OCM_modelvalidation

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This script demonstrates how the model was validated in PLCO. Unfortunately, the PLCO data cannot be shared, and therefore this script cannot be run. However, we provide the code for transparency.

Validation

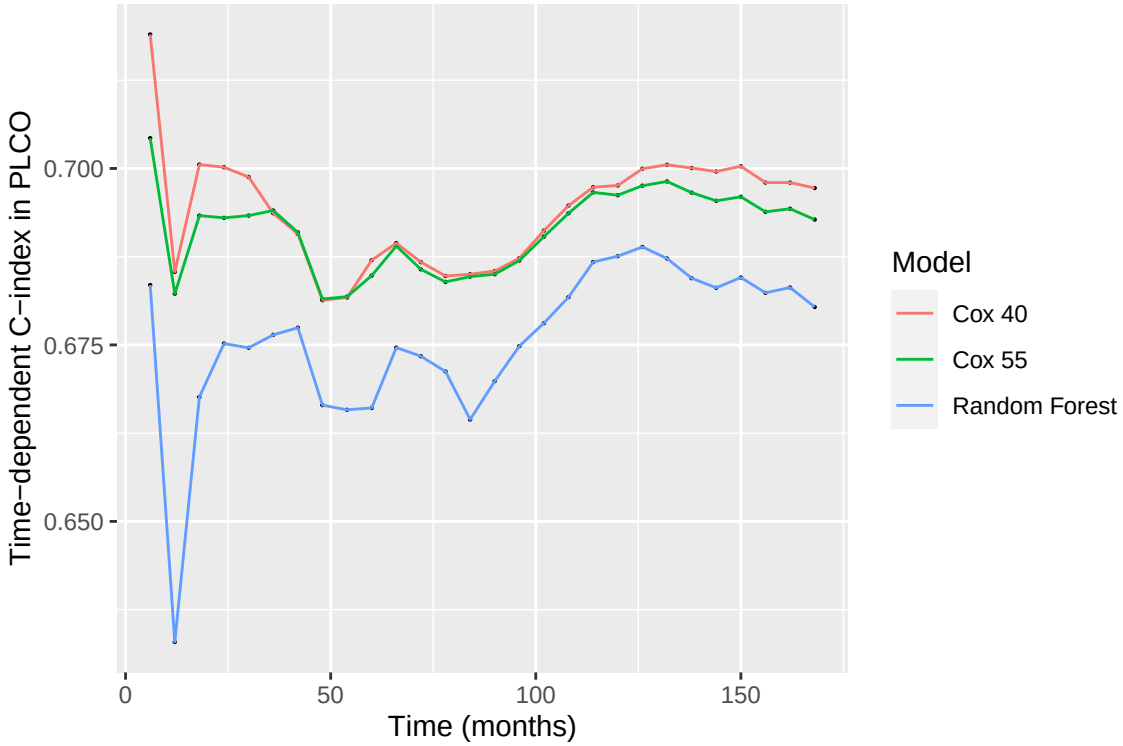
Now we validate each model. First, we look at C-index for the cause-specific formulation:

```
load("cox_55.RData")
load("cox_40.RData")
load("rforest_40.RData")

times <- seq(6, 168, by=6)
plco_clean$age_ctr_40 <- plco_clean$age - 60.34387 #scaling the age 40+ cohort
plco_clean$age_ctr_55 <- plco_clean$age - 68.35788 #scaling the age 55+ cohort

cox55_plco <- pec::cindex(object=cox_55, Surv(permth_exm, mortstat) ~ age_ctr_55 +
                            race2 + educ + marital2 + emphysema + diabetic +
                            stroke + smoker + underweight + overweight2 + obese2 +
                            pc + age_ctr_55*diabetic + age_ctr_55*educ +
                            age_ctr_55*marital2 + race2*educ, data = plco_clean,
                          eval.times = times)

cox40_plco <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                            age_ctr_40 + diabetic + educ + hypertension + marital2 +
                            underweight + overweight2 + obese2 + smoker + stroke +
                            age_ctr_40*diabetic + age_ctr_40*educ +
                            age_ctr_40*hypertension + age_ctr_40*stroke + pc,
                          data=plco_clean, eval.times = times)

forest_plco <- pec::cindex(object=rforest_40, formula = Surv(permth_exm, mortstat) ~
                             age + arthritis + bronch + diabetic + educ +
                             emphysema + hypertension + single + sep + mi_chd +
                             underweight + overweight_ex + obese + liver + black +
                             other + smoker + stroke + pc, data=plco_nf, eval.times = times)

valid_perf <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                         "Model" = c(rep("Cox 55", 28), rep("Cox 40", 28),
                                     rep("Random Forest", 28)),
                         "C" = c(cox55_plco$AppCindex$coxph, cox40_plco$AppCindex$coxph,
                                 forest_plco$AppCindex$rfsrc))

performance_plot <- ggplot(data=valid_perf, aes(x=Time, y=C)) + geom_point(size=0.1) +
```

Table 1: Time-dependent C-index in PLCO

Model	Year5	Year10	Year14
Cox 55	0.685	0.696	0.693
Cox 40	0.687	0.698	0.697
Random Forest	0.666	0.688	0.680

```
  geom_line(data=valid_perf, aes(group=Model, color=Model)) + xlab("Time (months)") +
  ylab("Time-dependent C-index in PLCO")

performance_plot
```



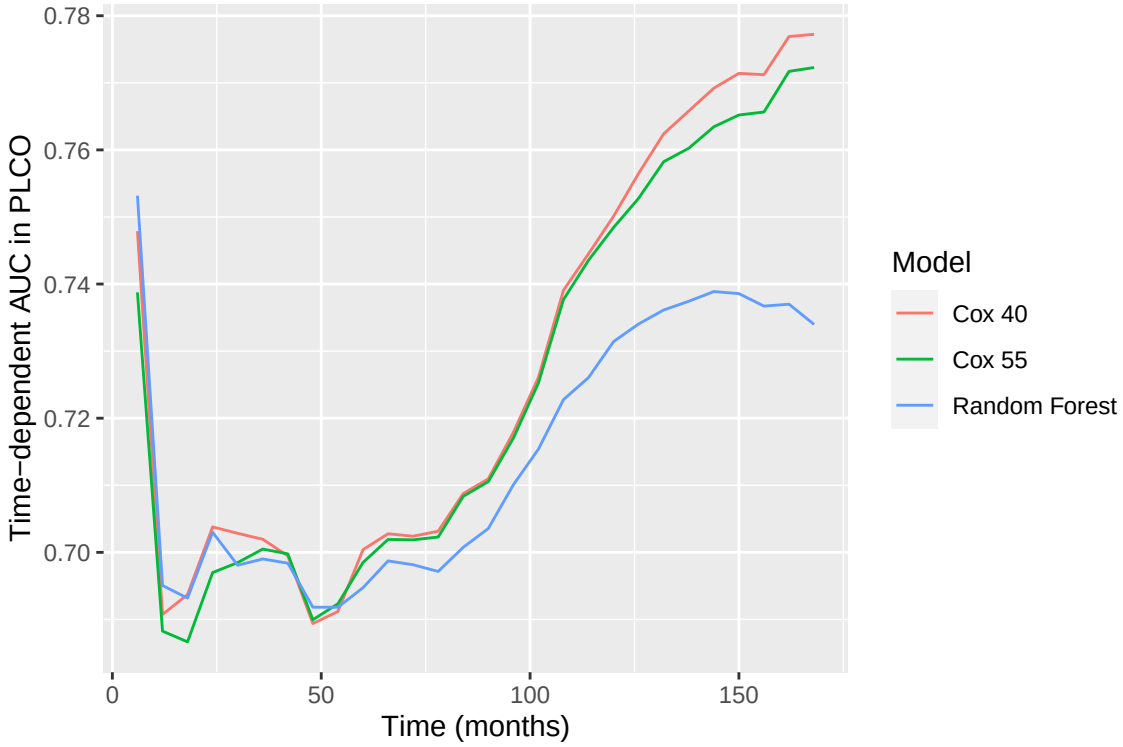

```
subperf <- data.frame("Model" = c("Cox 55", "Cox 40", "Random Forest"),
                      "Year5" = round(c(cox55_plco$AppCindex$coxph[10],
                                        cox40_plco$AppCindex$coxph[10],
                                        forest_plco$AppCindex$rfsrc[10]), digits=3),
                      "Year10" = round(c(cox55_plco$AppCindex$coxph[20],
                                         cox40_plco$AppCindex$coxph[20],
                                         forest_plco$AppCindex$rfsrc[20]), digits=3),
                      "Year14" = round(c(cox55_plco$AppCindex$coxph[28],
                                         cox40_plco$AppCindex$coxph[28],
                                         forest_plco$AppCindex$rfsrc[28]), digits=3))

kable(subperf, caption = "Time-dependent C-index in PLCO")
```

Based on C-index, our strongest performing model is the Cox model fit to men ages 40+. Now we look at time-dependent AUC:

```r
cox40predict <-
  predict(object = cox_40,
          newdata = plco_clean,
          type = "lp")
cox55predict <-
  predict(object = cox_55,
          newdata = plco_clean,
          type = "lp")
rforestpredict <-
  predict(object=rforest_40,
          newdata = plco_nf)

cox40roc <-
  timeROC(
    T = plco_clean$permth_exm,
    delta = plco_clean$mortstat,
    marker = cox40predict,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )
cox55roc <-
  timeROC(
    T = plco_clean$permth_exm,
    delta = plco_clean$mortstat,
    marker = cox55predict,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )
rforestroc <-
  timeROC(
    T = plco_nf$permth_exm,
    delta = plco_nf$mortstat,
    marker = rforestpredict$predicted,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

aucdat <-
  data.frame("Time" = rep(seq(6, 168, by = 6), 3),
             "Model" = c(rep("Cox 55", 28), rep("Cox 40", 28),
                                    rep("Random Forest", 28)),
             "AUC" = c(cox55roc$AUC[-1], cox40roc$AUC[-1],
                       rforestroc$AUC[-1]))

aucplot <-
  ggplot(data = aucdat, aes(x = Time, y = AUC, group = Model, color=Model)) +
  geom_line() + xlab("Time (months)") + ylab("Time-dependent AUC in PLCO")

aucplot
```

Table 2: Time-Dependent AUC in PLCO

Model	Year5	Year10	Year14
Cox 55	0.698	0.748	0.772
Cox 40	0.700	0.750	0.777
Random Forest	0.695	0.731	0.734




```
auc_table <- data.frame("Model" = c("Cox 55", "Cox 40", "Random Forest"),
                        "Year5" = round(c(cox55roc$AUC[11],
                                          cox40roc$AUC[11],
                                          rforestroc$AUC[11]), digits=3),
                        "Year10" = round(c(cox55roc$AUC[21],
                                           cox40roc$AUC[21],
                                           rforestroc$AUC[21]), digits=3),
                        "Year14" = round(c(cox55roc$AUC[29],
                                           cox40roc$AUC[29],
                                           rforestroc$AUC[29]), digits=3))

kable(auc_table, caption="Time-Dependent AUC in PLCO")
```

Based on time-dependent AUC, the Cox model fit to men ages 40+ is still the strongest performing model. We will now focus our attention on the Cox ages 40+ model for the rest of our model validation/performance assessment.

