

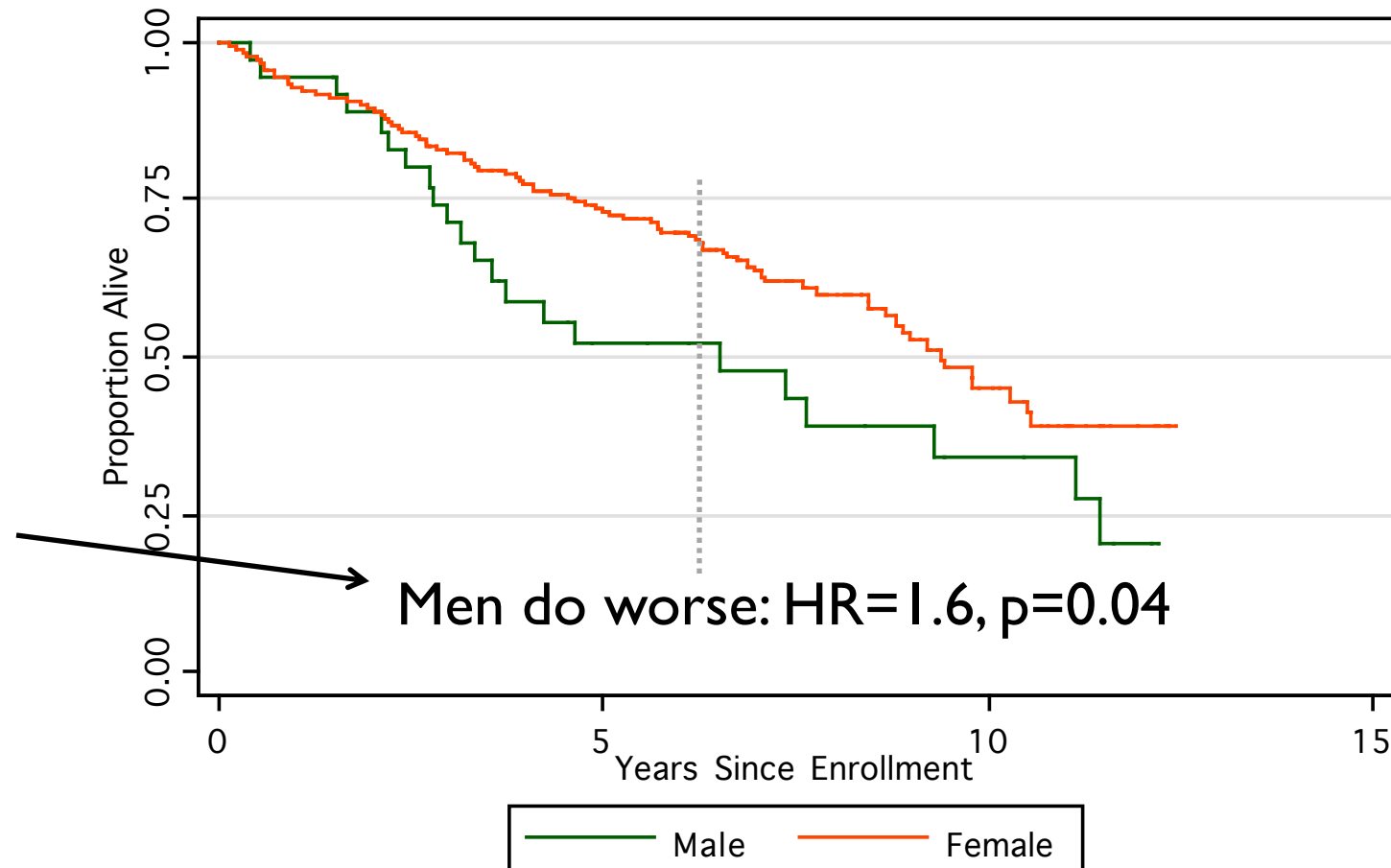
Adjusted Survival Curves

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

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

$h_0(t)$ = baseline hazard function

= hazard function when all predictors equal zero

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

= 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

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

(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: $S(t|x) = S_0(t) \exp(\beta_1 x_1 + \dots + \beta_2 x_2)$

Adjusted Survival Curves

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. stcox sex copper
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sex	1.171796	.2996835	0.62	0.535	.7098385	1.934391
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Coefficient for sex: $\hat{\beta}_1 = \log(\text{HR}) = \log(1.17) = 0.16$

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

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

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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)

