Adjusted Survival Curves

Effect of Sex: PBC data

(unadjusted comparison)

```
use pbc.dat
stset years,failure(status)
sts graph, by(sex)
```

```
stcox sex
```

(Cox model fit)

Cox Proportional Hazards Model

$x = (x_1, \ldots, x_p)$: the set of predictors

$h_0(t)$ = baseline hazard function

= hazard function when all predictors equal zero

$h(t|x) = h_0(t) \exp(\beta_1 x_1 + \ldots + \beta_p x_p)$

= hazard function of someone with predictors

- In Cox model we see estimates of $\exp(\beta_p)$
- In background, Stata calculates estimates of $h_0(t)$

Under the Cox Model

Consider $S(t|x)$: survival function (event-free proportion at time t) for someone with predictors x

$S_0(t)$ = baseline survival function
= survival function when all predictors equal zero

$$S(t|x) = S_0(t)^{\exp(\beta_1 x_1 + \ldots + \beta_p x_p)}$$

(β's are the coefficients from the Cox model)

- In Cox model we see estimates of $\exp(\beta_p)$
- In background, Stata calculates estimates of $S_0(t)$

Adjusted Survival Curves

```
. stcox sex copper

------------------------------------------------------------------------------
          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         sex |   1.171796   .2996835     0.62   0.535     .7098385    1.934391
      copper |   1.006935   .0008328     8.36   0.000     1.005304    1.008569
------------------------------------------------------------------------------
```

x_1: sex;

x_2: copper

Cox model: $h(t|x) = h_0(t) \exp(\beta_1 x_1 + \beta_2 x_2)$

Survival function: $S(t|x) = S_0(t)^{\exp(\beta_1 x_1 + \ldots + \beta_2 x_2)}$

Adjusted Survival Curves

```
. stcox sex copper

------------------------------------------------------------------------------
          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         sex |   1.171796   .2996835     0.62   0.535     .7098385    1.934391
      copper |   1.006935   .0008328     8.36   0.000     1.005304    1.008569
------------------------------------------------------------------------------
```

Coefficient for sex: $\widehat{\beta}_1$ = log(HR) = log(1.17) =0.16

Coefficient for copper: $\widehat{\beta}_2$ = log(1.01) = 0.01

x_1: sex;

x_2: copper

Cox model: $h(t|x) = h_0(t)\, \exp(\beta_1 x_1 + \beta_2 x_2)$

Survival function: $S(t|x) = S_0(t)^{\exp(\beta_1 x_1 + \beta_2 x_2)}$

Adjusted Survival Curves

```
. stcox sex copper

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          _t | Haz. Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
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------------------------------------------------------------------------------
```

```
. stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
```

stcurve: gives predicted curves

survival: graph survival (not hazard default)

at1: (predictor values for curve 1)

at2: (predictor values for curve 2)

Note that the copper default is fixed at overall mean(=97.6)

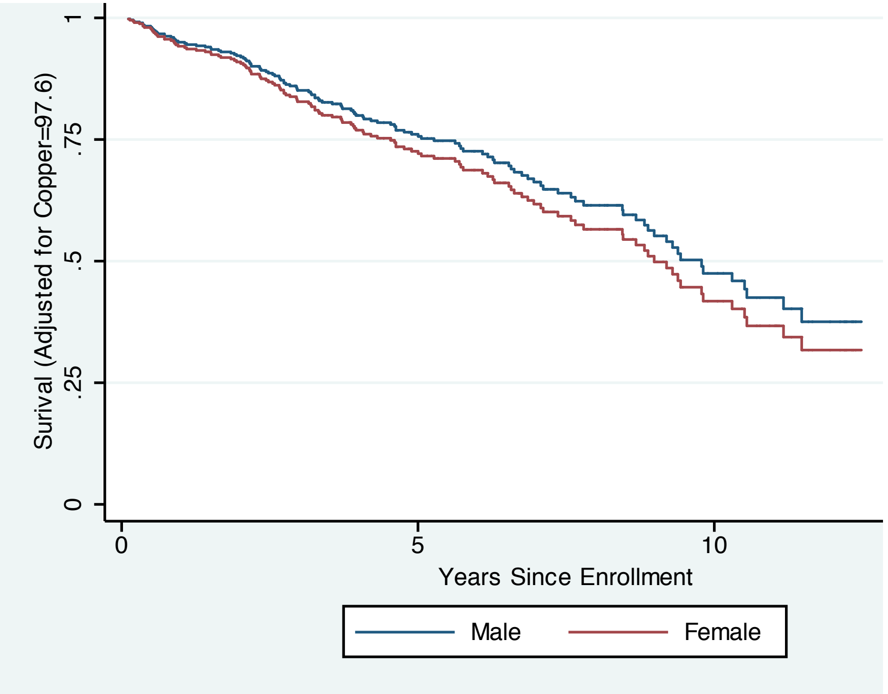
```
. stcurve, survival at1(sex=0) at2(sex=1)
```

gives same result

Adjusted Survival Curves

```
stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
```

copper set to 97.6 (mean value)