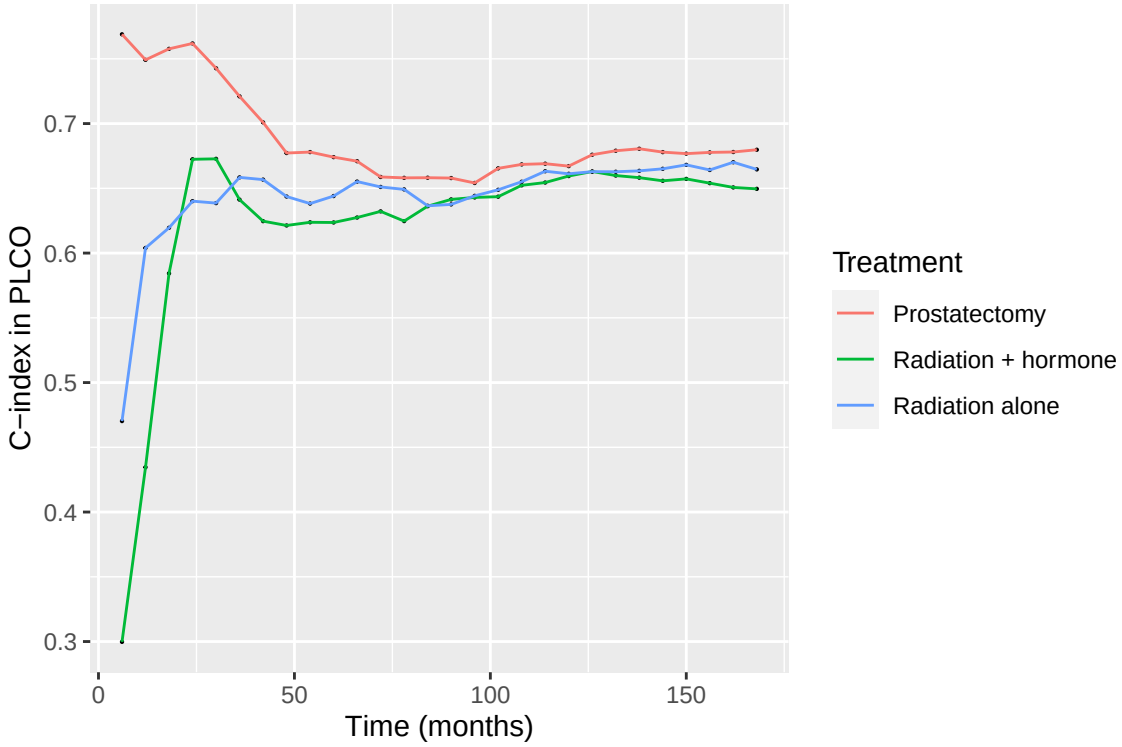
We look at C-index and time-dependent AUC stratified by treatment group:

```
cox40_prostatectomy <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                                     age_ctr_40 + diabetic + educ + hypertension +
                                     marital2 + underweight + overweight2 + obese2 +
                                     smoker + stroke + age_ctr_40*diabetic +
```

```
                                    age_ctr_40*educ + age_ctr_40*hypertension +
                                    age_ctr_40*stroke + pc,
                                  data=plco_clean[plco_clean$primary_tx=="Prostatectomy",],
                                  eval.times = times)

cox40_radiation <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                                 age_ctr_40 + diabetic + educ + hypertension +
                                 marital2 + underweight + overweight2 + obese2 +
                                 smoker + stroke + age_ctr_40*diabetic +
                                 age_ctr_40*educ + age_ctr_40*hypertension +
                                 age_ctr_40*stroke + pc,
                               data=plco_clean[plco_clean$primary_tx=="Radiation alone",],
                               eval.times = times)

cox40_rtadt <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                             age_ctr_40 + diabetic + educ + hypertension +
                             marital2 + underweight + overweight2 + obese2 +
                             smoker + stroke + age_ctr_40*diabetic +
                             age_ctr_40*educ + age_ctr_40*hypertension +
                             age_ctr_40*stroke + pc,
                           data=plco_clean[plco_clean$primary_tx=="Radiation + hormone",],
                           eval.times = times)

valid_perf_trt <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                             "Treatment" = c(rep("Prostatectomy", 28),
                                             rep("Radiation alone", 28),
                                             rep("Radiation + hormone", 28)),
                             "C" = c(cox40_prostatectomy$AppCindex$coxph,
                                     cox40_radiation$AppCindex$coxph,
                                     cox40_rtadt$AppCindex$coxph))

performance_plot_trt <- ggplot(data=valid_perf_trt, aes(x=Time, y=C)) +
  geom_point(size=0.1) + geom_line(data=valid_perf_trt, aes(group=Treatment,
                                                            color=Treatment)) +
  xlab("Time (months)") + ylab("C-index in PLCO")

performance_plot_trt
```

Table 3: PLCO Time-Dependent C-index, by Treatment

Treatment	Year5	Year10	Year14
Prostatectomy	0.674	0.667	0.680
Radiation alone	0.644	0.661	0.665
Radiation + hormone	0.624	0.659	0.650



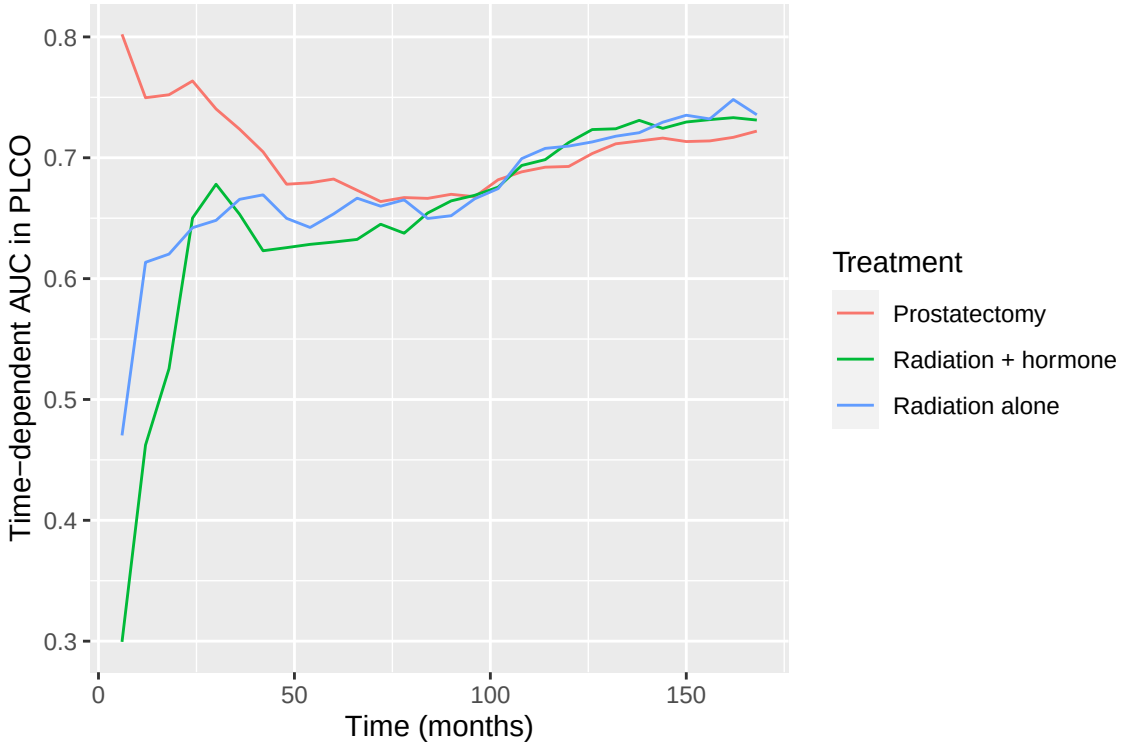

```
subperf_trt <- data.frame("Treatment" = c("Prostatectomy", "Radiation alone",
                                          "Radiation + hormone"),
                          "Year5" = round(c(cox40_prostatectomy$AppCindex$coxph[10],
                                            cox40_radiation$AppCindex$coxph[10],
                                            cox40_rtadt$AppCindex$coxph[10]), digits=3),
                          "Year10" = round(c(cox40_prostatectomy$AppCindex$coxph[20],
                                             cox40_radiation$AppCindex$coxph[20],
                                             cox40_rtadt$AppCindex$coxph[20]), digits=3),
                          "Year14" = round(c(cox40_prostatectomy$AppCindex$coxph[28],
                                             cox40_radiation$AppCindex$coxph[28],
                                             cox40_rtadt$AppCindex$coxph[28]), digits=3))

kable(subperf_trt, caption = "PLCO Time-Dependent C-index, by Treatment")
```

```
cox40predict_prostatectomy <- predict(object=cox_40, newdata =
                                        plco_clean[plco_clean$primary_tx=="Prostatectomy",],
                                      type="lp")

cox40predict_radiation <- predict(object=cox_40, newdata =
                                    plco_clean[plco_clean$primary_tx=="Radiation alone",],
                                  type="lp")
```

```r
cox40predict_rtadt <- predict(object=cox_40, newdata =
                                plco_clean[plco_clean$primary_tx=="Radiation + hormone",],
                              type="lp")

prostatectomy_roc <- timeROC(T = plco_clean$permth_exm[plco_clean$primary_tx=="Prostatectomy"],
                             delta = plco_clean$mortstat[plco_clean$primary_tx=="Prostatectomy"],
                             marker = cox40predict_prostatectomy, cause = 1,
                             weighting="marginal", times = seq(0, 168, by=6))

radiation_roc <- timeROC(T = plco_clean$permth_exm[plco_clean$primary_tx=="Radiation alone"],
                         delta = plco_clean$mortstat[plco_clean$primary_tx=="Radiation alone"],
                         marker = cox40predict_radiation, cause = 1,
                         weighting="marginal", times = seq(0, 168, by=6))

rtadt_roc <- timeROC(T = plco_clean$permth_exm[plco_clean$primary_tx=="Radiation + hormone"],
                     delta = plco_clean$mortstat[plco_clean$primary_tx=="Radiation + hormone"],
                     marker = cox40predict_rtadt, cause = 1, weighting="marginal",
                     times = seq(0, 168, by=6))

aucdat_trt <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                         "AUC" = c(prostatectomy_roc$AUC[-1], radiation_roc$AUC[-1],
                                   rtadt_roc$AUC[-1]),
                         "Treatment" = c(rep("Prostatectomy", 28),
                                         rep("Radiation alone", 28),
                                         rep("Radiation + hormone", 28)))

aucplot_trt <- ggplot(data=aucdat_trt, aes(x=Time, y=AUC, group=Treatment,
                                           color=Treatment)) + geom_line() +
  xlab("Time (months)") + ylab("Time-dependent AUC in PLCO")

aucplot_trt
```