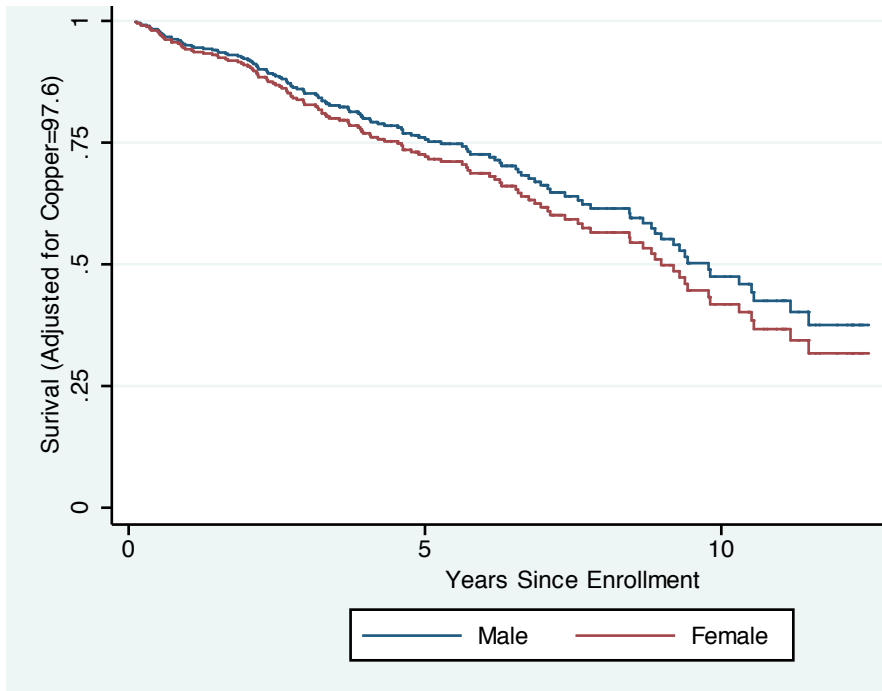
Note that the copper default is fixed at overall mean(=97.6)

```
. 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:

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

$S_0(t)$ 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

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

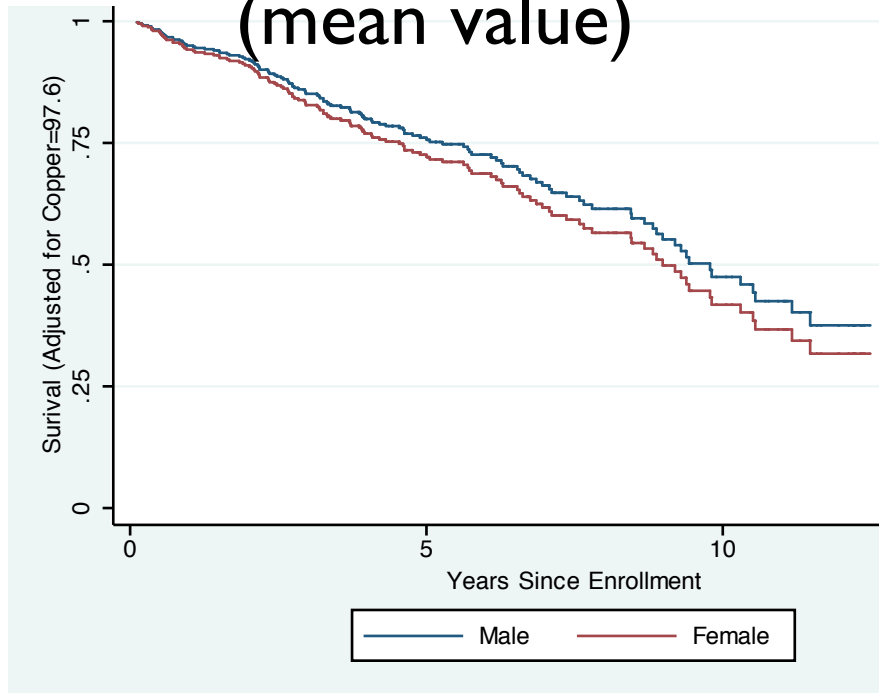
Adjusted Survival Curves

Let's compare mean vs. median copper as reference

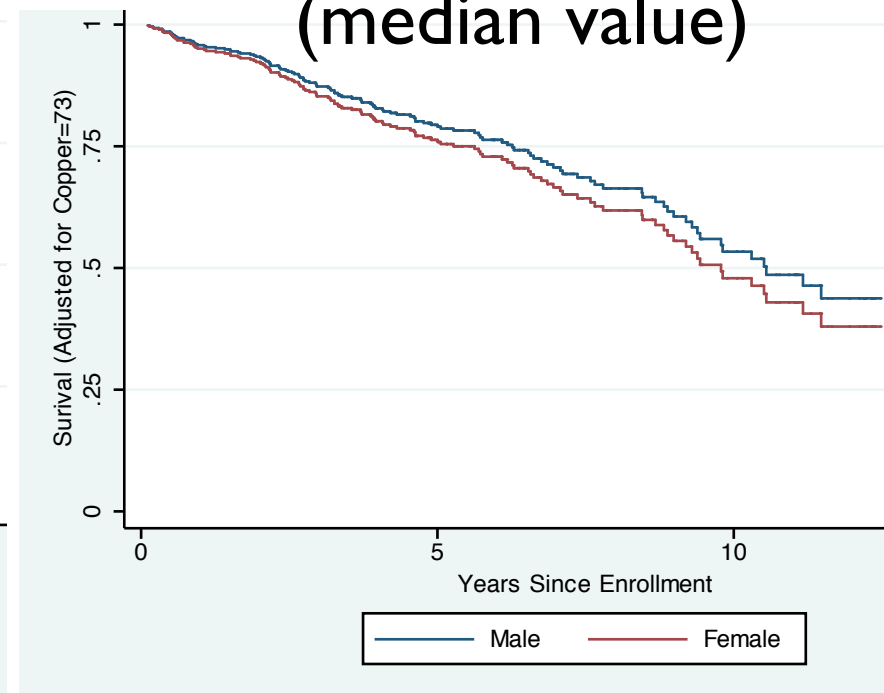
```
stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
```