Fitted Survival function:

$$S(t|x) = S_0(t)^{\exp(0.16\ sex + 0.01\ copper)}$$

$S_0(t)$ is the survival function for male (sex=0) with copper=0

Adjusted survival curve for

- male (sex=0) with a copper level of 97.6

$$S_0(t)^{\exp(0.16 * 0 + 0.01 * 97.6)}$$

- female (sex=1) with a copper level of 97.6

$$S_0(t)^{\exp(0.16 * 1 + 0.01 * 97.6)}$$

Adjusted Survival Curves

Let's compare mean vs. median copper as reference

```
stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
stcurve, survival at1(sex=0 copper=73) at2(sex=1 copper=73)
```

copper set to 97.6
(mean value)

copper set to 73
(median value)

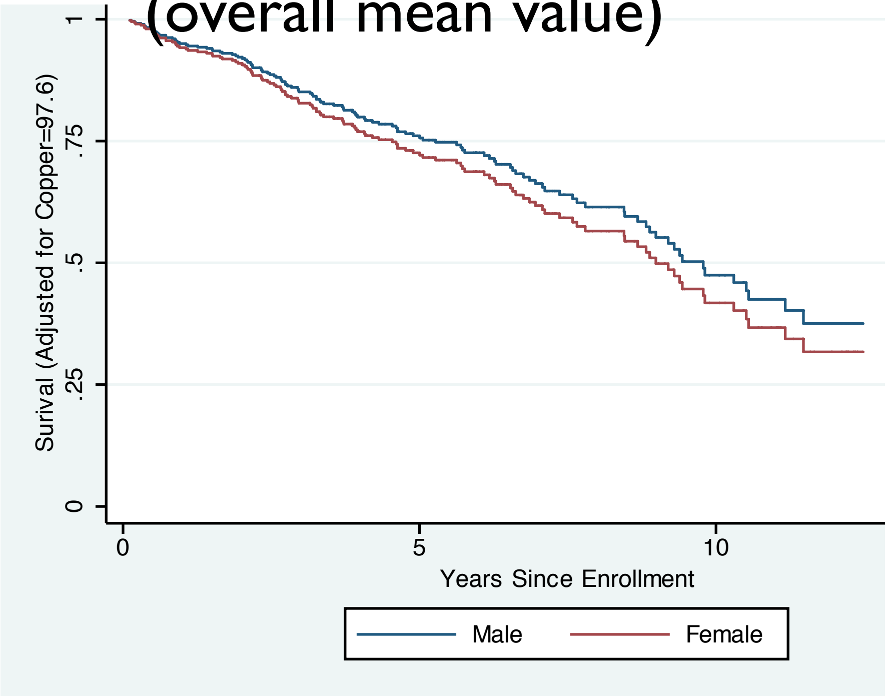
reference value for copper matters

Adjusted Survival Curves

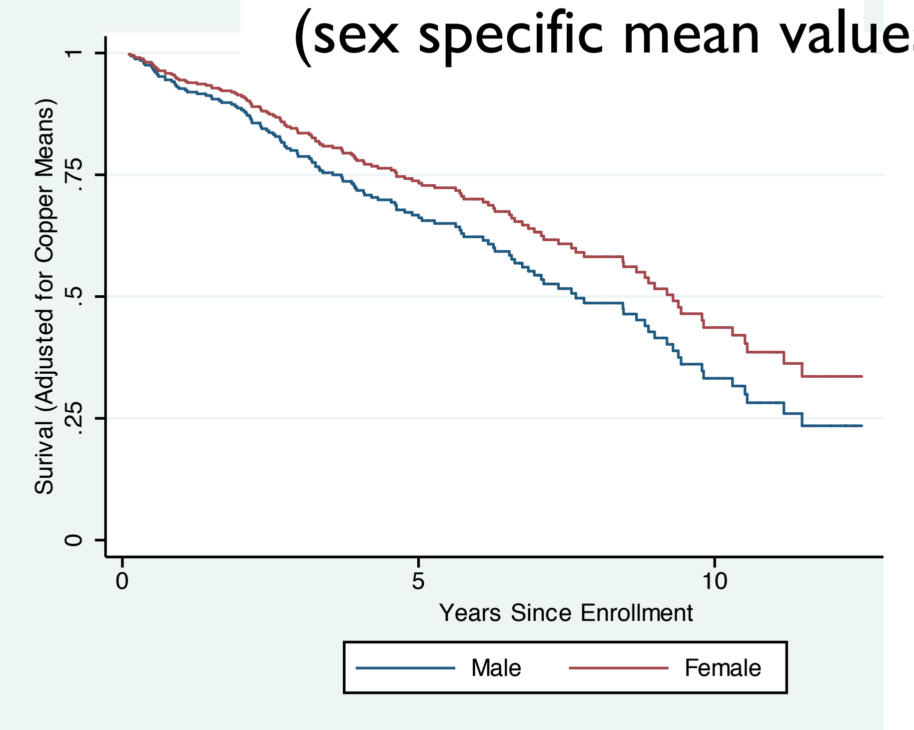
Now compare overall vs. group specific copper means as reference

```
stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
stcurve, survival at1(sex=0 copper=154) at2(sex=1 copper=90)
```