Table 4: Time-Dependent AUC in PLCO, by Treatment

Years	Prostatectomy	Radiation	Radiation_hormone
5	0.682	0.654	0.630
10	0.693	0.710	0.713
14	0.722	0.736	0.731




```
auc_table_trt <- data.frame("Years" = c(5, 10, 14),
                            "Prostatectomy" = round(c(prostatectomy_roc$AUC[11],
                                                      prostatectomy_roc$AUC[21],
                                                      prostatectomy_roc$AUC[29]),
                                                    digits = 3),
                            "Radiation" = round(c(radiation_roc$AUC[11],
                                                  radiation_roc$AUC[21],
                                                  radiation_roc$AUC[29]),
                                                digits = 3),
                            "Radiation_hormone" = round(c(rtadt_roc$AUC[11],
                                                          rtadt_roc$AUC[21],
                                                          rtadt_roc$AUC[29]),
                                                        digits = 3))

rownames(auc_table_trt) <- NULL
kable(auc_table_trt, caption="Time-Dependent AUC in PLCO, by Treatment")
```

```
cutTime <- 14*12   #14 yr cutoff point

plco_clean$pc_time_14yr <- ifelse(plco_clean$permth_exm > cutTime, cutTime,
                                  plco_clean$permth_exm)
```

```r
plco_clean$pc_status <- ifelse(plco_clean$permth_exm >= cutTime, 0,
                               plco_clean$mortstat2)
plco_clean$linpred <- cox40predict

dat <- plco_clean[, c("pc_status", "pc_time_14yr", "linpred")]
dat <- dat[complete.cases(dat), ]

eve.ocm <- dat$pc_status == 1
eve.pcsm <- dat$pc_status == 2
eve.cens <- dat$pc_status == 0

fstatus <- rep(0,times = nrow(dat))
fstatus[which(eve.ocm)] <- 1
fstatus[which(eve.pcsm)] <- 2
ftime <- dat$pc_time_14yr

fg_covariates <- dat$linpred

finegray_pc <- crr(ftime = ftime, fstatus = fstatus, cov1 = fg_covariates)
summary(finegray_pc)
## Competing Risks Regression
##
## Call:
## crr(ftime = ftime, fstatus = fstatus, cov1 = fg_covariates)
##
##                 coef exp(coef) se(coef)    z p-value
## fg_covariates1 1.02      2.76   0.0346 29.3       0
##
##                 exp(coef) exp(-coef) 2.5% 97.5%
## fg_covariates1      2.76      0.362 2.58  2.95
##
## Num. cases = 8220
## Pseudo Log-likelihood = -17432
## Pseudo likelihood ratio test = 936  on 1 df,

finegray_predictions <- predict(finegray_pc, cov1 = fg_covariates)

predict_5 <- finegray_predictions[finegray_predictions[,1]==60,-1]
predict_10 <- finegray_predictions[finegray_predictions[,1]==120,-1]
predict_14 <- finegray_predictions[finegray_predictions[,1]==167,-1]

group_5 <- case_when(
  predict_5 < 0.2 ~ 0.1,
  predict_5 >= 0.2 & predict_5 < 0.4 ~ 0.3,
  predict_5 >= 0.4 & predict_5 < 0.6 ~ 0.5,
  predict_5 >= 0.6 & predict_5 < 0.8 ~ 0.7,
  predict_5 >= 0.8 ~ 0.9
)

group_10 <- case_when(
  predict_10 < 0.2 ~ 0.1,
  predict_10 >= 0.2 & predict_10 < 0.4 ~ 0.3,
  predict_10 >= 0.4 & predict_10 < 0.6 ~ 0.5,
```

```
  predict_10 >= 0.6 & predict_10 < 0.8 ~ 0.7,
  predict_10 >= 0.8 ~ 0.9
)

group_14 <- case_when(
  predict_14 < 0.2 ~ 0.1,
  predict_14 >= 0.2 & predict_14 < 0.4 ~ 0.3,
  predict_14 >= 0.4 & predict_14 < 0.6 ~ 0.5,
  predict_14 >= 0.6 & predict_14 < 0.8 ~ 0.7,
  predict_14 >= 0.8 ~ 0.9
)

cuminc_5 <- cuminc(ftime, fstatus, group = group_5)
cuminc_10 <- cuminc(ftime, fstatus, group = group_10)
cuminc_14 <- cuminc(ftime, fstatus, group = group_14)

calibration5_data <- data.frame("Year" = rep("5 Years", 3),
                                "Group" = c(0.1, 0.3, 0.5),
                                "Est" = c(cuminc_5$`0.1 1`$est[cuminc_5$`0.1 1`$time==60][1],
                                          cuminc_5$`0.3 1`$est[cuminc_5$`0.3 1`$time==59][1],
                                          cuminc_5$`0.5 1`$est[cuminc_5$`0.5 1`$time==57][1]),
                                "Var" = c(cuminc_5$`0.1 1`$var[cuminc_5$`0.1 1`$time==60][1],
                                          cuminc_5$`0.3 1`$var[cuminc_5$`0.3 1`$time==59][1],
                                          cuminc_5$`0.5 1`$var[cuminc_5$`0.5 1`$time==57][1]))

calibration10_data <- data.frame("Year" = rep("10 Years", 4),
                                 "Group" = c(0.1, 0.3, 0.5, 0.7),
                                 "Est" = c(cuminc_10$`0.1 1`$est[cuminc_10$`0.1 1`$time==120][1],
                                           cuminc_10$`0.3 1`$est[cuminc_10$`0.3 1`$time==120][1],
                                           cuminc_10$`0.5 1`$est[cuminc_10$`0.5 1`$time==119][1],
                                           cuminc_10$`0.7 1`$est[cuminc_10$`0.7 1`$time==118][1]),
                                 "Var" = c(cuminc_10$`0.1 1`$var[cuminc_10$`0.1 1`$time==120][1],
                                           cuminc_10$`0.3 1`$var[cuminc_10$`0.3 1`$time==120][1],
                                           cuminc_10$`0.5 1`$var[cuminc_10$`0.5 1`$time==119][1],
                                           cuminc_10$`0.7 1`$var[cuminc_10$`0.7 1`$time==118][1]))

calibration14_data <- data.frame("Year" = rep("10 Years", 5),
                                 "Group" = c(0.1, 0.3, 0.5, 0.7, 0.9),
                                 "Est" = c(cuminc_14$`0.1 1`$est[cuminc_14$`0.1 1`$time==168][1],
                                           cuminc_14$`0.3 1`$est[cuminc_14$`0.3 1`$time==168][1],
                                           cuminc_14$`0.5 1`$est[cuminc_14$`0.5 1`$time==168][1],
                                           cuminc_14$`0.7 1`$est[cuminc_14$`0.7 1`$time==168][1],
                                           cuminc_14$`0.9 1`$est[cuminc_14$`0.9 1`$time==157][1]),
                                 "Var" = c(cuminc_14$`0.1 1`$var[cuminc_14$`0.1 1`$time==168][1],
                                           cuminc_14$`0.3 1`$var[cuminc_14$`0.3 1`$time==168][1],
                                           cuminc_14$`0.5 1`$var[cuminc_14$`0.5 1`$time==168][1],
                                           cuminc_14$`0.7 1`$var[cuminc_14$`0.7 1`$time==168][1],
                                           cuminc_14$`0.9 1`$var[cuminc_14$`0.9 1`$time==157][1]))

calibration5_data$Upper <- calibration5_data$Est + 1.96*sqrt(calibration5_data$Var)
calibration10_data$Upper <- calibration10_data$Est + 1.96*sqrt(calibration10_data$Var)
calibration14_data$Upper <- calibration14_data$Est + 1.96*sqrt(calibration14_data$Var)
calibration5_data$Lower <- calibration5_data$Est - 1.96*sqrt(calibration5_data$Var)
```

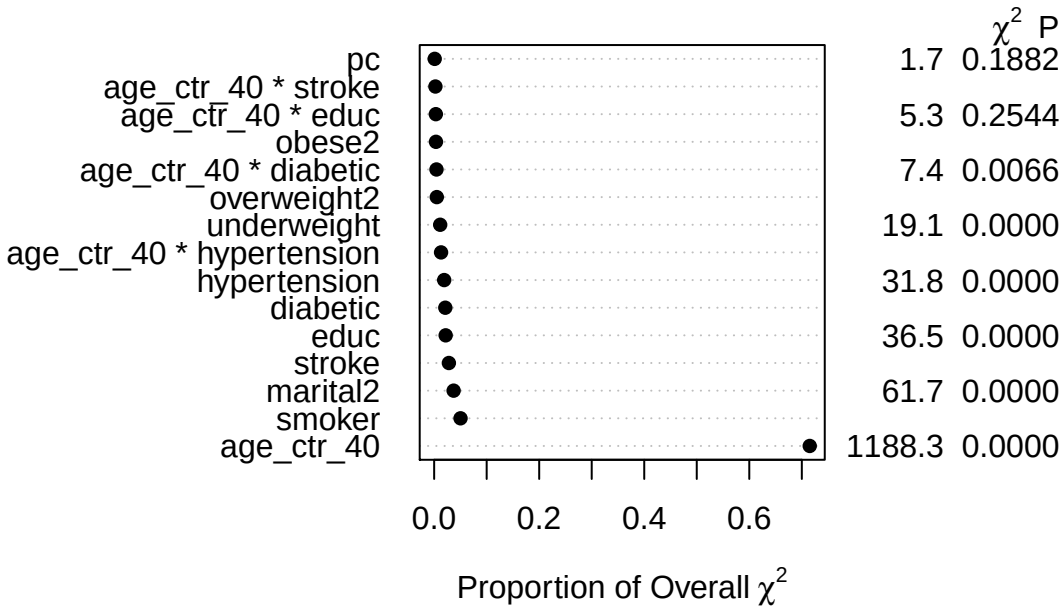
```
calibration10_data$Lower <- calibration10_data$Est - 1.96*sqrt(calibration10_data$Var)
calibration14_data$Lower <- calibration14_data$Est - 1.96*sqrt(calibration14_data$Var)

calibration5_data$Upper[calibration5_data$Upper>1] <- 1
calibration5_data$Lower[calibration5_data$Lower<0] <- 0
calibration10_data$Upper[calibration10_data$Upper>1] <- 1
calibration10_data$Lower[calibration10_data$Lower<0] <- 0
calibration14_data$Upper[calibration14_data$Upper>1] <- 1
calibration14_data$Lower[calibration14_data$Lower<0] <- 0

myplot <- ggplot() + geom_line(data = calibration5_data, aes(x=Group, y=Est),
                               color = "darkblue") +
  geom_errorbar(data = calibration5_data, aes(x = Group, ymin = Lower,
                                              ymax = Upper, width = 0.05),
                color = "darkblue") + geom_line(data = calibration10_data,
                                                aes(x=Group, y=Est),
                                                color = "mediumpurple4") +
  geom_errorbar(data = calibration10_data, aes(x = Group, ymin = Lower,
                                               ymax = Upper, width = 0.05),
                color = "mediumpurple4") + geom_line(data = calibration14_data,
                                                     aes(x=Group, y=Est),
                                                     color = "gray74") +
  geom_errorbar(data = calibration14_data, aes(x = Group, ymin = Lower,
                                               ymax = Upper), color = "gray74",
                width = 0.05) + scale_x_continuous(name = "Predicted Risk of OCM",
                                                   limits = c(0, 1),
                                                   breaks = seq(0, 1, by=0.2)) +
  scale_y_continuous(name = "Observed Risk of OCM", limits = c(0, 1),
                     breaks = seq(0, 1.2, by=0.2)) + theme_bw() +
  geom_abline(slope = 1, intercept = 0)  +
  labs(caption = "Black line: perfect calibration. Blue line: calibration at
       5 years. Purple line: calibration at 10 years. Gray line: calibration
       at 14 years.")

#myplot

#save(list=c("plco_clean", "plco_nf"), file = "~/Box/PLCO Data/Prostate/plco_data_clean.RData")
```