```
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

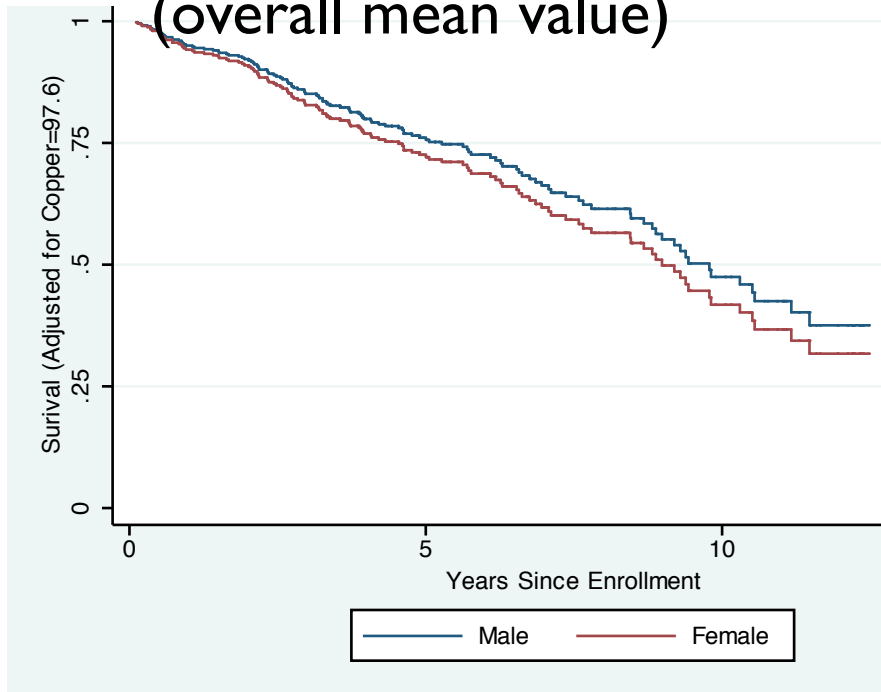
Adjusted Survival Curves

Now compare overall vs. group specific copper means as reference

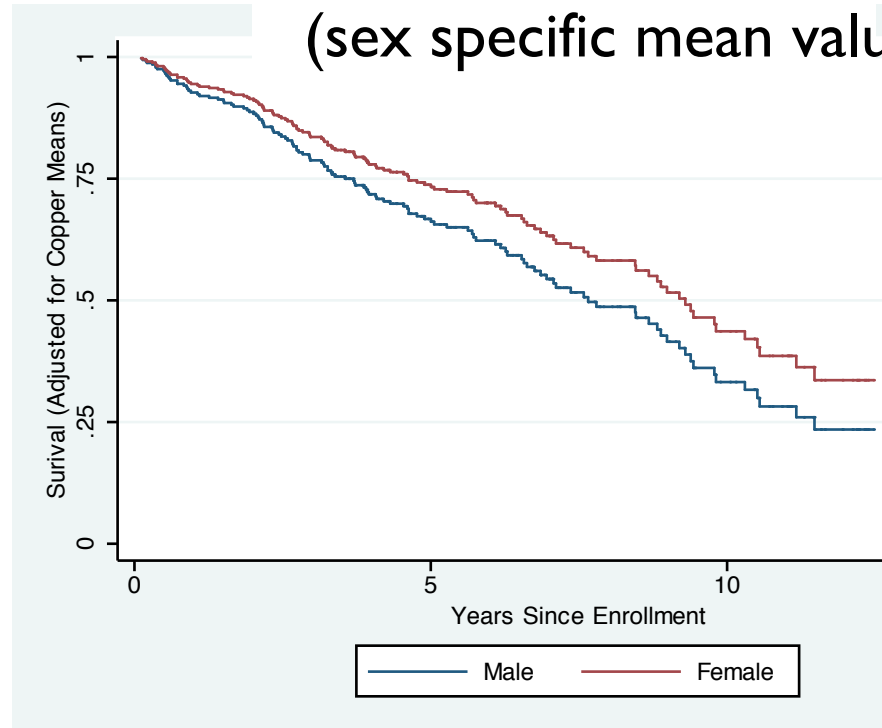
```
stcurve, survival at1(sex=0 copper=97.6) at2(sex=1 copper=97.6)
```

```
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

No interaction

	Drink = 0	Drink = 1