male and females= 97.6
(overall mean value)



male copper=154, female copper=90
(sex specific mean values)



adjusting for sex differences in copper matters

Interactions in regression with a continuous outcome

Binary Variable Interactions

Outcome = Systolic BP

$$Y = \alpha + x_{sm}\beta_{sm} + x_{dr}\beta_{dr} + x_{sm}x_{dr}\beta_{inter} + \epsilon$$

No interaction (β_{inter}=0)

	Drink = 0	Drink = 1
Smoke = 1	$\alpha + \beta_{sm}$	$\alpha + \beta_{sm} + \beta_{dr}$
Smoke = 0	α	$\alpha + \beta_{dr}$

β_{sm} = Smoking effect, β_{dr} = Drinking effect

Binary Variable Interactions

Outcome = Systolic BP

$$Y = \alpha + x_{sm}\beta_{sm} + x_{dr}\beta_{dr} + x_{sm}x_{dr}\beta_{inter} + \epsilon$$

Interaction ($\beta_{inter} \neq 0$)

	Drink = 0	Drink = 1
Smoke = 1	$\alpha + \beta_{sm}$	$\alpha + \beta_{sm} + \beta_{dr} + \beta_{inter}$
Smoke = 0	α	$\alpha + \beta_{dr}$

β_{inter} = interaction

$\beta_{inter} > 0$: synergistic;

