Biostat 200
Lecture 9

Chi-square test when the exposure has several levels

- E.g. Is sleep quality associated with having had at least one cold in the past month?

```
. tab coldany rested, col chi

+-------------------+
| Key               |
|-------------------|
|     frequency     |
| column percentage |
+-------------------+

           |                          rested
   coldany | Never res  Rarely (1  Half (3-4  Mostly (5     Always |     Total
-----------+-------------------------------------------------------+----------
        No |        13         82        119         93         12 |       319
           |     59.09      66.67      70.83      74.40      85.71 |     70.58
-----------+-------------------------------------------------------+----------
       Yes |         9         41         49         32          2 |       133
           |     40.91      33.33      29.17      25.60      14.29 |     29.42
-----------+-------------------------------------------------------+----------
     Total |        22        123        168        125         14 |       452
           |    100.00     100.00     100.00     100.00     100.00 |    100.00

          Pearson chi2(4) =   4.7331   Pr = 0.316

.
```

Odds ratio when the exposure has several levels

- One level is the “unexposed” or reference level

This is as if you partitioned your data off and did a chi-square test comparing colds in the rarely vs. never rested categories

```
. tabodds coldany rested, or

---------------------------------------------------------------------------
      rested |  Odds Ratio       chi2       P>chi2     [95% Conf. Interval]
-------------+-------------------------------------------------------------
   Never r~d |    1.000000          .            .             .          .
   Rarely ~) |    0.722222       0.47       0.4926      0.283916   1.837179
   Half (3~) |    0.594771       1.26       0.2620      0.237464   1.489714
   Mostly ~) |    0.497013       2.17       0.1412      0.192152   1.285553
      Always |    0.240741       2.78       0.0955      0.039025   1.485107
---------------------------------------------------------------------------
Test of homogeneity (equal odds): chi2(4)  =     4.72
                                  Pr>chi2  =   0.3170

Score test for trend of odds:     chi2(1)  =     4.37
                                  Pr>chi2  =   0.0365
```

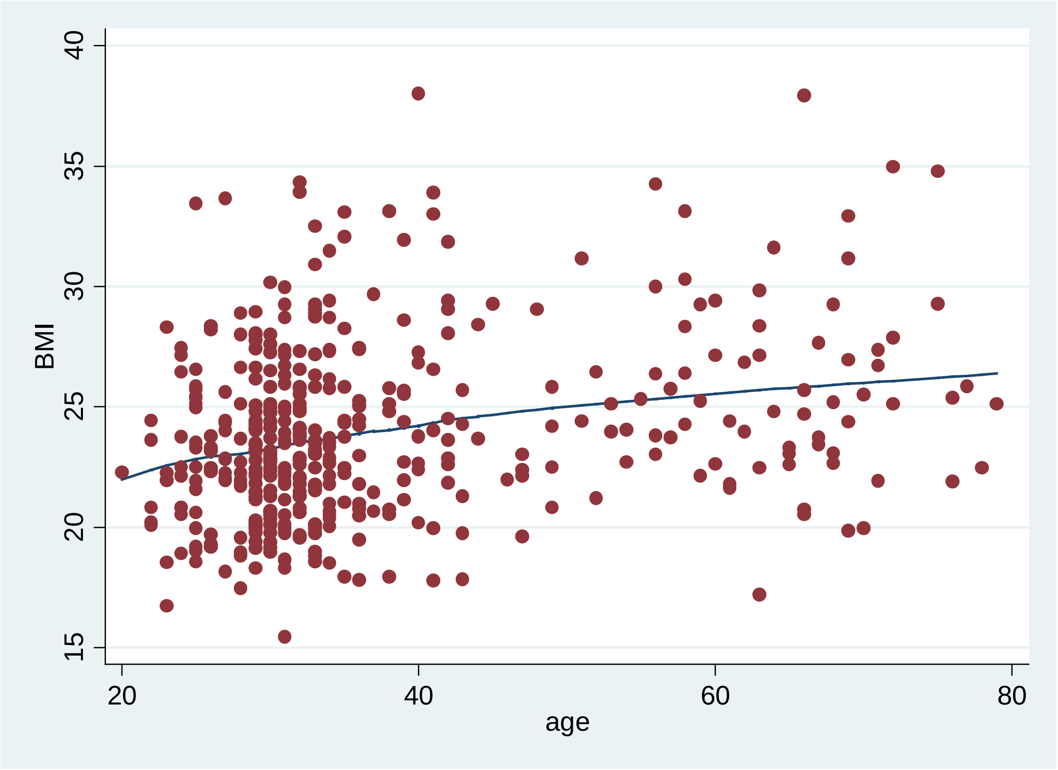
Stata lets you choose the reference level

```
. tabodds coldany rested, or base(2)

---------------------------------------------------------------------------
      rested |  Odds Ratio       chi2       P>chi2     [95% Conf. Interval]
-------------+-------------------------------------------------------------
   Never r~d |    1.384615       0.47       0.4926       0.544313   3.522165
   Rarely ~) |    1.000000          .            .              .          .
   Half (3~) |    0.823529       0.58       0.4482       0.498209   1.361278
   Mostly ~) |    0.688172       1.78       0.1824       0.396029   1.195823
      Always |    0.333333       2.10       0.1471       0.069979   1.587781
---------------------------------------------------------------------------
Test of homogeneity (equal odds): chi2(4)   =     4.72
                                  Pr>chi2   =   0.3170

Score test for trend of odds:     chi2(1)   =     4.37
                                  Pr>chi2   =   0.0365
```