Smoke = 1	$\mu + a$	$\mu + a + b$
Smoke = 0	μ	$\mu + b$

a = Smoking effect, b = Drinking effect

Binary Variable Interactions

Outcome = Systolic BP

Interaction

	Drink = 0	Drink = 1
Smoke = 1	$\mu + a$	$\mu + a + b + c$
Smoke = 0	μ	$\mu + b$

$c \neq 0$

a = Smoking effect, b = Drinking effect,

c = interaction

$c > 0$: synergistic;

$c < 0$: antagonistic

Binary Variable Interaction with a Continuous Variable

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

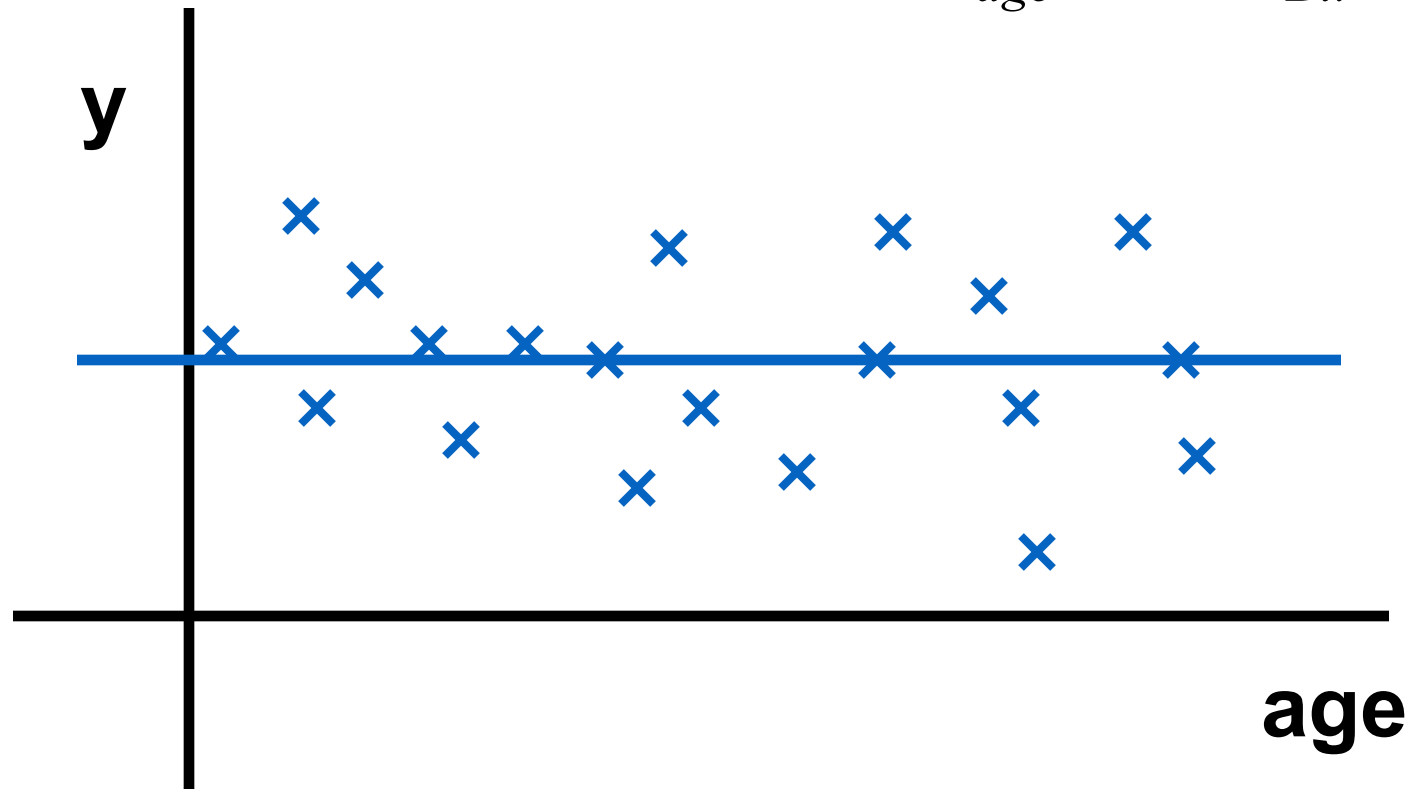
y = cognition score - outcome

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

$Dx = 0$, HC (Healthy Control)

Case 1

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



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

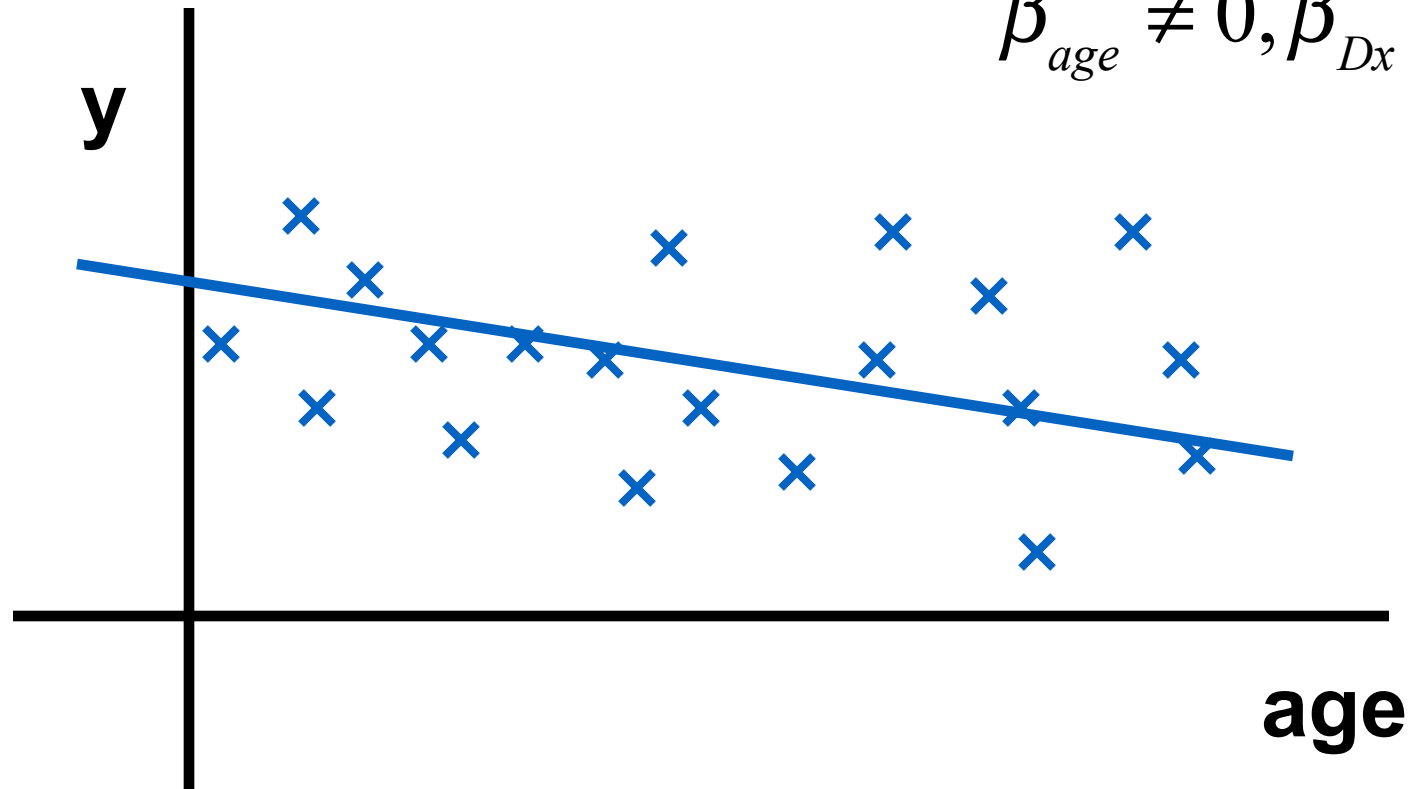
