, p= 6.5e-19
## Number of Newton-Raphson Iterations: 5
## n= 400

paste0("AIC of Main Effects (Univariate) Model: ", AIC(weibull_full_ti_uni))

## [1] "AIC of Main Effects (Univariate) Model: 1345.01438805026"

### Full model with Univariates - Step
weibull_full_ti_uni_step <- step(weibull_full_ti_uni,
                                scope = list(upper = ~ CD4 + drug + gender + prevOI + AZT), trace = 0)
summary(weibull_full_ti_uni_step)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI,
##      data = myaids.id, dist = "weibull")
##              Value Std. Error      z      p
## (Intercept)  2.9201      0.2456 11.89 < 2e-16
## CD4          0.0927      0.0183  5.06 4.3e-07
## drugddI     -0.1753      0.1096 -1.60 0.10976
## gendermale   0.2978      0.1738  1.71 0.08664
## prevOIAIDS  -0.6378      0.1666 -3.83 0.00013
## Log(scale)  -0.3714      0.0705 -5.27 1.4e-07
##
## Scale= 0.69
##
## Weibull distribution
## Loglik(model)= -666.4   Loglik(intercept only)= -712.9
## Chisq= 92.99 on 4 degrees of freedom, p= 3e-19
## Number of Newton-Raphson Iterations: 5
## n= 400

paste0("AIC of Main Effects (Univariate) Model with Stepwise Selection: ", AIC(cox_full_td_uni_step))

```

```
## [1] "AIC of Main Effects (Univariate) Model with Stepwise Selection: 1732.94301975638"
```

```
### Full model with Interactions
```

```
weibull_full_ti_int <- survreg(Surv(Time, death) ~ (CD4 + drug + gender + prevOI + AZT)^5, data = myaids)
summary(weibull_full_ti_int)
```

```
##
```

```
## Call:
```

```
## survreg(formula = Surv(Time, death) ~ (CD4 + drug + gender +
```

```
##     prevOI + AZT)^5, data = myaids.id, dist = "weibull")
```

```
##
```

	Value	Std. Error	z	p
## (Intercept)	3.82e+02	5.79e+04	0.01	0.995
## CD4	-2.20e+01	3.36e+03	-0.01	0.995
## drugddI	-3.80e+02	5.79e+04	-0.01	0.995
## gendermale	-3.79e+02	5.79e+04	-0.01	0.995
## prevOIAIDS	-3.80e+02	5.79e+04	-0.01	0.995
## AZTfailure	1.48e+01	3.26e+04	0.00	1.000
## CD4:drugddI	2.21e+01	3.36e+03	0.01	0.995
## CD4:gendermale	2.21e+01	3.36e+03	0.01	0.995
## CD4:prevOIAIDS	2.22e+01	3.36e+03	0.01	0.995
## CD4:AZTfailure	-4.52e-01	1.99e-01	-2.28	0.023
## drugddI:gendermale	3.79e+02	5.79e+04	0.01	0.995
## drugddI:prevOIAIDS	3.79e+02	5.79e+04	0.01	0.995
## drugddI:AZTfailure	7.46e-01	1.43e+00	0.52	0.602
## gendermale:prevOIAIDS	3.79e+02	5.79e+04	0.01	0.995
## gendermale:AZTfailure	-1.93e+00	1.07e+00	-1.79	0.073
## prevOIAIDS:AZTfailure	-1.33e+01	3.26e+04	0.00	1.000
## CD4:drugddI:gendermale	-2.21e+01	3.36e+03	-0.01	0.995
## CD4:drugddI:prevOIAIDS	-2.17e+01	3.36e+03	-0.01	0.995
## CD4:drugddI:AZTfailure	-6.76e-01	3.32e-01	-2.04	0.042
## CD4:gendermale:prevOIAIDS	-2.22e+01	3.36e+03	-0.01	0.995
## CD4:gendermale:AZTfailure	5.13e-01	2.08e-01	2.46	0.014
## CD4:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## drugddI:gendermale:prevOIAIDS	-3.78e+02	5.79e+04	-0.01	0.995
## drugddI:gendermale:AZTfailure	-6.28e-01	1.50e+00	-0.42	0.676
## drugddI:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## gendermale:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## CD4:drugddI:gendermale:prevOIAIDS	2.17e+01	3.36e+03	0.01	0.995
## CD4:drugddI:gendermale:AZTfailure	6.53e-01	3.44e-01	1.90	0.057
## CD4:drugddI:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## CD4:gendermale:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## drugddI:gendermale:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure	NA	0.00e+00	NA	NA
## Log(scale)	-4.41e-01	7.03e-02	-6.27	3.5e-10