Scatterplot

- Back to continuous outcomes
- T-test, ANOVA, Wilcoxon rank-sum test, Kruskal-Wallis test compare 2 or more independent samples
  - e.g. CD4 cell count by sex or alcohol consumption category
- The scatterplot is a simple method to examine the relationship between 2 continuous variables

Scatter plot




```
twoway (lowess bmi age) (scatter bmi age) if bmi<50,
ytitle(BMI) xtitle(age) legend(off)
```

Correlation

- Correlation is a method to examine the relationship between 2 continuous variables
  - Does one increase with the other?
    - E.g. Does BMI increase with increasing age?
- Both variables are measured on the same people (or unit of analysis)
- Correlation assumes a *linear* relationship between the two variables
- Correlation is symmetric
  - The correlation of A with B is the same as the correlation of B with A

Correlation

- Correlation is a measure of the relationship between two random variables X and Y
- If the variables increase together (or oppositely), then the average of X*Y will be large (in absolute terms)
- We subtract off the mean and divide by the standard deviation to standardize (i.e. so correlations will be between -1 and 1)

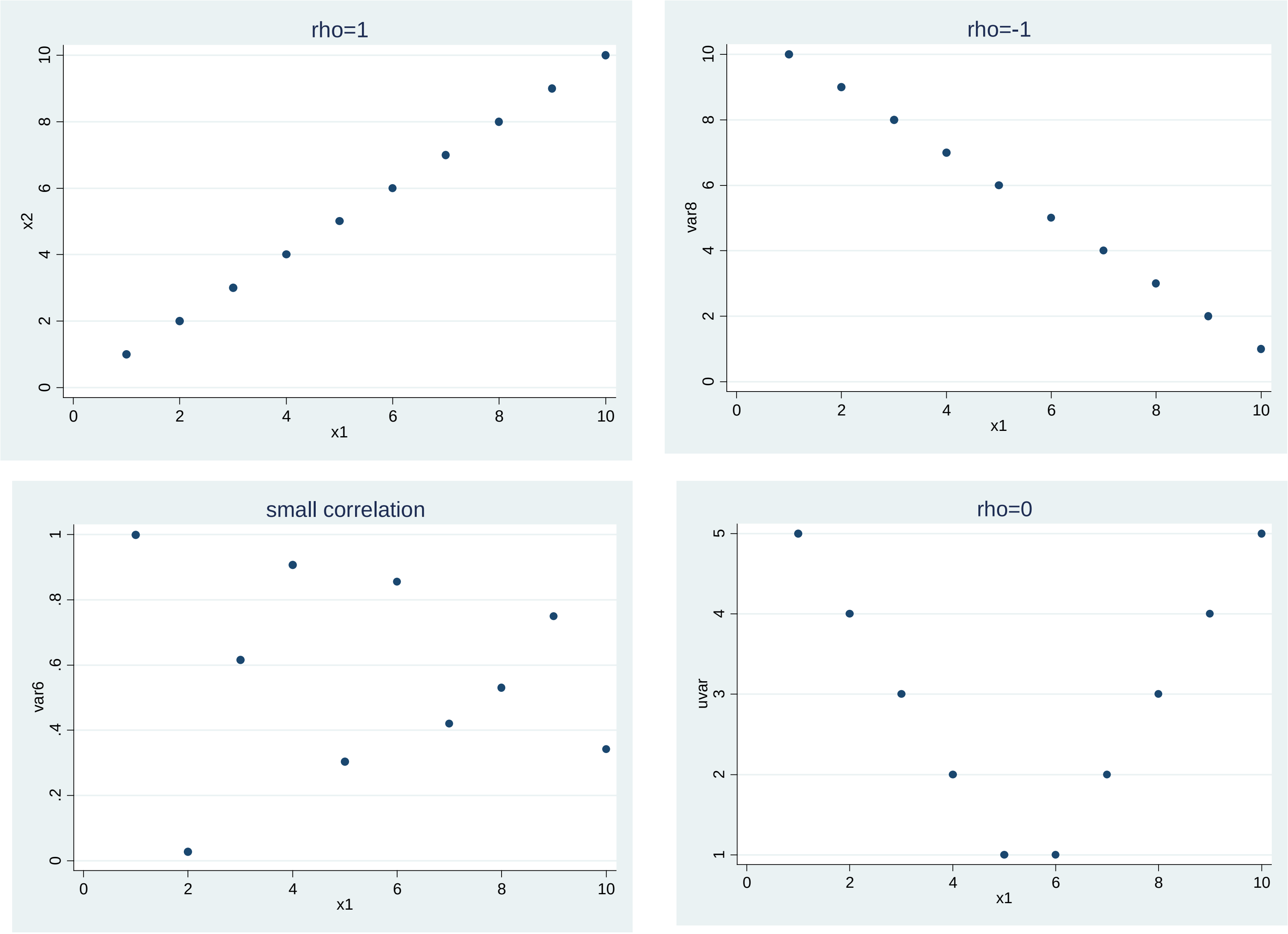
Correlation

- A correlation is defined as

$$\rho = average\left[\left(\frac{X-\mu_x}{\sigma_x}\right)\left(\frac{Y-\mu_y}{\sigma_y}\right)\right]$$

- Correlations can be comparable across variables with different means and variability
- Correlation does not imply causation

Correlation



Correlation

- ρ lies between -1 and 1
- -1 and 1 are perfect correlations, 0 is no correlation
- An estimator of the population correlation ρ is Pearson's correlation coefficient denoted r
- It is estimated by: $$r = \frac{1}{n-1}\sum_{i=1}^{n}\left(\frac{x_i - \bar{x}}{s_x}\right)\left(\frac{y_i - \bar{y}}{s_y}\right)$$

Correlation

$$r = \frac{1}{n-1}\sum_{i=1}^{n}\left(\frac{x_i - \bar{x}}{s_x}\right)\left(\frac{y_i - \bar{y}}{s_y}\right)$$

$$= \frac{1}{(n-1)}\frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\left[\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}\right]}\sqrt{\left[\frac{\sum_{i=1}^{n}(y_i - \bar{y})^2}{n-1}\right]}}$$

$$= \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\left[\sum_{i=1}^{n}(x_i - \bar{x})^2\right]}\sqrt{\left[\sum_{i=1}^{n}(y_i - \bar{y})^2\right]}}$$