y = cognition score - outcome

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

$Dx = 0$, HC (Healthy Control)

Case 2

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



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

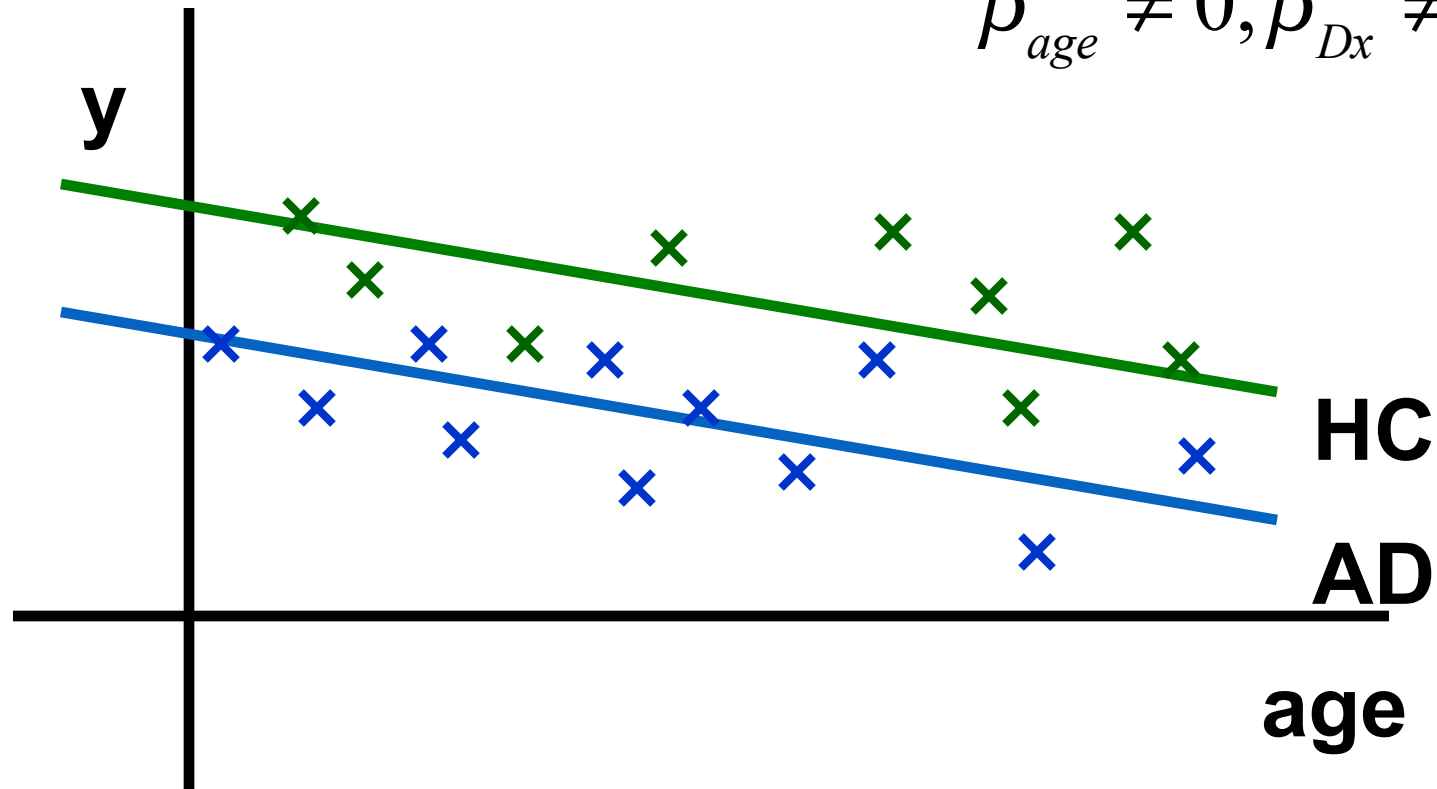
y = cognition score - outcome

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

$Dx = 0$, HC (Healthy Control)

Case 3