$\beta_{inter} < 0$: antagonistic

Binary Variable Interaction with a Continuous Variable

$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

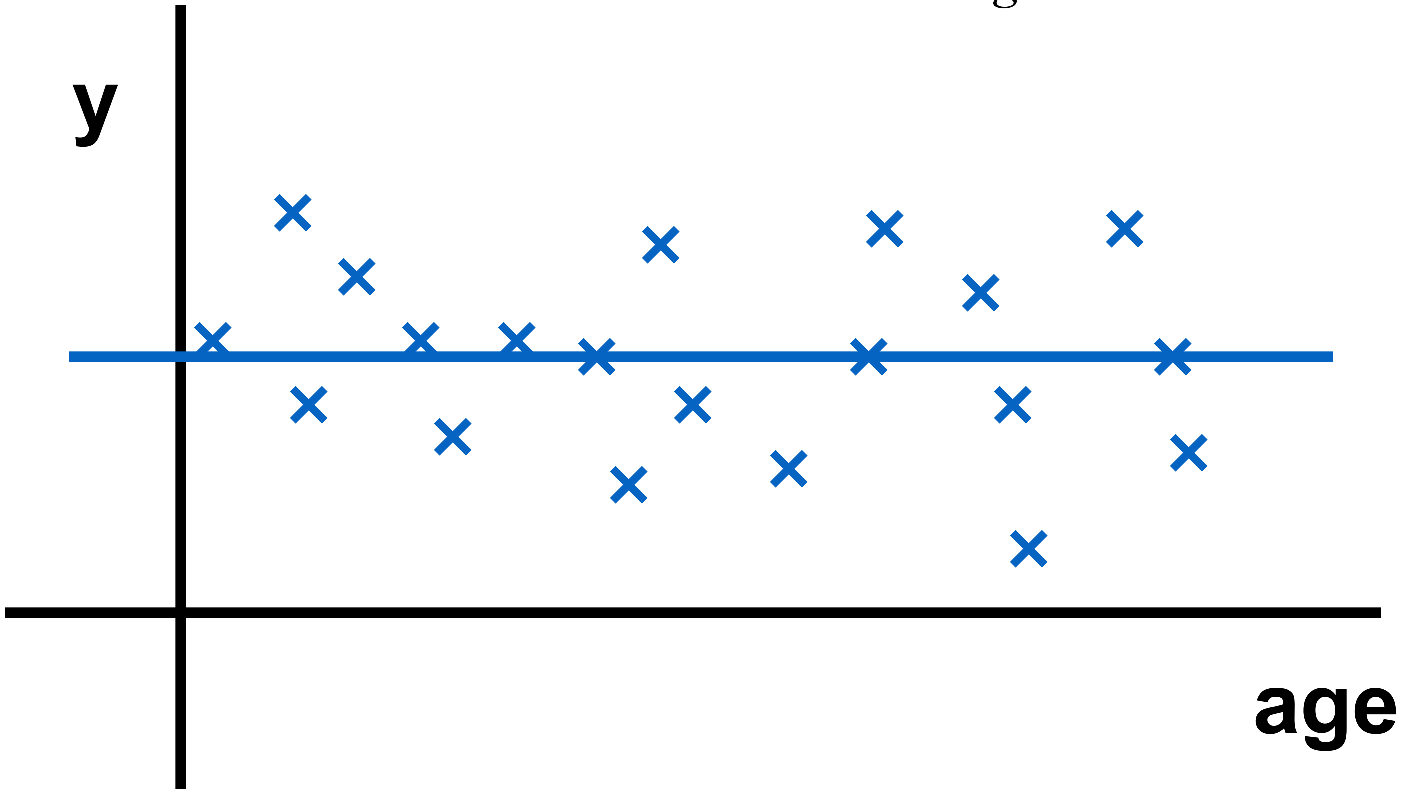
y = cognition score - outcome

$Dx = 1$, AD (Alzheimer's)

$Dx = 0$, HC (Healthy Control)