Correlation: hypothesis testing

- To test whether there is a correlation between two variables, our hypotheses are

  $H_0 : \rho=0$ and $H_A : \rho\neq 0$

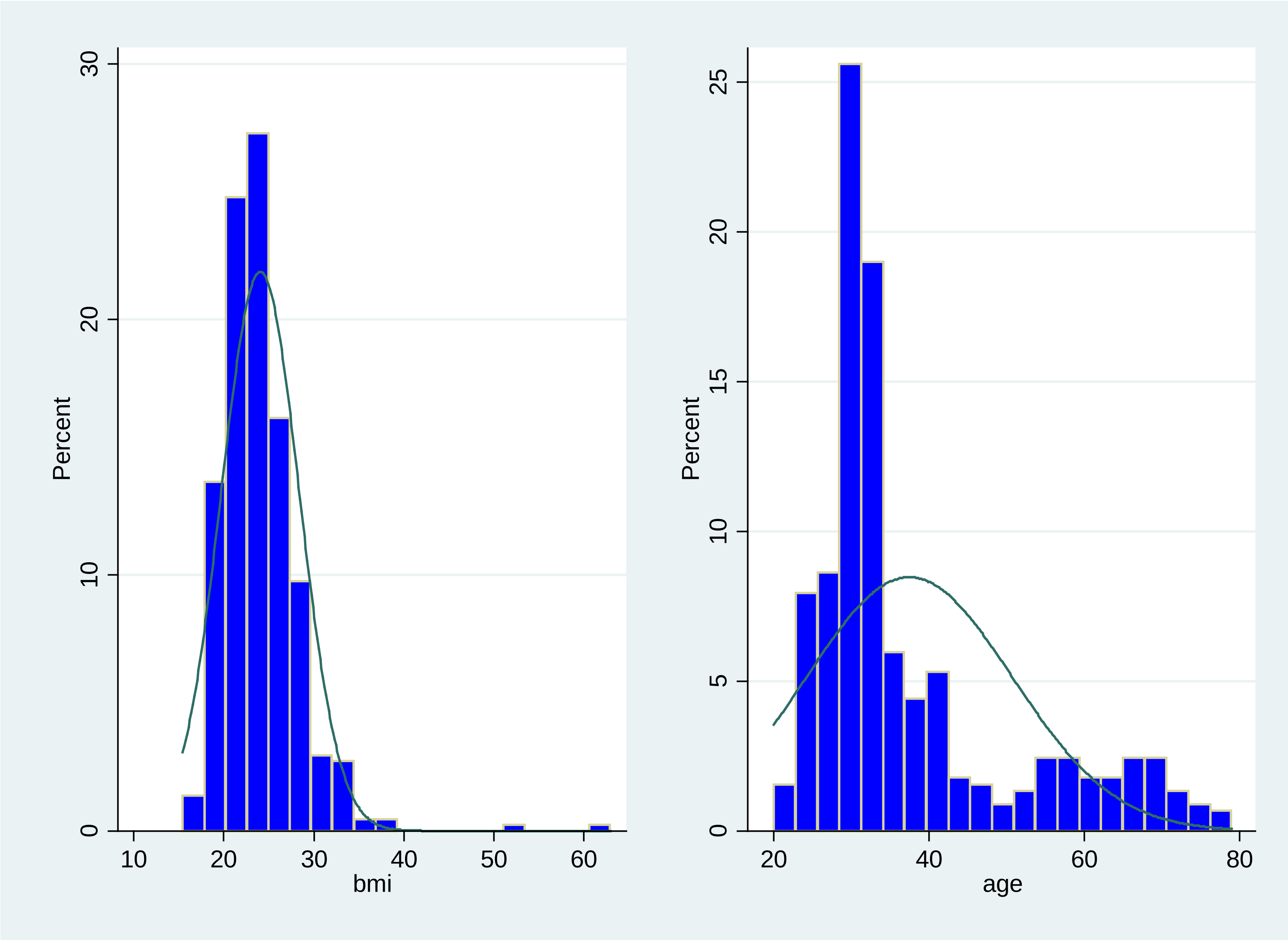
- We need to calculate a test statistic for r
- The test statistic is $t = \dfrac{r-0}{se(r)}$