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



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

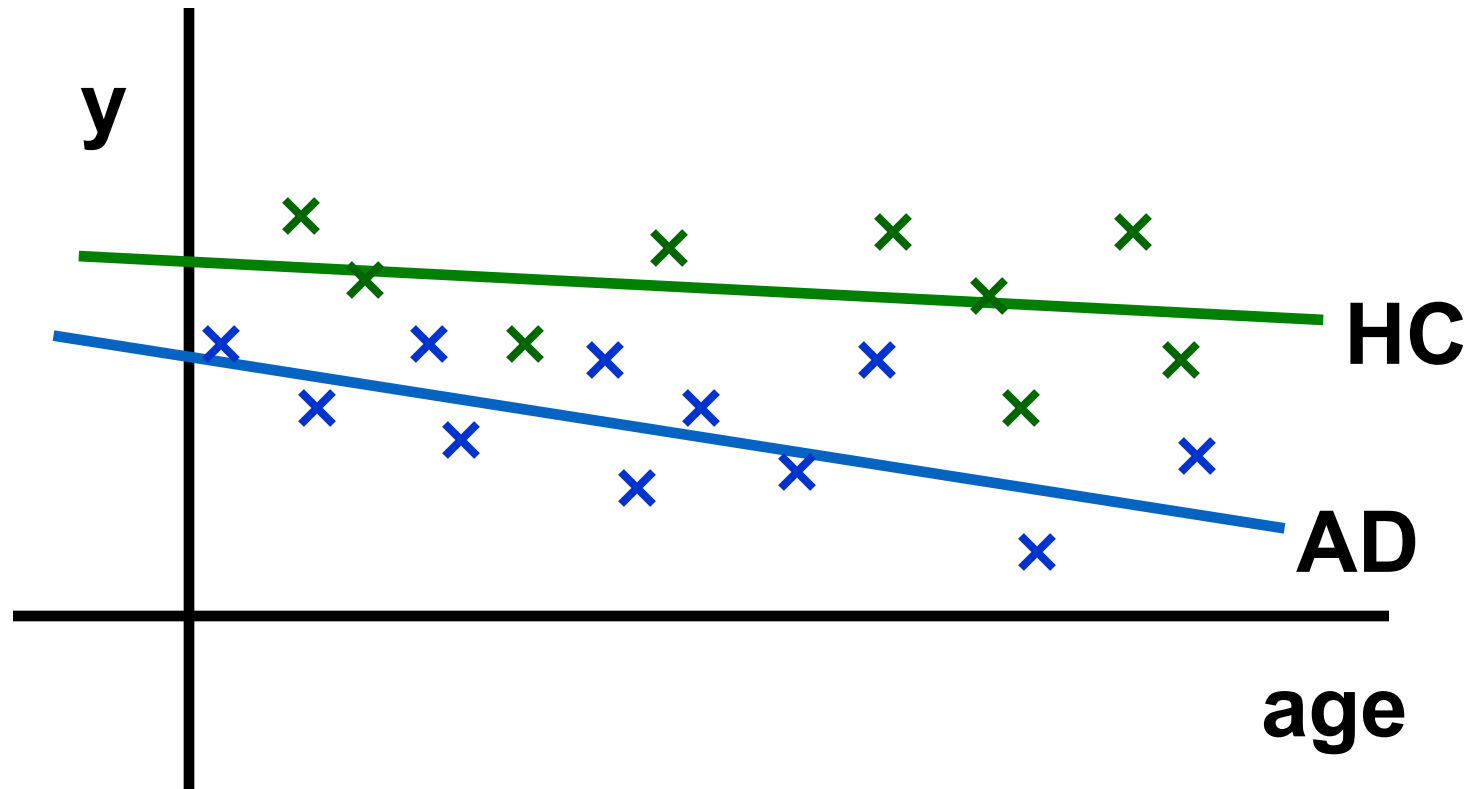
y = cognition score - outcome

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

$Dx = 0$, HC (Healthy Control)

Case 4

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



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