```
##
```

```
## Scale= 0.643
```

```
##
```

```
## Weibull distribution
```

```
## Loglik(model)= -646.1   Loglik(intercept only)= -712.9
```

```
##   Chisq= 133.58 on 31 degrees of freedom, p= 1.1e-14
```

```
## Number of Newton-Raphson Iterations: 20
```

```
## n= 400
```

```

paste0("AIC of Interactions Model: ", AIC(weibull_full_ti_int))

## [1] "AIC of Interactions Model: 1358.27156372946"
### Full model with Interactions - Step
weibull_full_ti_int_step <- step(weibull_full_ti_int,
                                scope = list(upper = ~ (CD4 + drug + gender + prevOI + AZT)^5), trace = 0)
summary(weibull_full_ti_int_step)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##      AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
##      drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
##      CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
##      drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id,
##      dist = "weibull")
##
##              Value Std. Error      z      p
## (Intercept)    9.8987      3.8546  2.57 0.0102
## CD4           -0.3874      0.2282 -1.70 0.0896
## drugddI       -7.1827      3.7221 -1.93 0.0536
## gendermale    -6.0541      3.8796 -1.56 0.1186
## prevOIAIDS    -7.8277      3.6161 -2.16 0.0304
## AZTfailure     1.4690      1.0010  1.47 0.1422
## CD4:drugddI    0.4330      0.2177  1.99 0.0467
## CD4:gendermale 0.4481      0.2338  1.92 0.0553
## CD4:prevOIAIDS 0.5293      0.1965  2.69 0.0071
## CD4:AZTfailure -0.4344      0.1885 -2.30 0.0212
## drugddI:gendermale 6.2664      3.7554  1.67 0.0952
## drugddI:prevOIAIDS 6.2094      3.2004  1.94 0.0524
## drugddI:AZTfailure 0.8917      1.3921  0.64 0.5218
## gendermale:prevOIAIDS 6.6213      3.6406  1.82 0.0690
## gendermale:AZTfailure -1.7867      1.0492 -1.70 0.0886
## CD4:drugddI:gendermale -0.4229      0.2235 -1.89 0.0584
## CD4:drugddI:AZTfailure -0.7276      0.3166 -2.30 0.0215
## CD4:gendermale:prevOIAIDS -0.5142      0.2023 -2.54 0.0110
## CD4:gendermale:AZTfailure 0.4848      0.1976  2.45 0.0141
## drugddI:gendermale:prevOIAIDS -5.4163      3.2242 -1.68 0.0930
## drugddI:gendermale:AZTfailure -0.8646      1.4505 -0.60 0.5512
## CD4:drugddI:gendermale:AZTfailure 0.7209      0.3255  2.22 0.0268
## Log(scale)    -0.4414      0.0703 -6.28 3.4e-10
##
## Scale= 0.643
##
## Weibull distribution
## Loglik(model)= -647.4   Loglik(intercept only)= -712.9
## Chisq= 130.95 on 21 degrees of freedom, p= 6.7e-18
## Number of Newton-Raphson Iterations: 6
## n= 400
paste0("AIC of Interactions Model with Stepwise Selection: ", AIC(weibull_full_ti_int_step))

## [1] "AIC of Interactions Model with Stepwise Selection: 1340.89427920678"

```

Final Time Independent Weibull Model

```
weibull_ti_final <- survreg(Surv(Time, death) ~ CD4 + drug + gender + prevOI +
  AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
  drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
  CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
  drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id,
  dist = "weibull")
summary(weibull_ti_final)
```