Case 1

$$\beta_{age} = 0, \beta_{Dx} = 0, \beta_{inter} = 0$$



$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

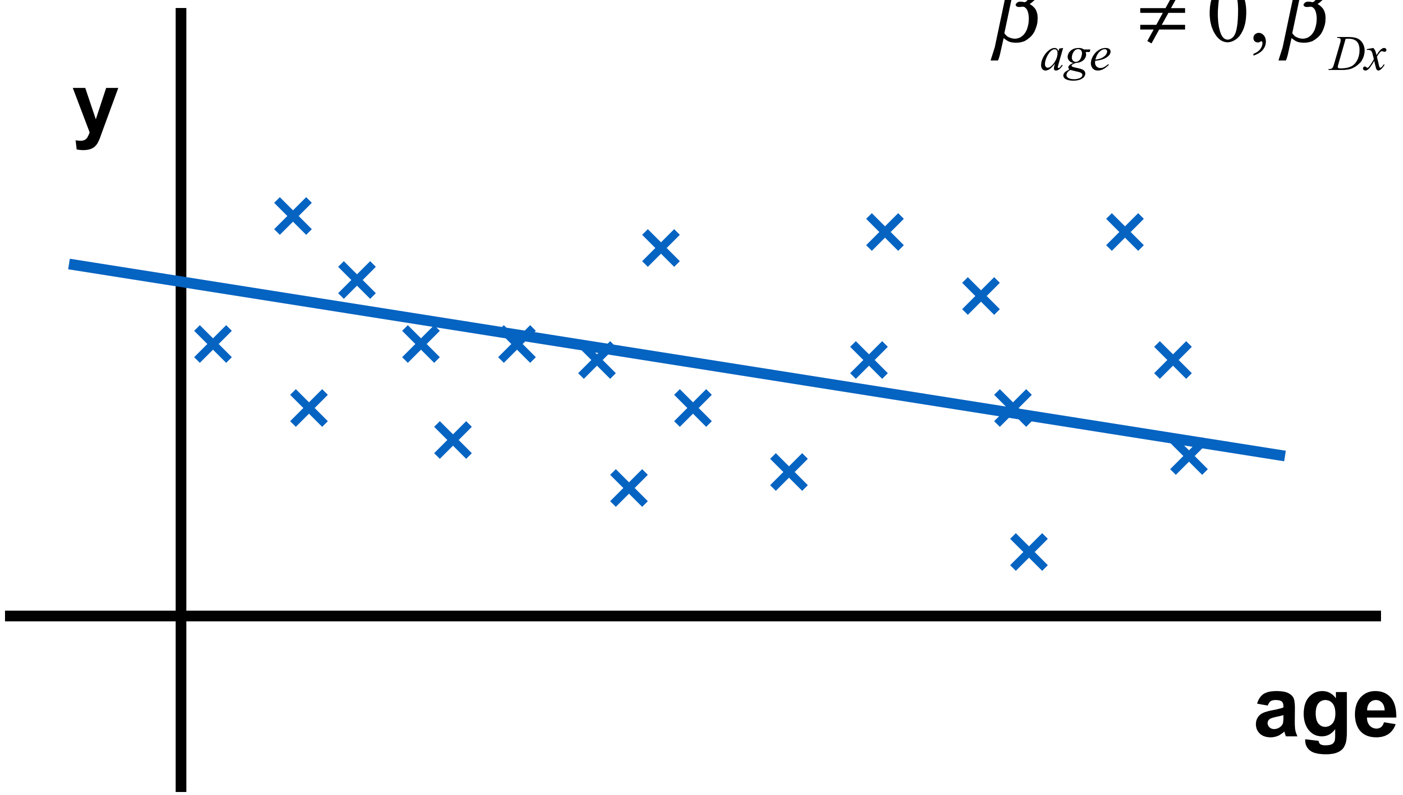
y = cognition score - outcome

$Dx = 1$, AD (Alzheimer's)

$Dx = 0$, HC (Healthy Control)