Variable Importance

We assess the variable importance of our Cox model:

```
load("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nhanes_data_clean.RData")
f <-
  cph(
    Surv(permth_exm, mortstat) ~ age_ctr_40 + diabetic + educ + hypertension +
      marital2 + underweight + overweight2 + obese2 + smoker + stroke +
      age_ctr_40 * diabetic + age_ctr_40 * educ + age_ctr_40 * hypertension +
      age_ctr_40 * stroke + pc,
    data = mydata[mydata$inmodel4 == 1, ],
    x = TRUE,
    y = TRUE
  )
```

```
plot(anova(f), what='proportion chisq')
```

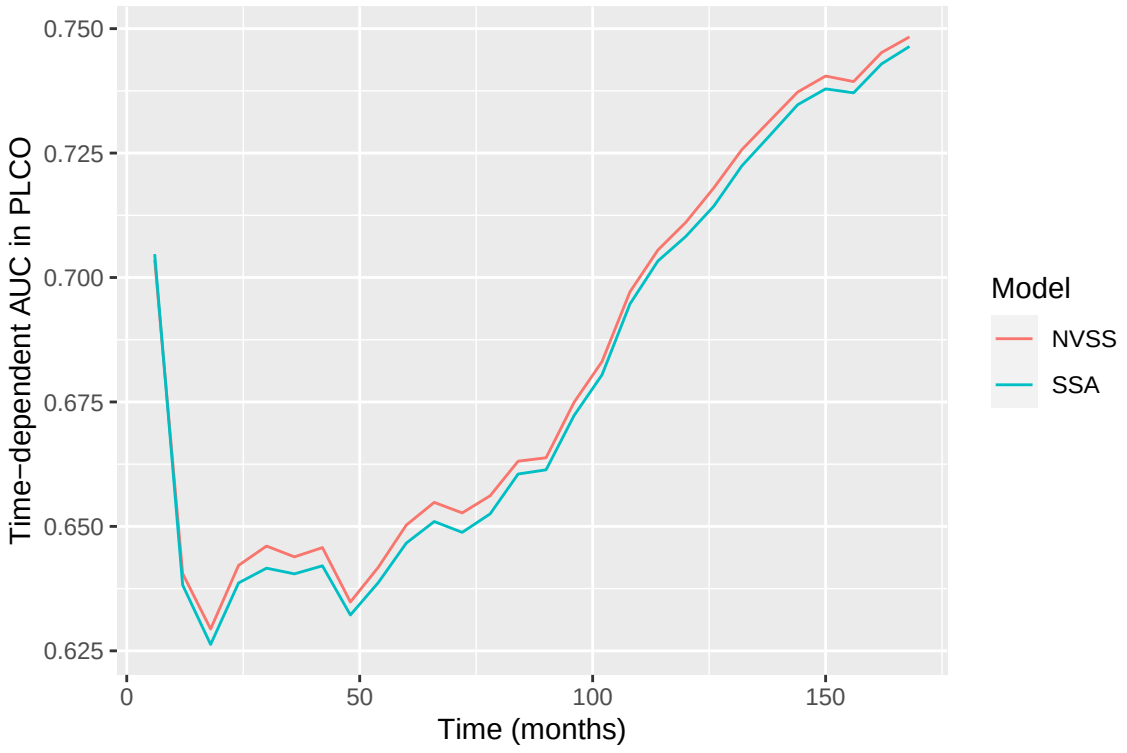


Comparison to SSA and NVSS Life Tables

We compare to the SSA and NVSS life tables:

```
ssa <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/ssa_2000.csv")
ssa$age <- seq(0, 119, by = 1)

nvss_black <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_blackma
nvss_white <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_whitema
nvss_other <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_allmal
nvss_other <- nvss_other[-102,]

nvss <- data.frame("Age" = seq(0, 100, by = 1), "White" = nvss_white$Expectancy, "Black" = nvss_black$E

plco_clean$ssa <- NA
plco_clean$nvss <- NA
for (i in 1:nrow(plco_clean)){
  plco_clean$ssa[i] <- ssa$Expectancy[which(ssa$age==plco_clean$age[i])]
  if (plco_clean$race2[i]=="NHW"){
    plco_clean$nvss[i] <- nvss$White[which(nvss$Age==plco_clean$age[i])]
  } else if (plco_clean$race2[i]=="NHB"){
    plco_clean$nvss[i] <- nvss$Black[which(nvss$Age==plco_clean$age[i])]
  } else if (plco_clean$race2[i]=="Other"){
    plco_clean$nvss[i] <- nvss$Other[which(nvss$Age==plco_clean$age[i])]
  }
}

ssa_roc <-
  timeROC(
    T = plco_clean$permth_exm,
    delta = plco_clean$mortstat,
```

```
    marker = 1/plco_clean$ssa,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

nvss_roc <-
  timeROC(
    T = plco_clean$permth_exm,
    delta = plco_clean$mortstat,
    marker = 1/plco_clean$nvss,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

aucdat <-
  data.frame("Time" = rep(seq(6, 168, by = 6), 2),
             "Model" = c(rep("SSA", 28), rep("NVSS", 28)),
             "AUC" = c(ssa_roc$AUC[-1], nvss_roc$AUC[-1]))

aucplot <-
  ggplot(data = aucdat, aes(x = Time, y = AUC, group = Model, color=Model)) +
  geom_line() + xlab("Time (months)") + ylab("Time-dependent AUC in PLCO")

aucplot
```



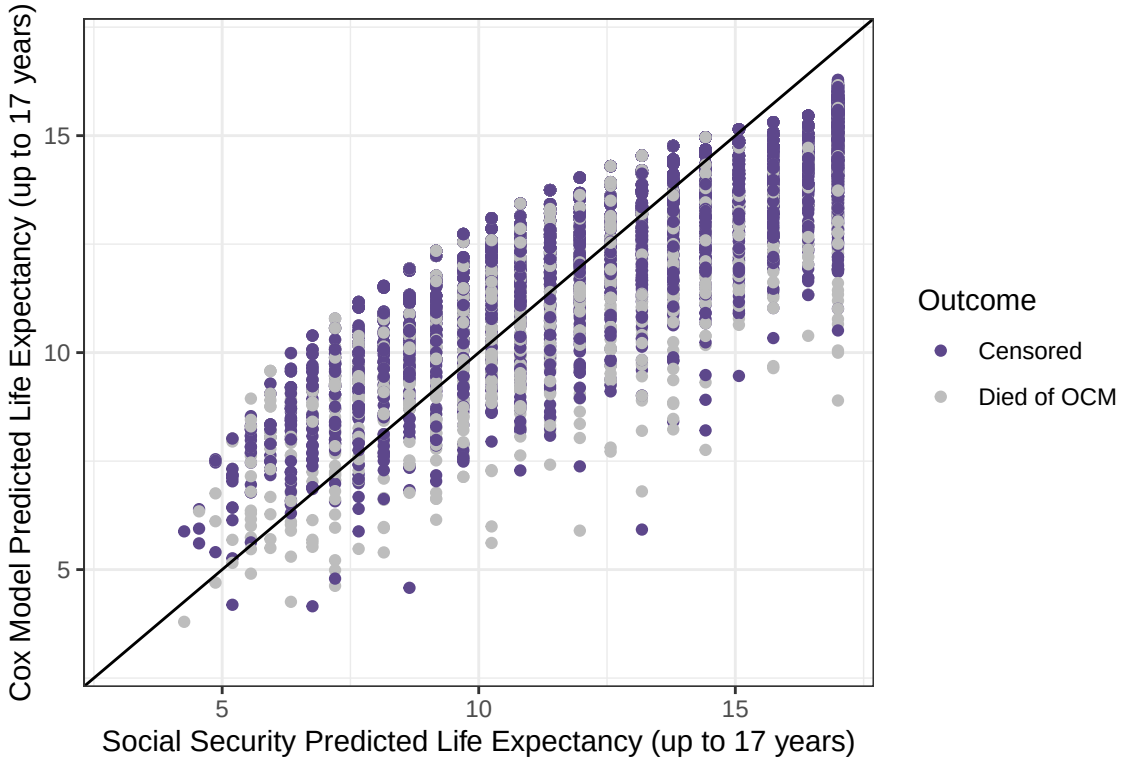

```
auc_table <- data.frame("Model" = c("SSA", "NVSS"),
                        "Year5" = round(c(ssa_roc$AUC[11],
```