```
##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##     AZT + CD4:drug + CD4:gender + CD4:prevOI + CD4:AZT + drug:gender +
##     drug:prevOI + drug:AZT + gender:prevOI + gender:AZT + CD4:drug:gender +
##     CD4:drug:AZT + CD4:gender:prevOI + CD4:gender:AZT + drug:gender:prevOI +
##     drug:gender:AZT + CD4:drug:gender:AZT, data = myaids.id,
##     dist = "weibull")
##
```

	Value	Std. Error	z	p
## (Intercept)	9.8987	3.8546	2.57	0.0102
## CD4	-0.3874	0.2282	-1.70	0.0896
## drugddI	-7.1827	3.7221	-1.93	0.0536
## gendermale	-6.0541	3.8796	-1.56	0.1186
## prevOIAIDS	-7.8277	3.6161	-2.16	0.0304
## AZTfailure	1.4690	1.0010	1.47	0.1422
## CD4:drugddI	0.4330	0.2177	1.99	0.0467
## CD4:gendermale	0.4481	0.2338	1.92	0.0553
## CD4:prevOIAIDS	0.5293	0.1965	2.69	0.0071
## CD4:AZTfailure	-0.4344	0.1885	-2.30	0.0212
## drugddI:gendermale	6.2664	3.7554	1.67	0.0952
## drugddI:prevOIAIDS	6.2094	3.2004	1.94	0.0524
## drugddI:AZTfailure	0.8917	1.3921	0.64	0.5218
## gendermale:prevOIAIDS	6.6213	3.6406	1.82	0.0690
## gendermale:AZTfailure	-1.7867	1.0492	-1.70	0.0886
## CD4:drugddI:gendermale	-0.4229	0.2235	-1.89	0.0584
## CD4:drugddI:AZTfailure	-0.7276	0.3166	-2.30	0.0215
## CD4:gendermale:prevOIAIDS	-0.5142	0.2023	-2.54	0.0110
## CD4:gendermale:AZTfailure	0.4848	0.1976	2.45	0.0141
## drugddI:gendermale:prevOIAIDS	-5.4163	3.2242	-1.68	0.0930
## drugddI:gendermale:AZTfailure	-0.8646	1.4505	-0.60	0.5512
## CD4:drugddI:gendermale:AZTfailure	0.7209	0.3255	2.22	0.0268
## Log(scale)	-0.4414	0.0703	-6.28	3.4e-10

```
##
## Scale= 0.643
##
## Weibull distribution
## Loglik(model)= -647.4   Loglik(intercept only)= -712.9
## Chisq= 130.95 on 21 degrees of freedom, p= 6.7e-18
## Number of Newton-Raphson Iterations: 6
## n= 400
```

```
paste0("AIC Final Selected Model: ", AIC(weibull_ti_final))
```

```
## [1] "AIC Final Selected Model: 1340.89427920678"
```

```

# -----
# Log-Normal distribution
# -----

# Null model
lognorm_ti_null <- survreg(Surv(Time, death) ~ 1, data = myaids.id, dist = "lognormal")
summary(lognorm_ti_null)

##
## Call:
## survreg(formula = Surv(Time, death) ~ 1, data = myaids.id, dist = "lognormal")
##               Value Std. Error      z      p
## (Intercept)  3.0665      0.0854 35.92 <2e-16
## Log(scale)   0.2002      0.0623  3.21 0.0013
##
## Scale= 1.22
##
## Log Normal distribution
## Loglik(model)= -713.7   Loglik(intercept only)= -713.7
## Number of Newton-Raphson Iterations: 3
## n= 400

paste0("AIC of Null Model: ", AIC(lognorm_ti_null))

## [1] "AIC of Null Model: 1431.49602720194"

# Full model with univariates
lognorm_full_ti_uni <- survreg(Surv(Time, death) ~ CD4 + drug + gender + prevOI + AZT,
                              data = myaids.id, dist = "lognormal")
summary(lognorm_full_ti_uni)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##      AZT, data = myaids.id, dist = "lognormal")
##               Value Std. Error      z      p
## (Intercept)   2.4940      0.2867  8.70 < 2e-16
## CD4            0.0872      0.0181  4.80 1.6e-06
## drugddI       -0.2162      0.1316 -1.64 0.1003
## gendermale     0.6297      0.2143  2.94 0.0033
## prevOIAIDS    -0.6115      0.1903 -3.21 0.0013
## AZTfailure    -0.1556      0.1508 -1.03 0.3021
## Log(scale)     0.0812      0.0611  1.33 0.1836
##
## Scale= 1.08
##
## Log Normal distribution
## Loglik(model)= -671   Loglik(intercept only)= -713.7
## Chisq= 85.52 on 5 degrees of freedom, p= 5.9e-17
## Number of Newton-Raphson Iterations: 4
## n= 400

paste0("AIC of Main Effects (Univariate) Model: ", AIC(lognorm_full_ti_uni))