Case 2

$$\beta_{age} \neq 0, \beta_{Dx} = 0, \beta_{inter} = 0$$



$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

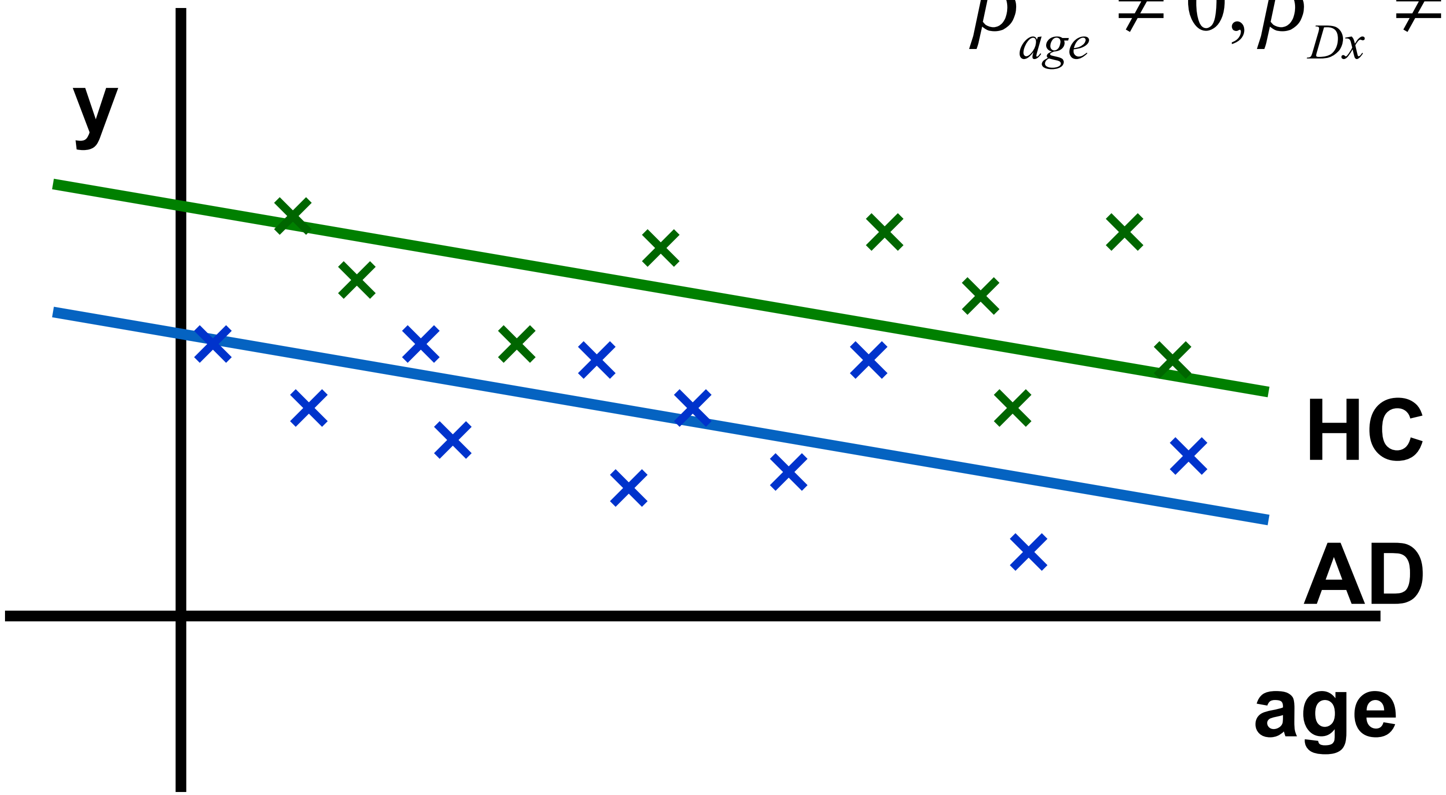
$y =$ cognition score - outcome

$Dx = 1$, AD (Alzheimer's)

$Dx = 0$, HC (Healthy Control)

Case 3

$$\beta_{age} \neq 0, \beta_{Dx} \neq 0, \beta_{inter} = 0$$



$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

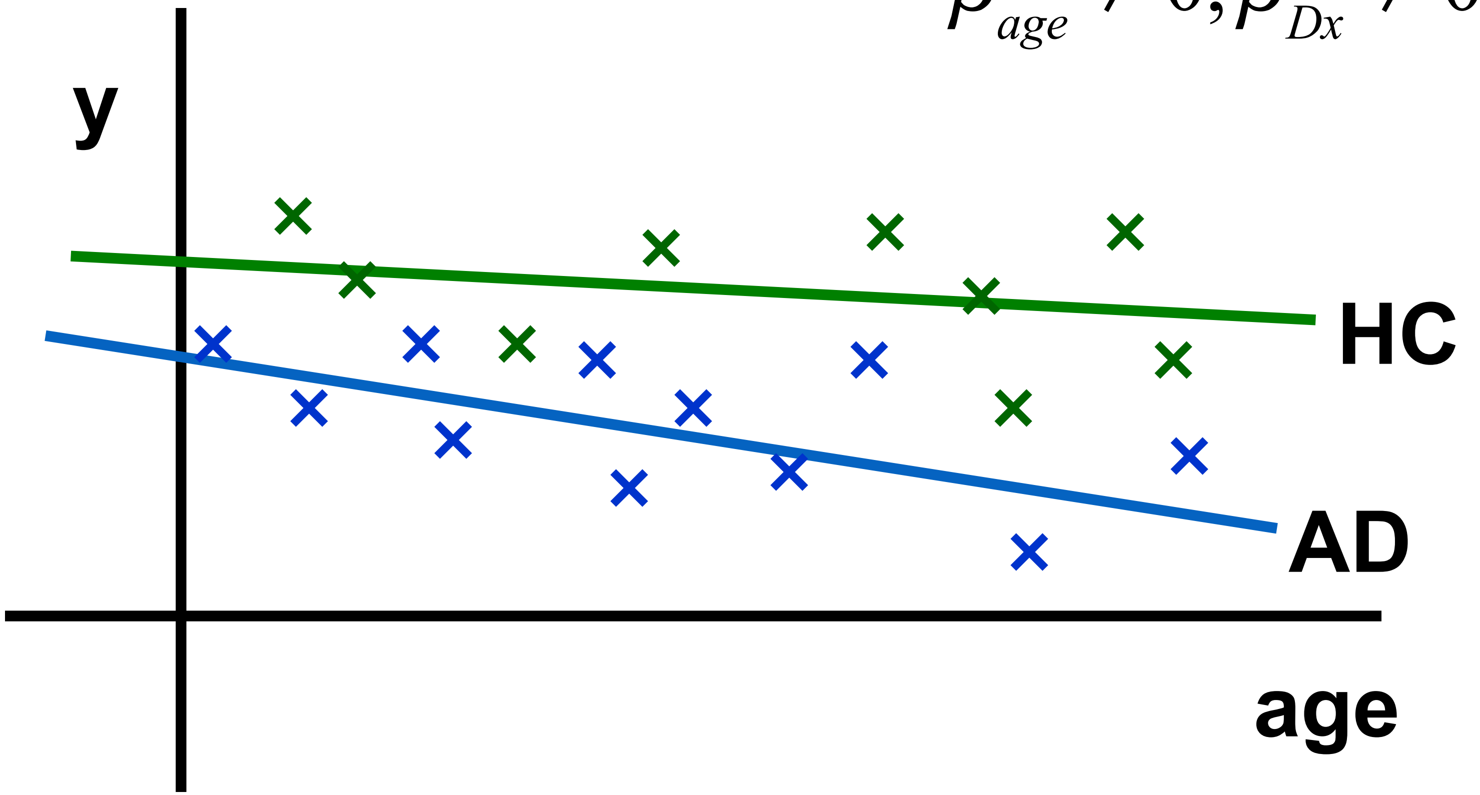
$y =$ cognition score - outcome

$Dx = 1$, AD (Alzheimer's)