$$\text{where } se(r) = \sqrt{\frac{1-r^2}{n-2}}$$

$$\text{so } t = r\sqrt{\frac{n-2}{1-r^2}}$$

Correlation: hypothesis testing

- The test statistic follows a t distribution with n-2 degrees of freedom under the null
- The assumptions
  - The pairs of observations (x_i , y_i) were obtained from a random sample
  - X and Y are normally distributed



Percent
0
10
20
30
10
20
30
40
50
60
bmi
Percent
0
5
10
15
20
25
20
40
60
80
age

Correlation example

pwcorr var1 var2, sig obs

```
. pwcorr age bmi, sig obs

             |      age      bmi
-------------+------------------
         age |   1.0000
             |
             |      453
             |
         bmi |   0.2103   1.0000
             |   0.0000
             |      438      440
```

Note that the hypothesis test is only of $\rho=0$, no other null
Also note that the correlation is the linear relationship only

Spearman rank correlation (nonparametric)

- Pearson's correlation coefficient is very sensitive to extreme values
- Spearman rank correlation calculates the Pearson correlation on the *ranks* of each variable
- The Pearson correlation coefficient is calculated, but the data values are replaced by the ranks
- The Spearman rank correlation coefficient is

$$r_s = \frac{1}{(n-1)} \sum_{i=1}^{n} \left(\frac{x_{ri} - \bar{x}_r}{s_{rx}} \right) \left(\frac{y_{ri} - \bar{y}_r}{s_{ry}} \right)$$

Spearman rank correlation (nonparametric)

- The Spearman rank correlation ranges between -1 and 1 as does the Pearson correlation
- We can test the null hypothesis that ρ=0
- The test statistic for n>10 is with n-2 degrees of freedom

$$t_s = r_s \sqrt{\frac{n-2}{1-r_s^2}}$$

is compared to the t distribution

```
. spearman  bmi age, stats(rho obs p)

 Number of obs =      438
Spearman's rho =        0.2522

Test of Ho: bmi and age are independent
    Prob > |t| =        0.0000
```

Matrix of Pearson correlations

- We can calculate a correlation matrix by listing multiple variable names
- Beware of which n's are used (use listwise option to get all n's equal)

```
pwcorr   sleep bmi age child6_n, sig obs

             |    sleep      bmi      age child6_n
-------------+------------------------------------
       sleep |   1.0000
             |
             |      452
             |
         bmi |  -0.0665   1.0000
             |   0.1655
             |      437      440
             |
         age |   0.0139   0.2103   1.0000
             |   0.7688   0.0000
             |      450      438      453
             |
    child6_n |  -0.1694   0.1912  -0.0326   1.0000
             |   0.0003   0.0001   0.4901
             |      449      437      450      452
             |
 |
```

