R code for Survival Lecture 4

Contents

Cause-specific hazard regression

- Load all the R packages

```
packages_to_load <- c("haven", "survival", "survminer", "pander", "gtsummary", "tidycmprsk", "ggsurvfit
 #"cmprsk",
lapply(packages_to_load, library, character.only = TRUE)
```

Load and check the MrOS dataset

```
mros <- read_dta("mros.dta")
head(mros)
```

Cox model for cause-specific hazard function (for fracture)

```
# Recode the status variable into a factor for event types
# 0 = censored, 1 = fracture (event of interest),
# 2 = death without fracture (competing risk)
mros$event <- factor(mros$status, 0:2, c("censor", "fracture", "death"))

# Create weight in 10 kg units
mros$weight10kg <- mros$weight / 10

# Convert bmd3 to a factor with levels labeled 1, 2, 3 tertiles of BMD
mros$bmd3 <- factor(mros$bmd3, levels=1:3, labels=1:3)
# Set up the survival object and fit a proportional cause-specific hazards model
cox_fracture <- coxph(Surv(years, event == "fracture") ~ bmd3 + weight10kg, data = mros)

# Display the model results
# Note: exp(coef) gives the cause-specific hazard ratios for the covariates
summary(cox_fracture)
```

Call: coxph(formula = Surv(years, event == “fracture”) ~ bmd3 + weight10kg, data = mros)

n= 5994, number of events= 531

```
           coef exp(coef) se(coef)      z Pr(>|z|)
```

bmd32 -0.86900 0.41937 0.10681 -8.136 4.1e-16 ***bmd33 -1.11165 0.32902 0.12050 -9.225 < 2e-16***
weight10kg 0.04138 1.04225 0.03605 1.148 0.251
— Signif. codes: 0 ‘’ ***0.001*** ’’ *0.01* ’’ 0.05 ‘.’ 0.1 ’ ’ 1

```
       exp(coef) exp(-coef) lower .95 upper .95
```

bmd32 0.4194 2.3845 0.3402 0.5170 bmd33 0.3290 3.0394 0.2598 0.4167 weight10kg 1.0422 0.9595 0.9711 1.1186

Concordance= 0.623 (se = 0.012) Likelihood ratio test= 121.2 on 3 df, p=<2e-16 Wald test = 120.9 on 3 df, p=<2e-16 Score (logrank) test = 130.6 on 3 df, p=<2e-16

Characteristic	cHR	95% CI	p-value
BMD Tertile			
1	—	—	
2	0.419	0.340, 0.517	0.000
3	0.329	0.260, 0.417	0.000
Weight (per 10 kg)	1.042	0.971, 1.119	0.251

```
# A nice table
cox_fracture %>%
  tbl_regression(
    label = list(bmd3 = "BMD Tertile", weight10kg = "Weight (per 10 kg)"),
    exponentiate = TRUE,
    estimate_fun = purrr::partial(style_ratio, digits = 3),
    pvalue_fun = purrr::partial(style_sigfig, digits = 3)
  ) %>%
  modify_header(estimate = "**cHR**") %>%  # Custom column label
  bold_labels() %>%
  modify_footnote(everything() ~ NA, abbreviation = TRUE) #supress footnote
```

Cox model for cause-specific hazard function (for death without fracture)

```
# Set up the survival object and fit a proportional cause-specific hazards model
cox_death <- coxph(Surv(years, event == "death") ~ bmd3 + weight10kg, data = mros)

# Display the model results
# Note: exp(coef) gives the cause-specific hazard ratios for the covariates
summary(cox_death)
```

```
## Call:
## coxph(formula = Surv(years, event == "death") ~ bmd3 + weight10kg,
##     data = mros)
##
##   n= 5994, number of events= 657
##
##                coef exp(coef) se(coef)      z Pr(>|z|)
## bmd32      -0.05364   0.94778  0.09442 -0.568 0.569993
## bmd33      -0.19111   0.82604  0.10426 -1.833 0.066795 .
## weight10kg -0.12982   0.87825  0.03368 -3.855 0.000116 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
##            exp(coef) exp(-coef) lower .95 upper .95
## bmd32         0.9478      1.055    0.7877    1.1404
## bmd33         0.8260      1.211    0.6734    1.0133
## weight10kg    0.8782      1.139    0.8221    0.9382
##
## Concordance= 0.564  (se = 0.012 )
## Likelihood ratio test= 27.64  on 3 df,   p=4e-06
```

Characteristic	cHR	95% CI	p-value
BMD Tertile			
1	—	—	
2	0.948	0.788, 1.140	0.570
3	0.826	0.673, 1.013	0.067
Weight (per 10 kg)	0.878	0.822, 0.938	0.000

```
## Wald test            = 26.65  on 3 df,   p=7e-06
## Score (logrank) test = 26.72  on 3 df,   p=7e-06
```

```
# A nice table
cox_death %>%
  tbl_regression(
                 label = list(bmd3 = "BMD Tertile", weight10kg = "Weight (per 10 kg)"),
                 exponentiate = TRUE,
                 estimate_fun = purrr::partial(style_ratio, digits = 3),
                 pvalue_fun = purrr::partial(style_sigfig, digits = 3)) %>%
  modify_header(estimate = "**cHR**") %>%  # Replace default "log(HR)" header
  bold_labels() %>%
  modify_footnote(everything() ~ NA, abbreviation = TRUE) #supress footnote
```