$Dx = 0$, HC (Healthy Control)

Case 4

$$\beta_{age} \neq 0, \beta_{Dx} \neq 0, \beta_{inter} \neq 0$$

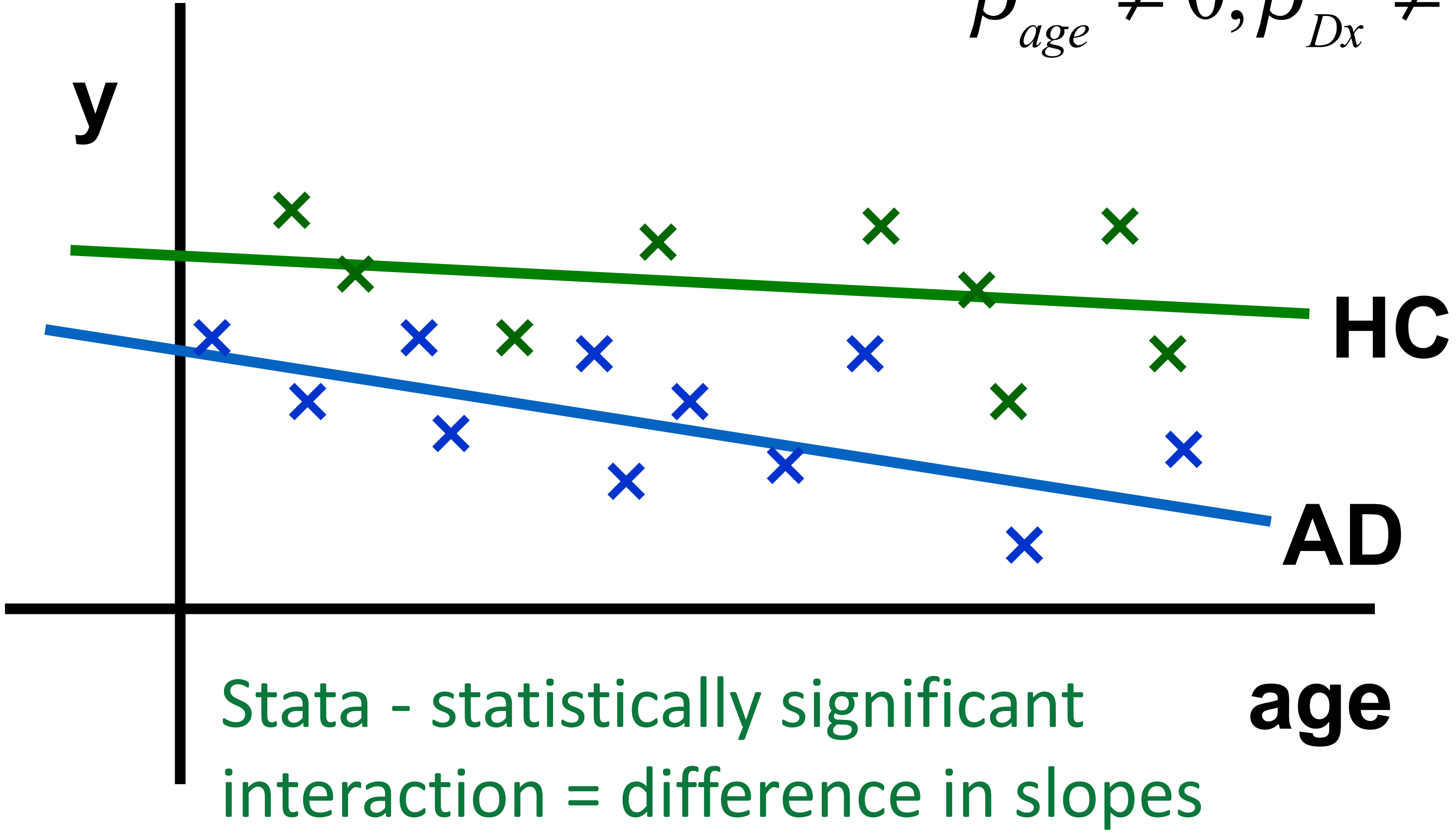


$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

y = cognition score - outcome
$Dx = 1$, AD (Alzheimer's)
$Dx = 0$, HC (Healthy Control)

