Biostatistics 209, Lab #2

1. Background

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

2. Data

- Use the dataset `pbc.dta` from the website (for Homework #1).

3. Confounding

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

```
stset years, failure(status)   -- don't forget to declare the data as survival!!
sts graph, by(sex)
stcox sex
```

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

```
stcox sex age logbili trigli
```

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

4. Interaction

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

- Fit the interaction model
  `stcox sex##c.copper, nolog`
- Does there appear to be a significant interaction?
- Consider the use of the following tables to derive the `lincom` statements for **a 10 unit change** in urine copper for female and male subjects

	Female Subjects			*Male Subjects*		
	sex	**copper**	**interaction**	**sex**	**copper**	**interaction**
copper = x+10	1	x+10	x+10	0	x+10	0
copper = x	1	x	x	0	x	0
difference	0	10	10	0	10	0

- Verify that the correct `lincom` for the 10-unit increase in copper

  for male subjects is `lincom 10*copper, hr`
  for female subjects is `lincom 10*copper + 10* 1.sex#c.copper, hr`

- Interpret the results you obtain when you run the `lincom` commands above.
- Fill out the following tables to derive the relative hazard between the sexes at a copper of 17, 73 and 256 (the 5%, 50%, and 95%-ile of copper values)

Copper of	***17***			***73***		
	sex	**copper**	**interaction**	**sex**	**copper**	**interaction**
Female						
Male						
difference						

Copper of	***256***		
	sex	**copper**	**interaction**
Female			
Male			
difference			

- Verify the appropriate `lincom` statements are

```
lincom 1.sex +  17* 1.sex#c.copper, hr
lincom 1.sex +  73* 1.sex#c.copper, hr
lincom 1.sex + 256* 1.sex#c.copper, 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**.

```
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 on “X axis” and then click on “Reference lines”
- Check “Add lines to graph at specified x axis values” and type “17 73 153 256” in box
- Pattern select “Dash dot”
- Color select “Green”
- Click "submit"

- The specifications on the previous page yield the following command

```
twoway (line out copper if sex==0, sort lcolor(red)) (line out copper if
sex==1, sort lcolor(blue)), ytitle(Log Hazard Ratio) xline(17 73 153
256, lpattern(dash_dot) lcolor(green)) legend(order(1 "Male" 2
"Female"))
```

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

5. Adjusted Survival Curves

Return to the issue we considered in question 3, the effect of sex on mortality after adjusting for log bilirubin, age and triglycerides.

- Re-run (or restore) the adjusted regression

```
stcox sex age logbili trigli
```

- Graph the adjusted survival curve

```
stcurve, survival at1(sex=0) at2(sex=1)
```

- Regraph the unadjusted Kaplan-Meiers for comparison

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