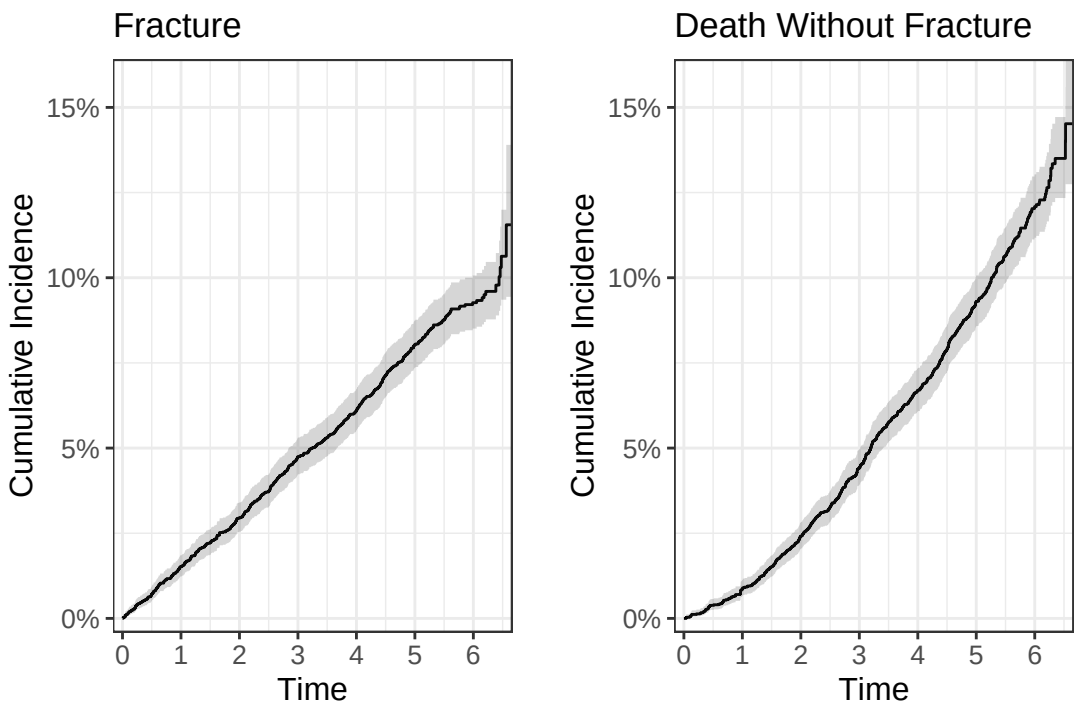
CIF-based analysis

Cumulative incidence functions

```
p1 <- cuminc(Surv(years, event) ~ 1, mros) %>%
  ggcuminc(outcome = "fracture") +
  ggtitle("Fracture") +
  coord_cartesian(xlim = c(0, 6.5), ylim = c(0, 0.16))  +
  add_confidence_interval() +
  add_risktable() +
  scale_ggsurvfit()


p2 <- cuminc(Surv(years, event) ~ 1, mros) %>%
  ggcuminc(outcome = "death") +
  ggtitle("Death Without Fracture") +
  coord_cartesian(xlim = c(0, 6.5), ylim = c(0, 0.16))  +
  add_confidence_interval() +
  add_risktable() +
  scale_ggsurvfit()

wrap_elements(p1) + wrap_elements(p2)
```



Characteristic	sHR	95% CI	p-value
BMD Tertile			
1	—	—	
2	0.422	0.343, 0.519	0.000
3	0.337	0.267, 0.425	0.000
Weight (per 10 kg)	1.048	0.975, 1.126	0.200

Fine-Gray models for cumulative incidence function

- Subdistribution hazard ratios for fracture

```
# Fit a Fine-Gray model for the subdistribution hazard of fracture
# failcode = "fracture" assumes mros$event is a factor with levels including "fracture"
fg_fracture <- crr(Surv(years, event) ~ bmd3 + weight10kg, failcode = "fracture", mros)

# Generate a polished regression summary table using gtsummary
fg_fracture %>%
  tbl_regression(
    label = list( bmd3 = "BMD Tertile", weight10kg = "Weight (per 10 kg)" ),
    exponentiate = TRUE,  # Exponentiate coefficients to show sHRs
    estimate_fun = purrr::partial(style_ratio, digits = 3),
    pvalue_fun = purrr::partial(style_sigfig, digits = 3)
  ) %>%
  modify_header(
    estimate = "**sHR**"  # Rename the "estimate" column header to "sHR"
  ) %>%
  bold_labels() %>%  # Bold the variable labels for better visual hierarchy
  modify_footnote(
    everything() ~ NA, abbreviation = TRUE  # Suppress all footnotes, including default abbreviations
  )
```

- Subdistribution hazard ratios for death

```
# Fit Fine-Gray competing risks model
fg_death <- crr(Surv(years, event) ~ bmd3 + weight10kg, failcode = "death", mros)

fg_death %>%
  tbl_regression(
                 label = list(bmd3 = "BMD Tertile", weight10kg = "Weight (per 10 kg)"),
                 exponentiate = TRUE,
                 estimate_fun = purrr::partial(style_ratio, digits = 3),
                 pvalue_fun = purrr::partial(style_sigfig, digits = 3)) %>%
  modify_header(estimate = "**sHR**") %>%  # Replace default "log(HR)" header
  bold_labels()%>%
  modify_footnote(everything() ~ NA, abbreviation = TRUE) #supress footnote
```

Characteristic	sHR	95% CI	p-value
BMD Tertile			
1	—	—	
2	1.009	0.837, 1.216	0.920
3	0.886	0.723, 1.086	0.240
Weight (per 10 kg)	0.878	0.816, 0.945	0.001