Table 5: Time-Dependent AUC in PLCO

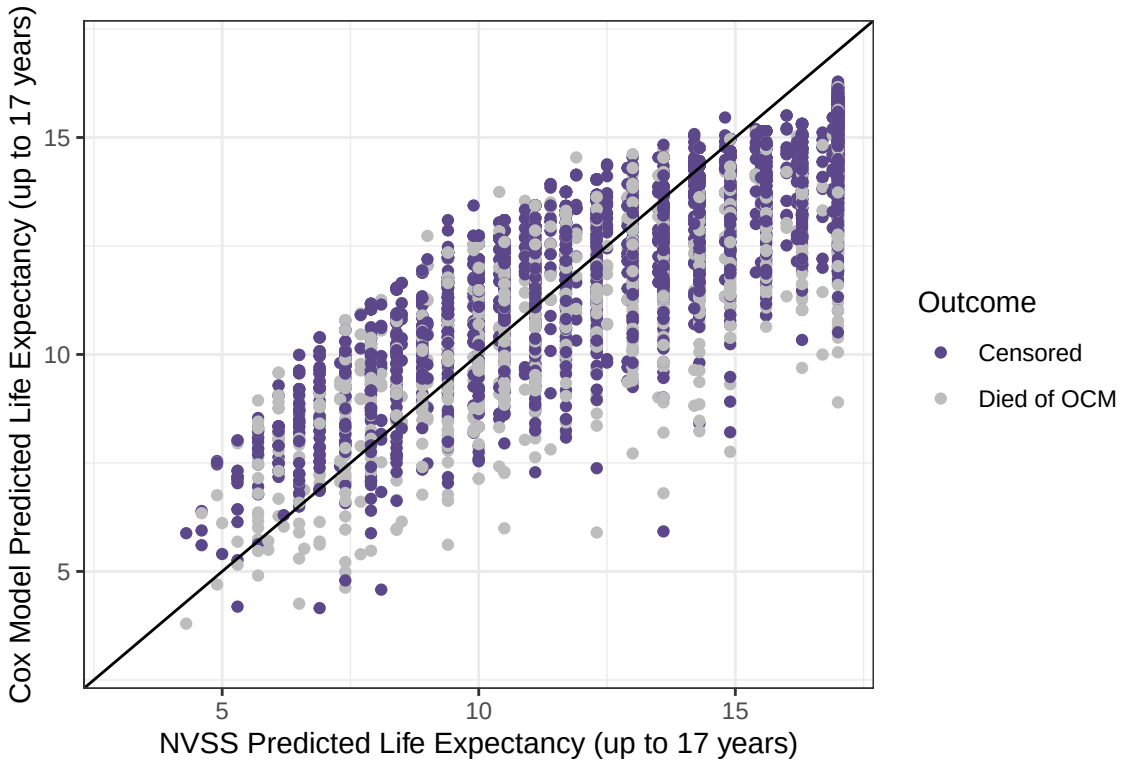
Model	Year5	Year10	Year14
SSA	0.647	0.708	0.746
NVSS	0.650	0.711	0.748

```
                                    nvss_roc$AUC[11]), digits=3),
                    "Year10" = round(c(ssa_roc$AUC[21],
                                    nvss_roc$AUC[21]), digits=3),
                    "Year14" = round(c(ssa_roc$AUC[29],
                                    nvss_roc$AUC[29]), digits=3))

kable(auc_table, caption="Time-Dependent AUC in PLCO")
```

```
km_predictions <- survfit(cox_40, plco_clean)
incs2 <- km_predictions$time[2:length(km_predictions$time)] - km_predictions$time[1:(length(km_predictio
rmst2 <- (incs2 %*% (km_predictions$surv[-nrow(km_predictions$surv),]))/12

expectancy_dat <- data.frame("Cox_40" = rmst2[1,], "SSA" = plco_clean$ssa, "NVSS" = plco_clean$nvss, "A

expectancy_dat$SSA[expectancy_dat$SSA > 17] <- 17
expectancy_dat$NVSS[expectancy_dat$NVSS > 17] <- 17

comparison_plot <- ggplot(data=expectancy_dat, aes(x = SSA, y = Cox_40, color = factor(Outcome))) + geo

comparison_plot
```



```
comparison_plot2 <- ggplot(data=expectancy_dat, aes(x = NVSS, y = Cox_40, color = factor(Outcome))) + g

comparison_plot2
```



Performance Assessment in Presence of Competing Risks

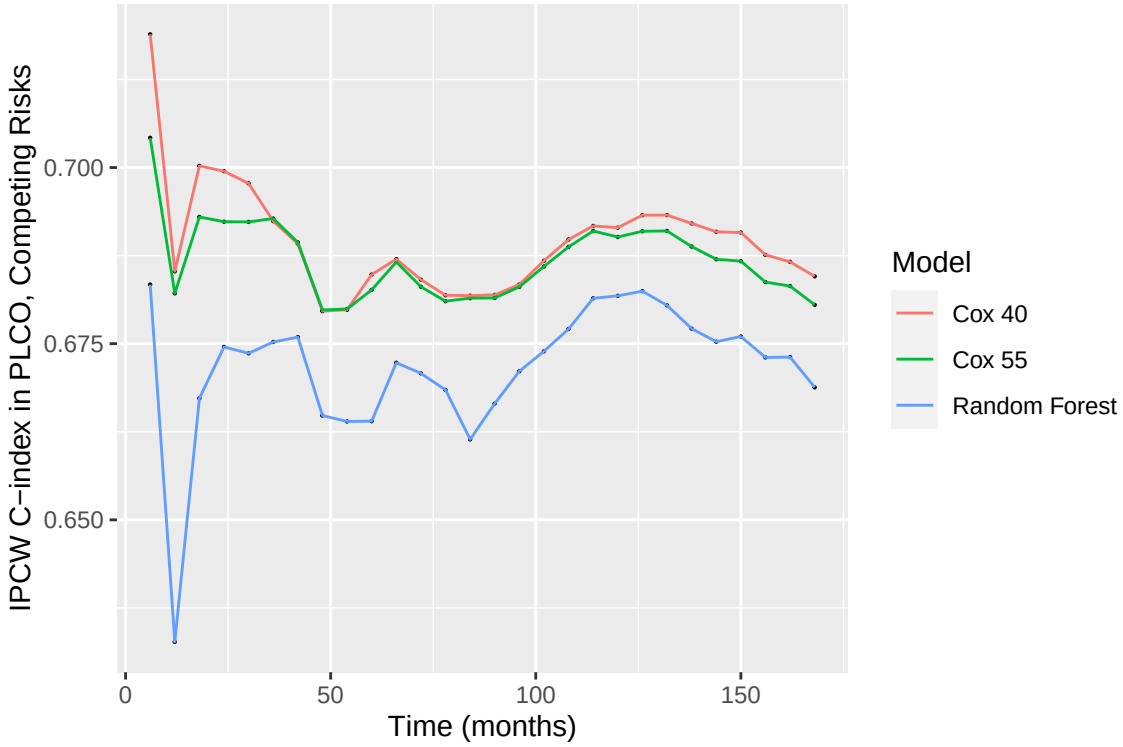
Now we redo all of the above analyses, but accounting for the competing risks using the lengthened survival time:

```
plco_clean2 <- plco_clean
plco_nf2 <- plco_nf

plco_clean2$permth_exm <- case_when(
  plco_clean$mortstat2==0 | plco_clean$mortstat2==1 ~ plco_clean$permth_exm,
  plco_clean$mortstat2==2 ~ 1000
)

plco_nf2$permth_exm <- case_when(
  plco_nf$mortstat2==0 | plco_nf$mortstat2==1 ~ plco_nf$permth_exm,
  plco_nf$mortstat2==2 ~ 1000
)

obs_surv <- Surv(plco_clean2$permth_exm, plco_clean2$mortstat)
rf_predictor <- predict(rforest_40, plco_nf2)
cox_40_predictor <- survfit(cox_40, plco_clean2)
cox_55_predictor <- survfit(cox_55, plco_clean2)

cox_40_5 <- rcorr.cens(cox_40_predictor$surv[cox_40_predictor$time==60,], obs_surv)
```

```
cox_40_10 <- rcorr.cens(cox_40_predictor$surv[cox_40_predictor$time==120,], obs_surv)
cox_40_14 <- rcorr.cens(cox_40_predictor$surv[cox_40_predictor$time==168,], obs_surv)

cox_55_5 <- rcorr.cens(cox_55_predictor$surv[cox_55_predictor$time==60,], obs_surv)
cox_55_10 <- rcorr.cens(cox_55_predictor$surv[cox_55_predictor$time==120,], obs_surv)
cox_55_14 <- rcorr.cens(cox_55_predictor$surv[cox_55_predictor$time==168,], obs_surv)

rforest_40_5 <- rcorr.cens(rf_predictor$survival[, rf_predictor$time.interest==60], obs_surv)
rforest_40_10 <- rcorr.cens(rf_predictor$survival[, rf_predictor$time.interest==120], obs_surv)
rforest_40_14 <- rcorr.cens(rf_predictor$survival[, rf_predictor$time.interest==168], obs_surv)

cox55_plco <- pec::cindex(object=cox_55, Surv(permth_exm, mortstat) ~ age_ctr_55 +
                            race2 + educ + marital2 + emphysema + diabetic +
                            stroke + smoker + underweight + overweight2 + obese2 +
                            pc + age_ctr_55*diabetic + age_ctr_55*educ +
                            age_ctr_55*marital2 + race2*educ, data = plco_clean2,
                          eval.times = times)

cox40_plco <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                            age_ctr_40 + diabetic + educ + hypertension + marital2 +
                            underweight + overweight2 + obese2 + smoker + stroke +
                            age_ctr_40*diabetic + age_ctr_40*educ +
                            age_ctr_40*hypertension + age_ctr_40*stroke + pc,
                          data=plco_clean2, eval.times = times)

forest_plco <- pec::cindex(object=rforest_40, formula = Surv(permth_exm, mortstat) ~
                             age + arthritis + bronch + diabetic + educ +
                             emphysema + hypertension + single + sep + mi_chd +
                             underweight + overweight_ex + obese + liver + black +
                             other + smoker + stroke + pc, data=plco_nf2, eval.times = times)

valid_perf <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                         "Model" = c(rep("Cox 55", 28), rep("Cox 40", 28),
                                     rep("Random Forest", 28)),
                         "C" = c(cox55_plco$AppCindex$coxph, cox40_plco$AppCindex$coxph,
                                 forest_plco$AppCindex$rfsrc))

performance_plot <- ggplot(data=valid_perf, aes(x=Time, y=C)) + geom_point(size=0.1) +
  geom_line(data=valid_perf, aes(group=Model, color=Model)) + xlab("Time (months)") +
  ylab("IPCW C-index in PLCO, Competing Risks")

performance_plot
```

Table 6: IPCW C-index in PLCO, Competing Risks

Model	Year5	Year10	Year14
Cox 55	0.683	0.690	0.681
Cox 40	0.685	0.691	0.685
Random Forest	0.664	0.682	0.669




```
subperf <- data.frame("Model" = c("Cox 55", "Cox 40", "Random Forest"),
                      "Year5" = round(c(cox55_plco$AppCindex$coxph[10],
                                        cox40_plco$AppCindex$coxph[10],
                                        forest_plco$AppCindex$rfsrc[10]), digits=3),
                      "Year10" = round(c(cox55_plco$AppCindex$coxph[20],
                                         cox40_plco$AppCindex$coxph[20],
                                         forest_plco$AppCindex$rfsrc[20]), digits=3),
                      "Year14" = round(c(cox55_plco$AppCindex$coxph[28],
                                         cox40_plco$AppCindex$coxph[28],
                                         forest_plco$AppCindex$rfsrc[28]), digits=3))

kable(subperf, caption = "IPCW C-index in PLCO, Competing Risks")
```

```
subperf2 <- data.frame("Model" = c("Cox 55", "Cox 40", "Random Forest"),
                      "Year5" = round(c(cox_55_5[1],
                                        cox_40_5[1],
                                        rforest_40_5[1]), digits=3),
                      "Year10" = round(c(cox_55_10[1],
                                         cox_40_10[1],
                                         rforest_40_10[1]), digits=3),
                      "Year14" = round(c(cox_55_14[1],
```