## [1] "AIC of Main Effects (Univariate) Model: 1355.97981393027"

```

```

# Stepwise selection from full univariate model
lognorm_full_ti_step <- step(lognorm_full_ti_step,
                             scope = list(upper = ~ CD4 + drug + gender + prevOI + AZT), trace = 0)
summary(lognorm_full_ti_step)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI,
## data = myaids.id, dist = "lognormal")
##
## Value Std. Error z p
## (Intercept) 2.4930 0.2870 8.69 < 2e-16
## CD4 0.0879 0.0182 4.84 1.3e-06
## drugddI -0.2102 0.1314 -1.60 0.1098
## gendermale 0.6180 0.2140 2.89 0.0039
## prevOIAIDS -0.6959 0.1727 -4.03 5.6e-05
## Log(scale) 0.0819 0.0611 1.34 0.1798
##
## Scale= 1.09
##
## Log Normal distribution
## Loglik(model)= -671.5 Loglik(intercept only)= -713.7
## Chisq= 84.45 on 4 degrees of freedom, p= 2e-17
## Number of Newton-Raphson Iterations: 4
## n= 400

paste0("AIC of Interactions Model with Stepwise Selection: ", AIC(lognorm_full_ti_step))

## [1] "AIC of Interactions Model with Stepwise Selection: 1355.04881235274"

# Full interaction model
lognorm_full_ti_int <- survreg(Surv(Time, death) ~ (CD4 + drug + gender + prevOI + AZT)^5,
                              data = myaids.id, dist = "lognormal")
summary(lognorm_full_ti_int)

##
## Call:
## survreg(formula = Surv(Time, death) ~ (CD4 + drug + gender +
## prevOI + AZT)^5, data = myaids.id, dist = "lognormal")
##
## Value Std. Error z p
## (Intercept) 2.07e+02 2.70e+04 0.01 0.994
## CD4 -1.19e+01 1.57e+03 -0.01 0.994
## drugddI -2.03e+02 2.70e+04 -0.01 0.994
## gendermale -2.03e+02 2.70e+04 -0.01 0.994
## prevOIAIDS -2.06e+02 2.70e+04 -0.01 0.994
## AZTfailure 7.91e+00 1.44e+04 0.00 1.000
## CD4:drugddI 1.18e+01 1.57e+03 0.01 0.994
## CD4:gendermale 1.19e+01 1.57e+03 0.01 0.994
## CD4:prevOIAIDS 1.21e+01 1.57e+03 0.01 0.994
## CD4:AZTfailure -5.27e-01 2.36e-01 -2.23 0.026
## drugddI:gendermale 2.03e+02 2.70e+04 0.01 0.994
## drugddI:prevOIAIDS 2.03e+02 2.70e+04 0.01 0.994
## drugddI:AZTfailure 6.22e-02 2.10e+00 0.03 0.976
## gendermale:prevOIAIDS 2.05e+02 2.70e+04 0.01 0.994
## gendermale:AZTfailure -2.45e+00 1.24e+00 -1.97 0.048
## prevOIAIDS:AZTfailure -5.88e+00 1.44e+04 0.00 1.000

```



```
## CD4:drugddI:gendermale -1.18e+01 1.57e+03 -0.01 0.994
## CD4:drugddI:prevOIAIDS -1.14e+01 1.57e+03 -0.01 0.994
## CD4:drugddI:AZTfailure -5.89e-01 5.01e-01 -1.18 0.240
## CD4:gendermale:prevOIAIDS -1.21e+01 1.57e+03 -0.01 0.994
## CD4:gendermale:AZTfailure 6.19e-01 2.45e-01 2.53 0.011
## CD4:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## drugddI:gendermale:prevOIAIDS -2.02e+02 2.70e+04 -0.01 0.994
## drugddI:gendermale:AZTfailure -1.47e-01 2.17e+00 -0.07 0.946
## drugddI:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## gendermale:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## CD4:drugddI:gendermale:prevOIAIDS 1.14e+01 1.57e+03 0.01 0.994
## CD4:drugddI:gendermale:AZTfailure 5.69e-01 5.09e-01 1.12 0.264
## CD4:drugddI:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## CD4:gendermale:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## drugddI:gendermale:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## CD4:drugddI:gendermale:prevOIAIDS:AZTfailure NA 0.00e+00 NA NA
## Log(scale) -6.59e-03 6.09e-02 -0.11 0.914
##
## Scale= 0.993
##
## Log Normal distribution
## Loglik(model)= -650.2 Loglik(intercept only)= -713.7
## Chisq= 127.06 on 31 degrees of freedom, p= 1.4e-13
## Number of Newton-Raphson Iterations: 18
## n= 400
```