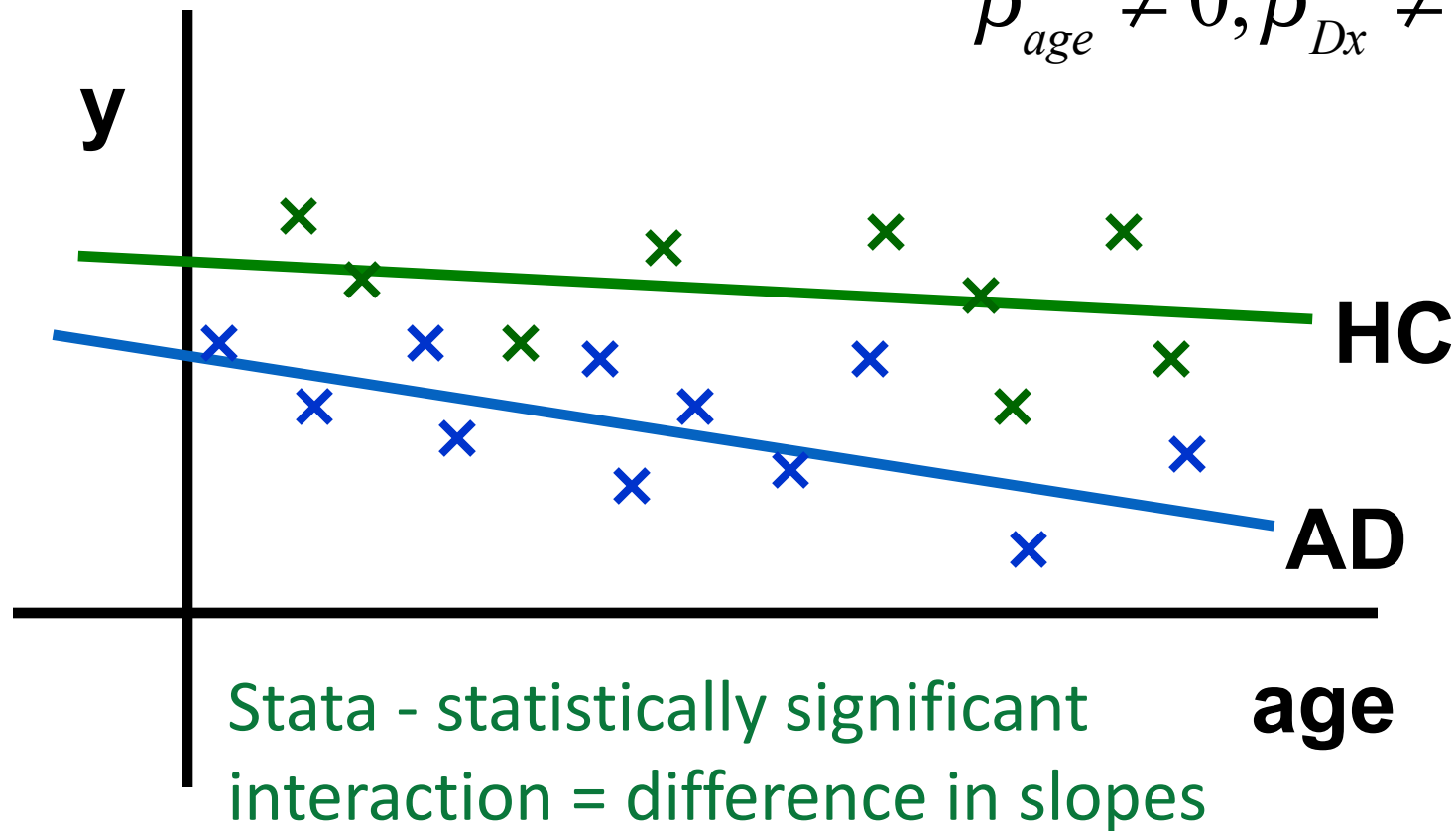
y = cognition score - outcome

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

$Dx = 0$, HC (Healthy Control)

Case 4

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



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

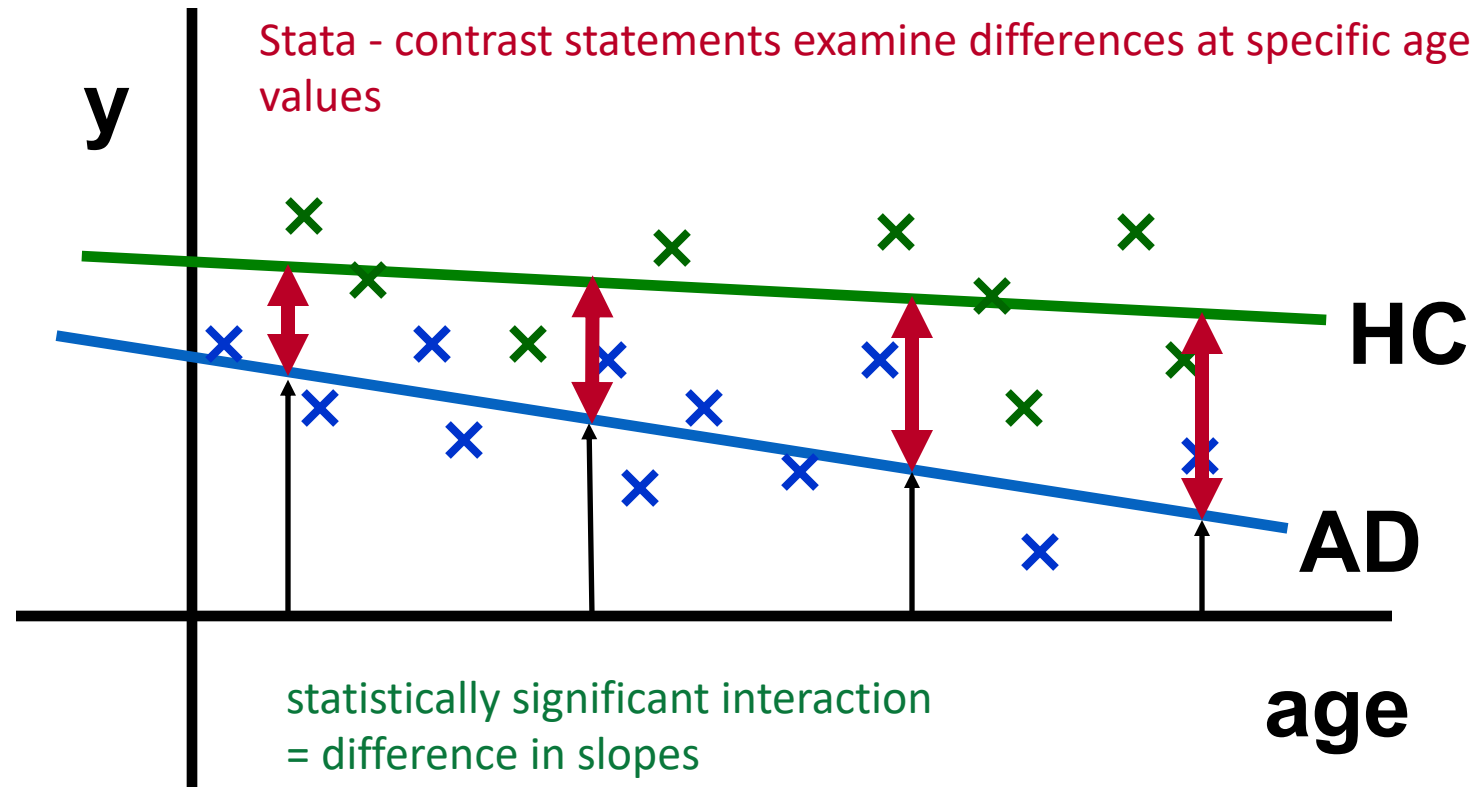
y = cognition score - outcome

$Dx = 1$, 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