Table 7: No IPCW C-index in PLCO, Competing Risks

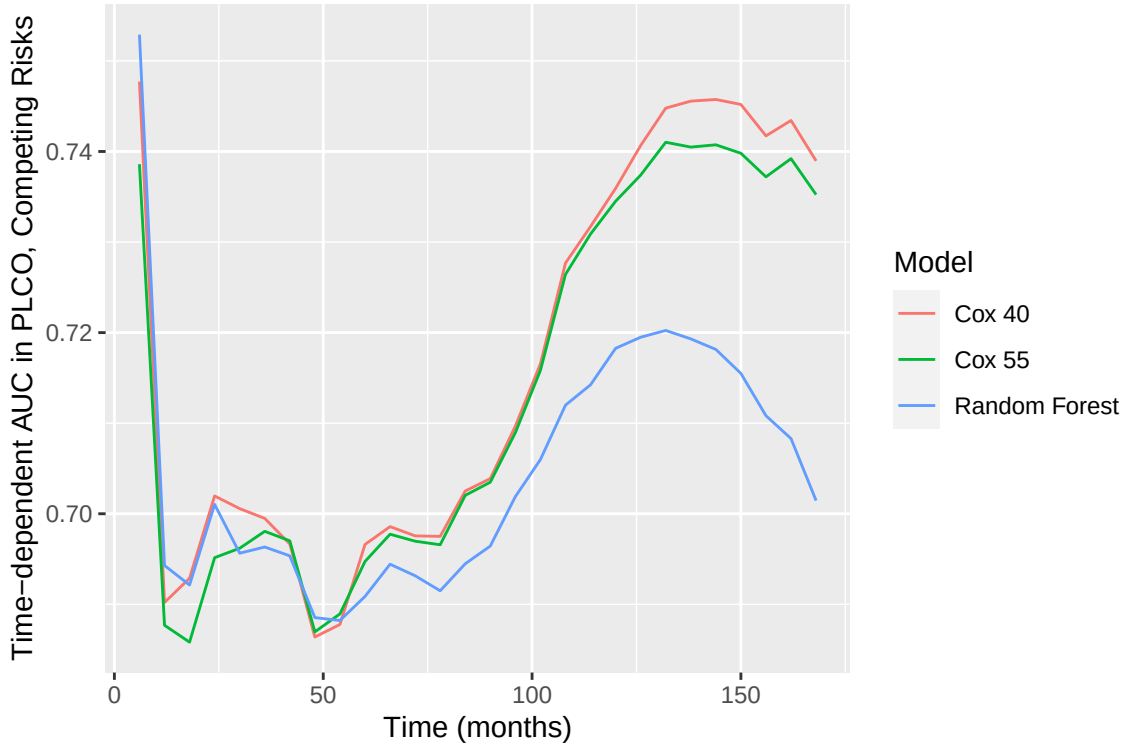
Model	Year5	Year10	Year14
Cox 55	0.680	0.680	0.680
Cox 40	0.683	0.683	0.683
Random Forest	0.652	0.670	0.673

```
                                        cox_40_14[1],
                                        rforest_40_14[1]), digits=3))

kable(subperf2, caption = "No IPCW C-index in PLCO, Competing Risks")
```

Based on C-index, our strongest performing model is the Cox model fit to men ages 40+. Now we look at time-dependent AUC:

```
cox40predict <-
  predict(object = cox_40,
          newdata = plco_clean2,
          type = "lp")
cox55predict <-
  predict(object = cox_55,
          newdata = plco_clean2,
          type = "lp")
rforestpredict <-
  predict(object=rforest_40,
          newdata = plco_nf2)

cox40roc <-
  timeROC(
    T = plco_clean2$permth_exm,
    delta = plco_clean2$mortstat,
    marker = cox40predict,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )
cox55roc <-
  timeROC(
    T = plco_clean2$permth_exm,
    delta = plco_clean2$mortstat,
    marker = cox55predict,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )
rforestroc <-
  timeROC(
    T = plco_nf2$permth_exm,
    delta = plco_nf2$mortstat,
    marker = rforestpredict$predicted,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
```

```
  )

aucdat <-
  data.frame("Time" = rep(seq(6, 168, by = 6), 3),
             "Model" = c(rep("Cox 55", 28), rep("Cox 40", 28),
                                    rep("Random Forest", 28)),
             "AUC" = c(cox55roc$AUC[-1], cox40roc$AUC[-1],
                       rforestroc$AUC[-1]))

aucplot <-
  ggplot(data = aucdat, aes(x = Time, y = AUC, group = Model, color=Model)) +
  geom_line() + xlab("Time (months)") + ylab("Time-dependent AUC in PLCO, Competing Risks")

aucplot
```




```
auc_table <- data.frame("Model" = c("Cox 55", "Cox 40", "Random Forest"),
                        "Year5" = round(c(cox55roc$AUC[11],
                                          cox40roc$AUC[11],
                                          rforestroc$AUC[11]), digits=3),
                        "Year10" = round(c(cox55roc$AUC[21],
                                           cox40roc$AUC[21],
                                           rforestroc$AUC[21]), digits=3),
                        "Year14" = round(c(cox55roc$AUC[29],
                                           cox40roc$AUC[29],
                                           rforestroc$AUC[29]), digits=3))

kable(auc_table, caption="Time-Dependent AUC in PLCO, Competing Risks")
```

Based on time-dependent AUC, the Cox model fit to men ages 40+ is still the strongest performing model. We will now focus our attention on the Cox ages 40+ model for the rest of our model validation/performance

Table 8: Time-Dependent AUC in PLCO, Competing Risks

Model	Year5	Year10	Year14
Cox 55	0.695	0.735	0.735
Cox 40	0.697	0.736	0.739
Random Forest	0.691	0.718	0.701

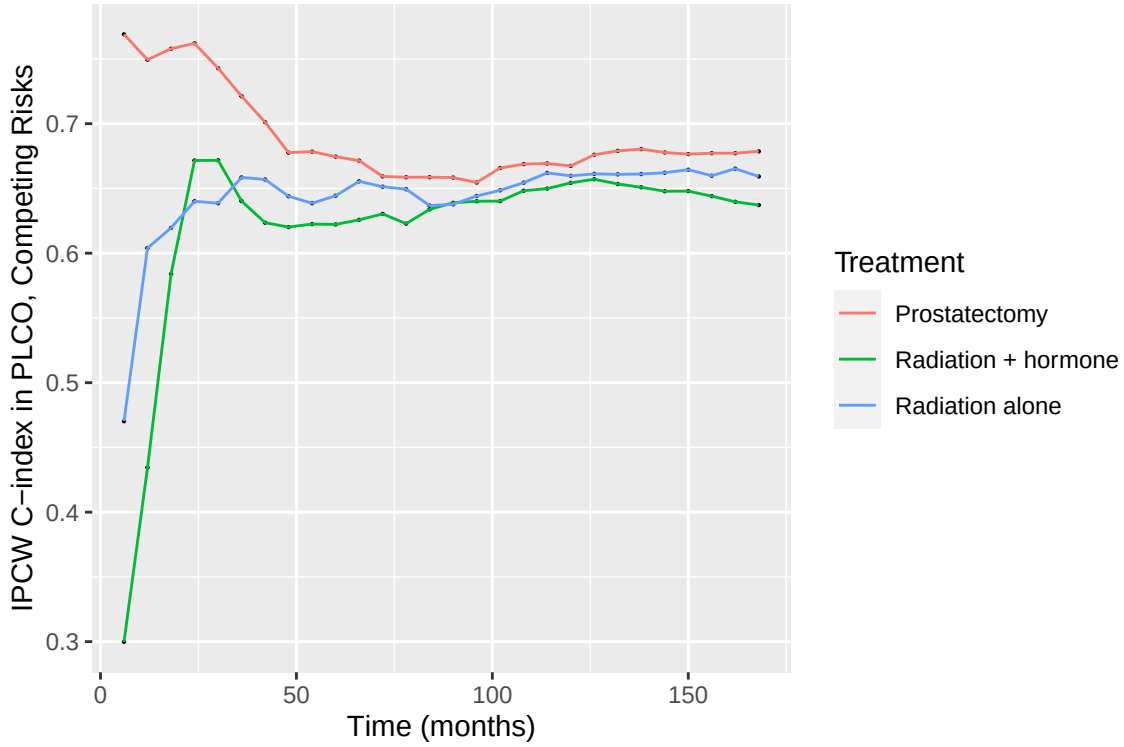
assessment.

We look at C-index and time-dependent AUC stratified by treatment group:

```
cox40_prostatectomy <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                                     age_ctr_40 + diabetic + educ + hypertension +
                                     marital2 + underweight + overweight2 + obese2 +
                                     smoker + stroke + age_ctr_40*diabetic +
                                     age_ctr_40*educ + age_ctr_40*hypertension +
                                     age_ctr_40*stroke + pc,
                                   data=plco_clean2[plco_clean2$primary_tx=="Prostatectomy",],
                                   eval.times = times)

cox40_radiation <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                                 age_ctr_40 + diabetic + educ + hypertension +
                                 marital2 + underweight + overweight2 + obese2 +
                                 smoker + stroke + age_ctr_40*diabetic +
                                 age_ctr_40*educ + age_ctr_40*hypertension +
                                 age_ctr_40*stroke + pc,
                               data=plco_clean2[plco_clean2$primary_tx=="Radiation alone",],
                               eval.times = times)

cox40_rtadt <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                             age_ctr_40 + diabetic + educ + hypertension +
                             marital2 + underweight + overweight2 + obese2 +
                             smoker + stroke + age_ctr_40*diabetic +
                             age_ctr_40*educ + age_ctr_40*hypertension +
                             age_ctr_40*stroke + pc,
                           data=plco_clean2[plco_clean2$primary_tx=="Radiation + hormone",],
                           eval.times = times)

valid_perf_trt <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                             "Treatment" = c(rep("Prostatectomy", 28),
                                             rep("Radiation alone", 28),
                                             rep("Radiation + hormone", 28)),
                             "C" = c(cox40_prostatectomy$AppCindex$coxph,
                                     cox40_radiation$AppCindex$coxph,
                                     cox40_rtadt$AppCindex$coxph))

performance_plot_trt <- ggplot(data=valid_perf_trt, aes(x=Time, y=C)) +
  geom_point(size=0.1) + geom_line(data=valid_perf_trt, aes(group=Treatment,
                                                            color=Treatment)) +
  xlab("Time (months)") + ylab("IPCW C-index in PLCO, Competing Risks")

performance_plot_trt
```