```
paste0("AIC of Interactions Model: ", AIC(lognorm_full_ti_int))
```

```
## [1] "AIC of Interactions Model: 1366.43313674881"
```

```
# Stepwise interaction model
```

```
lognorm_full_ti_int_step <- step(lognorm_full_ti_int,
                                scope = list(upper = ~ (CD4 + drug + gender + prevOI + AZT)^5), trace = FALSE)
summary(lognorm_full_ti_int_step)
```

```
##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##       AZT + CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:prevOI +
##       gender:AZT + CD4:gender:prevOI + CD4:gender:AZT, data = myaids.id,
##       dist = "lognormal")
##
##              Value Std. Error      z      p
## (Intercept)    4.6525      0.8149  5.71 1.1e-08
## CD4           -0.0858      0.0608 -1.41 0.1579
## drugddI       -0.8655      0.2804 -3.09 0.0020
## gendermale    -1.0702      0.8375 -1.28 0.2013
## prevOIAIDS   -3.2253      1.0062 -3.21 0.0013
## AZTfailure     1.6130      0.9655  1.67 0.0948
## CD4:gendermale  0.1602      0.0692  2.32 0.0206
## CD4:prevOIAIDS  0.3733      0.1496  2.50 0.0126
## CD4:AZTfailure -0.6159      0.2143 -2.87 0.0041
## drugddI:prevOIAIDS  0.8318      0.3135  2.65 0.0080
## gendermale:prevOIAIDS  2.0272      1.0412  1.95 0.0515
## gendermale:AZTfailure -2.0650      1.0033 -2.06 0.0396
## CD4:gendermale:prevOIAIDS -0.3709      0.1566 -2.37 0.0179
```

```
## CD4:gendermale:AZTfailure 0.6968      0.2195  3.18  0.0015
## Log(scale)                0.0161      0.0607  0.26  0.7913
##
## Scale= 1.02
##
## Log Normal distribution
## Loglik(model)= -655.5   Loglik(intercept only)= -713.7
## Chisq= 116.43 on 13 degrees of freedom, p= 1e-18
## Number of Newton-Raphson Iterations: 4
## n= 400

paste0("AIC of Interactions Model with Stepwise Selection: ", AIC(lognorm_full_ti_int_step))

## [1] "AIC of Interactions Model with Stepwise Selection: 1341.06676972302"

# Final log-normal model
lognorm_ti_final <- survreg(Surv(Time, death) ~ CD4 + drug + gender + prevOI +
  AZT + CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:prevOI +
  gender:AZT + CD4:gender:prevOI + CD4:gender:AZT, data = myaids.id,
  dist = "lognormal")
summary(lognorm_ti_final)

##
## Call:
## survreg(formula = Surv(Time, death) ~ CD4 + drug + gender + prevOI +
##      AZT + CD4:gender + CD4:prevOI + CD4:AZT + drug:prevOI + gender:prevOI +
##      gender:AZT + CD4:gender:prevOI + CD4:gender:AZT, data = myaids.id,
##      dist = "lognormal")
##
##              Value Std. Error      z      p
## (Intercept)      4.6525      0.8149  5.71 1.1e-08
## CD4              -0.0858      0.0608 -1.41 0.1579
## drugddI          -0.8655      0.2804 -3.09 0.0020
## gendermale       -1.0702      0.8375 -1.28 0.2013
## prevOIAIDS       -3.2253      1.0062 -3.21 0.0013
## AZTfailure        1.6130      0.9655  1.67 0.0948
## CD4:gendermale    0.1602      0.0692  2.32 0.0206
## CD4:prevOIAIDS    0.3733      0.1496  2.50 0.0126
## CD4:AZTfailure   -0.6159      0.2143 -2.87 0.0041
## drugddI:prevOIAIDS 0.8318      0.3135  2.65 0.0080
## gendermale:prevOIAIDS 2.0272      1.0412  1.95 0.0515
## gendermale:AZTfailure -2.0650      1.0033 -2.06 0.0396
## CD4:gendermale:prevOIAIDS -0.3709      0.1566 -2.37 0.0179
## CD4:gendermale:AZTfailure 0.6968      0.2195  3.18 0.0015
## Log(scale)        0.0161      0.0607  0.26 0.7913
##
## Scale= 1.02
##
## Log Normal distribution
## Loglik(model)= -655.5   Loglik(intercept only)= -713.7
## Chisq= 116.43 on 13 degrees of freedom, p= 1e-18
## Number of Newton-Raphson Iterations: 4
## n= 400

paste0("AIC Final Selected Model: ", AIC(lognorm_ti_final))

## [1] "AIC Final Selected Model: 1341.06676972302"
```