Case 4

$$\beta_{age} \neq 0, \beta_{Dx} \neq 0, \beta_{inter} \neq 0$$

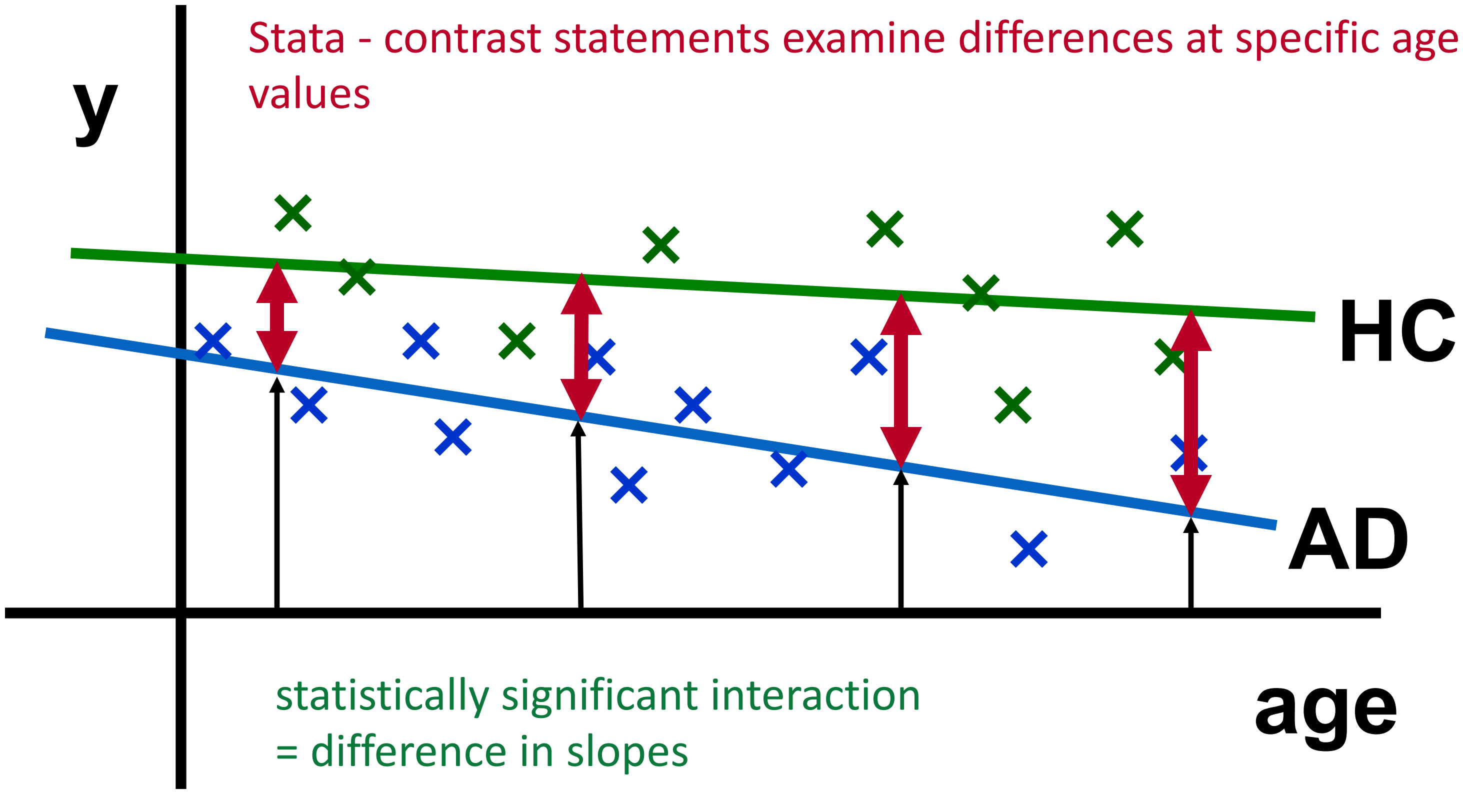


$$y = \alpha + x_{age}\beta_{age} + x_{Dx}\beta_{Dx} + x_{age}x_{diag.}\beta_{inter} + \varepsilon$$

y = cognition score - outcome
$Dx = 1$, AD (Alzheimer's)
$Dx = 0$, HC (Healthy Control)

Case 4

$$\beta_{age} \neq 0, \beta_{Dx} \neq 0, \beta_{inter} \neq 0$$



Note: continuous variable by continuous variable interaction even trickier to interpret – we won't go there