Table 9: PLCO Time-Dependent C-index, by Treatment, Competing Risks

Treatment	Year5	Year10	Year14
Prostatectomy	0.675	0.667	0.679
Radiation alone	0.644	0.660	0.659
Radiation + hormone	0.622	0.654	0.637



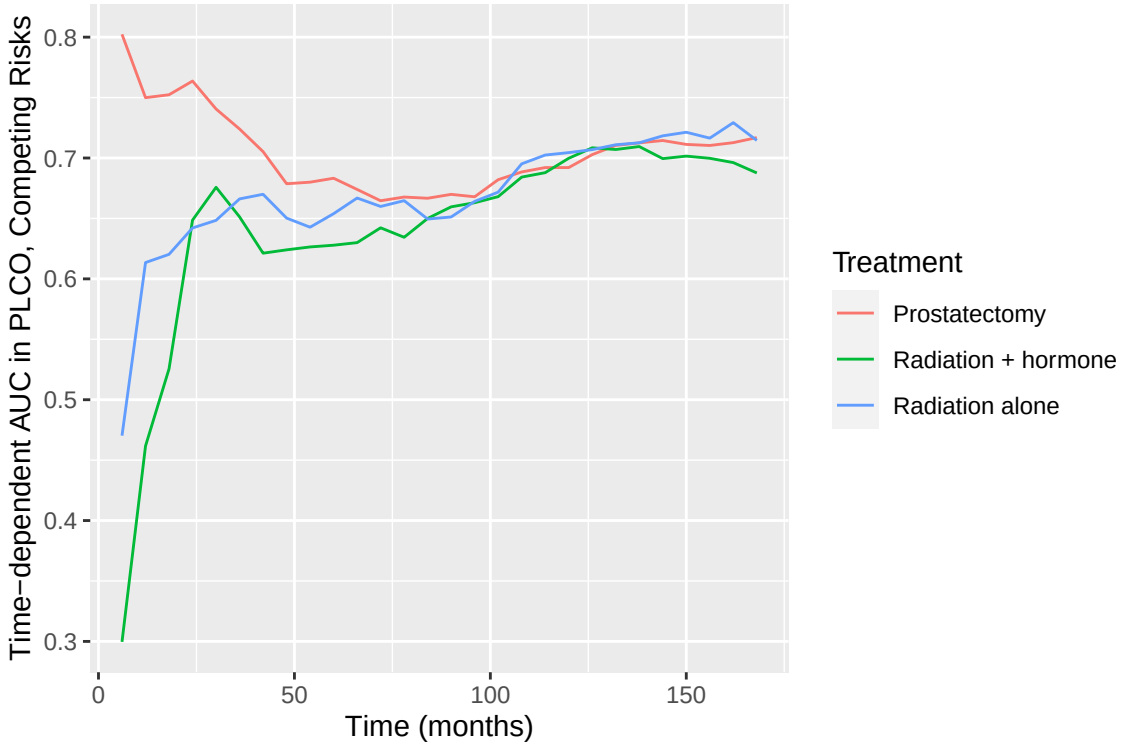

```
subperf_trt <- data.frame("Treatment" = c("Prostatectomy", "Radiation alone",
                                          "Radiation + hormone"),
                          "Year5" = round(c(cox40_prostatectomy$AppCindex$coxph[10],
                                            cox40_radiation$AppCindex$coxph[10],
                                            cox40_rtadt$AppCindex$coxph[10]), digits=3),
                          "Year10" = round(c(cox40_prostatectomy$AppCindex$coxph[20],
                                             cox40_radiation$AppCindex$coxph[20],
                                             cox40_rtadt$AppCindex$coxph[20]), digits=3),
                          "Year14" = round(c(cox40_prostatectomy$AppCindex$coxph[28],
                                             cox40_radiation$AppCindex$coxph[28],
                                             cox40_rtadt$AppCindex$coxph[28]), digits=3))

kable(subperf_trt, caption = "PLCO Time-Dependent C-index, by Treatment, Competing Risks")
```

```
cox40predict_prostatectomy <- predict(object=cox_40, newdata =
                                        plco_clean2[plco_clean2$primary_tx=="Prostatectomy",],
                                      type="lp")

cox40predict_radiation <- predict(object=cox_40, newdata =
                                    plco_clean2[plco_clean2$primary_tx=="Radiation alone",],
                                  type="lp")
```

```
cox40predict_rtadt <- predict(object=cox_40, newdata =
                                plco_clean2[plco_clean2$primary_tx=="Radiation + hormone",],
                              type="lp")

prostatectomy_roc <- timeROC(T = plco_clean2$permth_exm[plco_clean2$primary_tx=="Prostatectomy"],
                             delta = plco_clean2$mortstat[plco_clean2$primary_tx=="Prostatectomy"],
                             marker = cox40predict_prostatectomy, cause = 1,
                             weighting="marginal", times = seq(0, 168, by=6))

radiation_roc <- timeROC(T = plco_clean2$permth_exm[plco_clean2$primary_tx=="Radiation alone"],
                         delta = plco_clean2$mortstat[plco_clean2$primary_tx=="Radiation alone"],
                         marker = cox40predict_radiation, cause = 1,
                         weighting="marginal", times = seq(0, 168, by=6))

rtadt_roc <- timeROC(T = plco_clean2$permth_exm[plco_clean2$primary_tx=="Radiation + hormone"],
                     delta = plco_clean2$mortstat[plco_clean2$primary_tx=="Radiation + hormone"],
                     marker = cox40predict_rtadt, cause = 1, weighting="marginal",
                     times = seq(0, 168, by=6))

aucdat_trt <- data.frame("Time" = rep(seq(6, 168, by=6), 3),
                         "AUC" = c(prostatectomy_roc$AUC[-1], radiation_roc$AUC[-1],
                                   rtadt_roc$AUC[-1]),
                         "Treatment" = c(rep("Prostatectomy", 28),
                                         rep("Radiation alone", 28),
                                         rep("Radiation + hormone", 28)))

aucplot_trt <- ggplot(data=aucdat_trt, aes(x=Time, y=AUC, group=Treatment,
                                           color=Treatment)) + geom_line() +
  xlab("Time (months)") + ylab("Time-dependent AUC in PLCO, Competing Risks")

aucplot_trt
```

Table 10: Time-Dependent AUC in PLCO, by Treatment, Competing Risks

Years	Prostatectomy	Radiation	Radiation_hormone
5	0.683	0.654	0.628
10	0.692	0.704	0.700
14	0.717	0.715	0.688




```
auc_table_trt <- data.frame("Years" = c(5, 10, 14),
                            "Prostatectomy" = round(c(prostatectomy_roc$AUC[11],
                                                      prostatectomy_roc$AUC[21],
                                                      prostatectomy_roc$AUC[29]),
                                                    digits = 3),
                            "Radiation" = round(c(radiation_roc$AUC[11],
                                                  radiation_roc$AUC[21],
                                                  radiation_roc$AUC[29]),
                                                digits = 3),
                            "Radiation_hormone" = round(c(rtadt_roc$AUC[11],
                                                          rtadt_roc$AUC[21],
                                                          rtadt_roc$AUC[29]),
                                                        digits = 3))

rownames(auc_table_trt) <- NULL
kable(auc_table_trt, caption="Time-Dependent AUC in PLCO, by Treatment, Competing Risks")
```

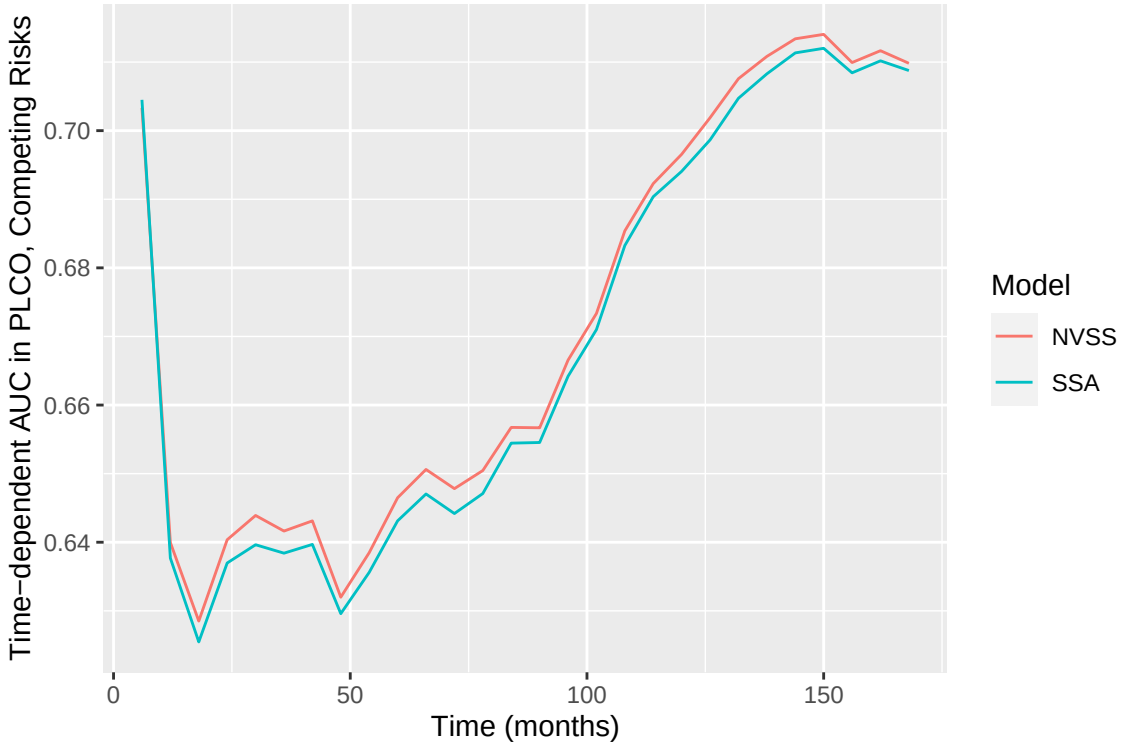
We compare to the SSA and NVSS life tables:

```
ssa <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/ssa_2000.csv")
ssa$age <- seq(0, 119, by = 1)
```

```r
nvss_black <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_blackma
nvss_white <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_whitema
nvss_other <- read_csv("/Users/ecchase/Desktop/Research/Matt Prostate OCM/PCOtherCause/Data/nvss_allmal
nvss_other <- nvss_other[-102,]

nvss <- data.frame("Age" = seq(0, 100, by = 1), "White" = nvss_white$Expectancy, "Black" = nvss_black$E

plco_clean$ssa <- NA
plco_clean$nvss <- NA
for (i in 1:nrow(plco_clean)){
  plco_clean$ssa[i] <- ssa$Expectancy[which(ssa$age==plco_clean$age[i])]
  if (plco_clean$race2[i]=="NHW"){
    plco_clean$nvss[i] <- nvss$White[which(nvss$Age==plco_clean$age[i])]
  } else if (plco_clean$race2[i]=="NHB"){
    plco_clean$nvss[i] <- nvss$Black[which(nvss$Age==plco_clean$age[i])]
  } else if (plco_clean$race2[i]=="Other"){
    plco_clean$nvss[i] <- nvss$Other[which(nvss$Age==plco_clean$age[i])]
  }
}

ssa_roc <-
  timeROC(
    T = plco_clean2$permth_exm,
    delta = plco_clean2$mortstat,
    marker = 1/plco_clean$ssa,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

nvss_roc <-
  timeROC(
    T = plco_clean2$permth_exm,
    delta = plco_clean2$mortstat,
    marker = 1/plco_clean$nvss,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

aucdat <-
  data.frame("Time" = rep(seq(6, 168, by = 6), 2),
             "Model" = c(rep("SSA", 28), rep("NVSS", 28)),
             "AUC" = c(ssa_roc$AUC[-1], nvss_roc$AUC[-1]))

aucplot <-
  ggplot(data = aucdat, aes(x = Time, y = AUC, group = Model, color=Model)) +
  geom_line() + xlab("Time (months)") + ylab("Time-dependent AUC in PLCO, Competing Risks")

aucplot
```

