

Biostatistics 209, Lab #2

0. Background

The purpose of this lab is to give you practice in addressing interaction and confounding in Cox regression models.

1. Download Data

- Download the dataset `lab2-pbc.dta` from the website.

Double click on the file to open it in `stata`. The dataset is based nearly 10 years of follow of 312 subject with primary biliary cirrhosis around 20 predictor variables were collected to develop a natural history of survival in subjects with PBC.

2. Confounding

- Examine the effect of `sex` (1=female, 0=male) on survival both graphically and in a Cox model

```
sts graph, by(sex)
stcox sex
```

- Fit a model adjusting for the effect of sex on the following possible confounding variables: log bilirubin (`logbili`), age and triglycerides (`trigli`)

```
stcox sex age logbili trigli
```

- Interpret the results. Do these variables appear to confound the relationship between sex and mortality?

3. Interaction

Consider an interaction between `sex` and baseline level of copper in the urine (`copper`).

- Generate a product term

```
gen sex_cop=sex*copper
```
- Fit the interaction model

```
stcox sex copper sex_cop
```
- Does there appear to be a significant interaction?

- Consider the following tables to derive the `lincom` statements for **a 10 unit change** in urine copper for female and male subjects

Female Subjects

	sex	copper	sex_cop
copper = x+10			
copper = x			

Male Subjects

	sex	copper	sex_cop
copper = x+10			
copper = x			

- Verify that the correct `lincom` for the 10-unit increase in copper for female subjects is `lincom 10*copper + 10* sex_cop, hr`
- Verify that the correct `lincom` for the 10-unit increase in copper for male subjects is `lincom 10*copper, hr`
- Interpret the results you obtain when you run the `lincom` commands above.
- Consider the following tables to derive the relative hazard between the sexes at a copper of 17, 73 and 251 (the 5%, 50%, and 95%-tile of copper values)

Copper of 17

	sex	copper	sex_cop
Female			
Male			

Copper of 73

	sex	copper	sex_cop
Female			
Male			

Copper of 251

	sex	copper	sex_cop
Female			
Male			

- Verify the appropriate `lincom` statements are
`lincom sex + 17* sex_cop, hr`
`lincom sex + 73* sex_cop, hr`
`lincom sex + 251* sex_cop, hr`
- Interpret the results you obtain when you run the `lincom` commands above.
- It can be helpful to graph the interaction. It is most easily visualized **on the log hazard scale**.
`stcox sex copper sex_cop` *(re run the Cox regression)*
`predict out, xb` *(calculate the log hazard and put them in variable "out")*
- Now, use the Stata menus to graphs the log hazards for female and male subjects by copper.
 - Go to, "Graphics", "Twoway graph"
 - Click "Create", select "Basic Plot" and "Line" as plot type
 - Y-variable: `out` , X-variable: `copper` Click on box "Sort on x variable"
 - Click on the tab "if/in", fill in "**sex=0**" and click "Accept"
 - Click "Edit"
 - Click on "Line Properties" , select "Red" for Line Color and click "Accept"
 - Click "Accept"

- Click “Create” again (*repeating the above steps for another line in different color*), select “Basic Plot” and “Line” as plot type
- Y-variable: `out` , X-variable: `copper` Click on box “Sort on x variable”
- Click on the tab “if/in”, fill in “**sex==1**” and click “Accept”
- Look at the Tabs at the Top
- Click on “Y-axis” , fill in **Log Hazard Ratio** under Title
- Click on Legend, Check “Override Default Keys”
- Fill in **1 "Male" 2 "Female"** under “Specify order of keys.....”
- Click "submit"
- The specifications on the previous page yield the following command


```
twoway (line out copper if sex==0, lcolor(red)) (line out copper if
sex==1, lcolor(blue)), ytitle(Log Hazard Ratio) legend(order(1 "Male"
2 "Female"))
```

Feel free to experiment with other options to further customize the graph.

4. Adjusted Survival Curves

Return to the issue we considered in (2), the effect of sex on mortality after adjusting for log bilirubin, age and triglycerides.

- Rerun the adjusted regression and save the baseline survival in the variable “`surv0`”


```
stcox logbili trigli sex age, basesurv(surv0)
```
- Graph the adjusted survival curve


```
stcurve, survival at1(sex=1) at2(sex=0)
```
- Regraph the unadjusted Kaplan-Meiers for comparison


```
sts graph, by(sex)
```