Table 11: Time-Dependent AUC in PLCO, Competing Risks

Model	Year5	Year10	Year14
SSA	0.643	0.694	0.709
NVSS	0.646	0.697	0.710




```
auc_table <- data.frame("Model" = c("SSA", "NVSS"),
                        "Year5" = round(c(ssa_roc$AUC[11],
                                          nvss_roc$AUC[11]), digits=3),
                        "Year10" = round(c(ssa_roc$AUC[21],
                                           nvss_roc$AUC[21]), digits=3),
                        "Year14" = round(c(ssa_roc$AUC[29],
                                           nvss_roc$AUC[29]), digits=3))

kable(auc_table, caption="Time-Dependent AUC in PLCO, Competing Risks")
```

PCSM Prediction

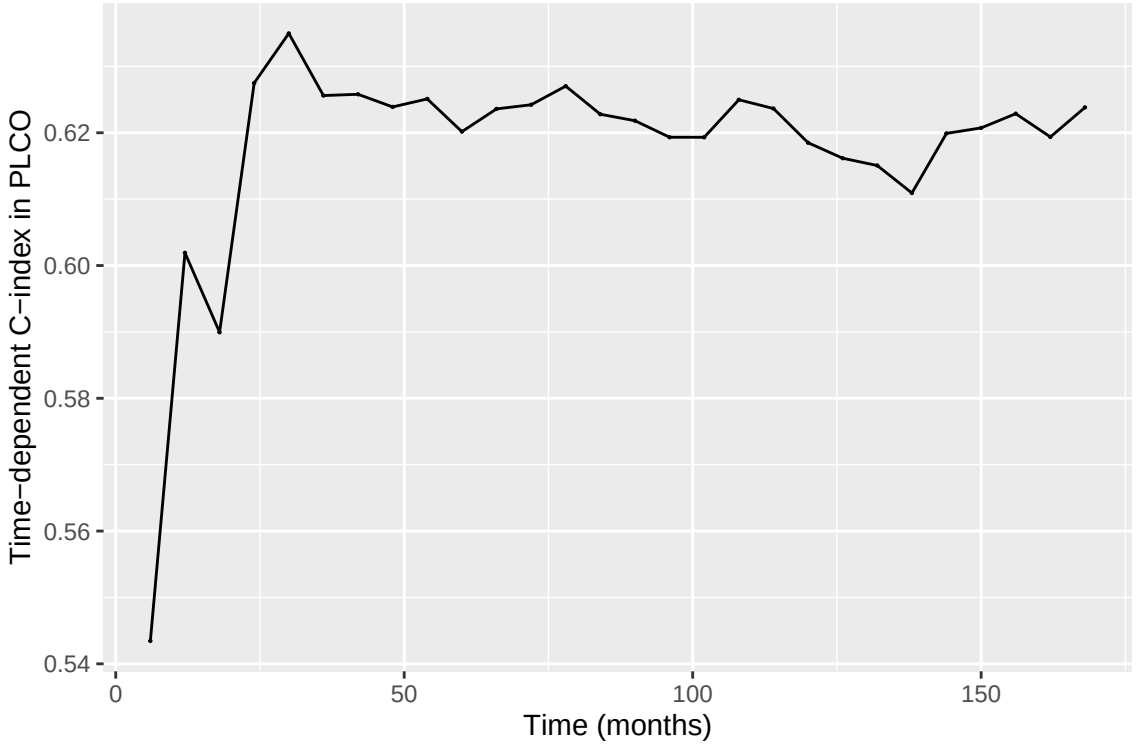
We get the C-index for the linear predictor for PCSM:

```
#Indicator for death from prostate cancer (other cause mortality censored)
plco_clean$mortstat <- case_when(
  plco_clean$mortstat2==2 ~ 1,
  plco_clean$mortstat2==1 | plco_clean$mortstat2==0 ~ 0
)

times <- seq(6, 168, by=6)
```

Table 12: Time-dependent C-index for PCSM

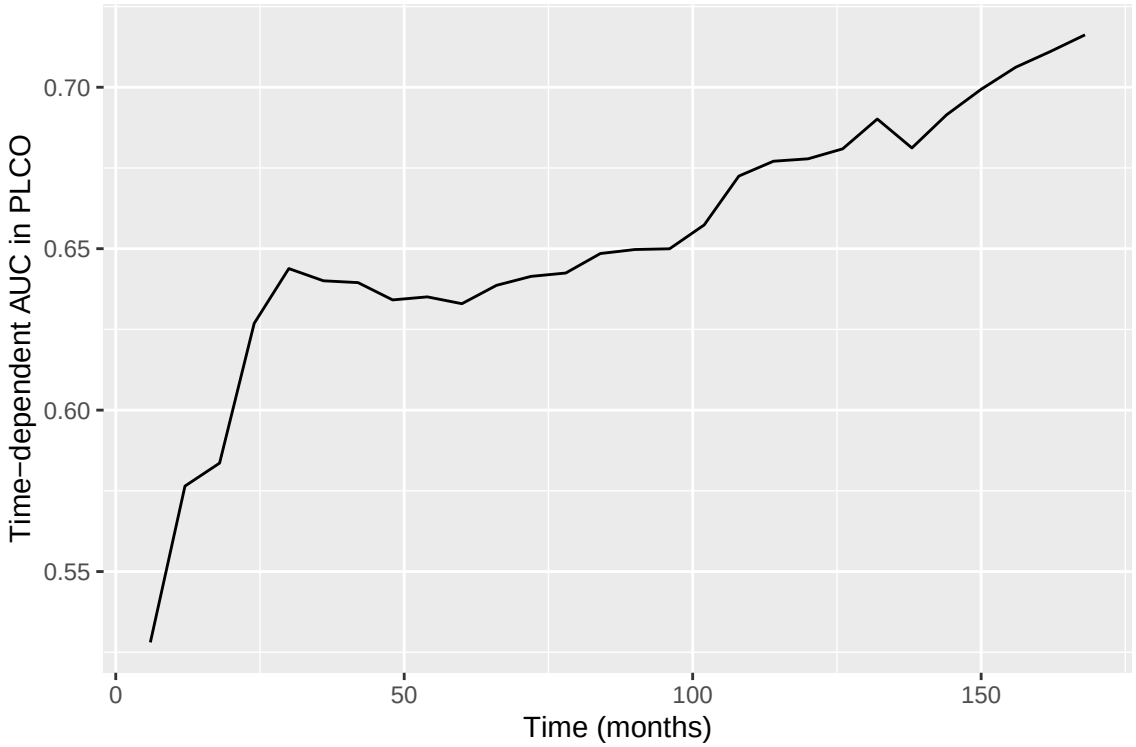
Model	Year5	Year10	Year14
Cox 40	0.62	0.619	0.624

```
cox40_plco_pcsm <- pec::cindex(object=cox_40, formula = Surv(permth_exm, mortstat) ~
                           age_ctr_40 + diabetic + educ + hypertension + marital2 +
                           underweight + overweight2 + obese2 + smoker + stroke +
                           age_ctr_40*diabetic + age_ctr_40*educ +
                           age_ctr_40*hypertension + age_ctr_40*stroke + pc,
                         data=plco_clean, eval.times = times)

valid_perf <- data.frame("Time" = seq(6, 168, by=6),
                         "C" = cox40_plco_pcsm$AppCindex$coxph)

performance_plot <- ggplot(data=valid_perf, aes(x=Time, y=C)) + geom_point(size=0.1) +
  geom_line(data=valid_perf) + xlab("Time (months)") + ylab("Time-dependent C-index in PLCO")

performance_plot
```




```
subperf <- data.frame("Model" = "Cox 40",
                      "Year5" = round(cox40_plco_pcsm$AppCindex$coxph[10], digits=3),
                      "Year10" = round(cox40_plco_pcsm$AppCindex$coxph[20], digits=3),
                      "Year14" = round(cox40_plco_pcsm$AppCindex$coxph[28], digits=3))

kable(subperf, caption = "Time-dependent C-index for PCSM")
```

```r
cox40predict <-
  predict(object = cox_40,
          newdata = plco_clean,
          type = "lp")

cox40roc <-
  timeROC(
    T = plco_clean$permth_exm,
    delta = plco_clean$mortstat,
    marker = cox40predict,
    cause = 1,
    weighting = "marginal",
    times = seq(0, 168, by = 6)
  )

aucdat <-
  data.frame("Time" = seq(6, 168, by = 6),
             "AUC" = cox40roc$AUC[-1])

aucplot <-
  ggplot(data = aucdat, aes(x = Time, y = AUC)) + geom_line() +
  xlab("Time (months)") + ylab("Time-dependent AUC in PLCO")

aucplot
```




```r
auc_table <- data.frame("Model" = "Cox 40",
                        "Year5" = round(cox40roc$AUC[11], digits=3),
                        "Year10" = round(cox40roc$AUC[21], digits=3),
                        "Year14" = round(cox40roc$AUC[29], digits=3))
```

Table 13: Time-Dependent AUC for PCSM

	Model	Year5	Year10	Year14
t=60	Cox 40	0.633	0.678	0.716

```
kable(auc_table, caption="Time-Dependent AUC for PCSM")
```