Matrix of Spearman correlations

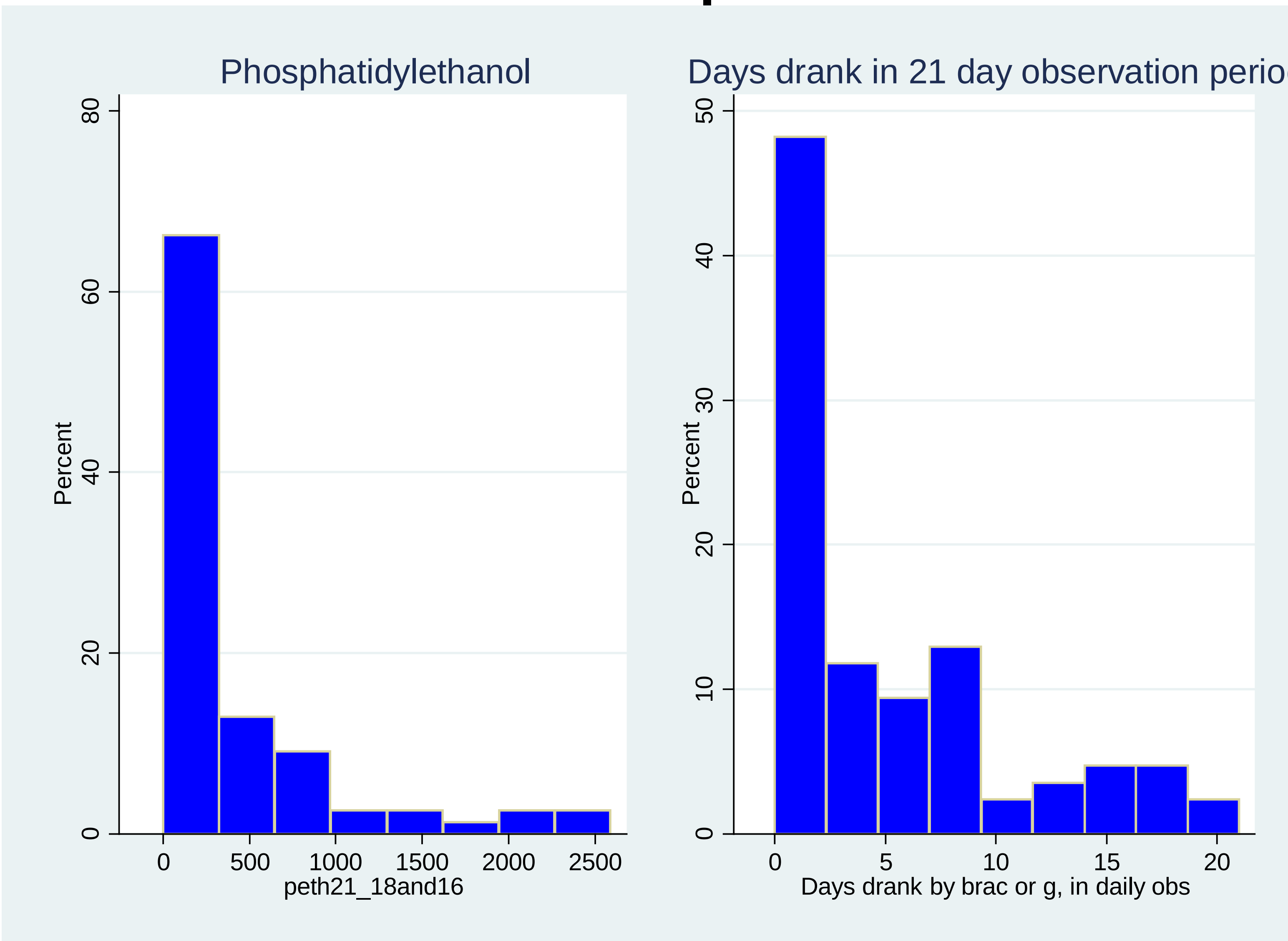
```
. . spearman sleep bmi age child6_n, pw stats(rho obs p)

+-----------------+
|  Key            |
|-----------------|
|   rho           |
|   Number of obs |
|   Sig. level    |
+-----------------+

             |    sleep      bmi      age child6_n
-------------+------------------------------------
       sleep |   1.0000
             |      452
             |
             |
         bmi |  -0.0270   1.0000
             |      437      440
             |   0.5734
             |
         age |  -0.0406   0.2522   1.0000
             |      450      438      453
             |   0.3900   0.0000
             |
    child6_n |  -0.1169   0.0577   0.1555   1.0000
             |      449      437      450      452
             |   0.0131   0.2289   0.0009
             |
```

Here if you drop the “pw” option you get all n’s equal

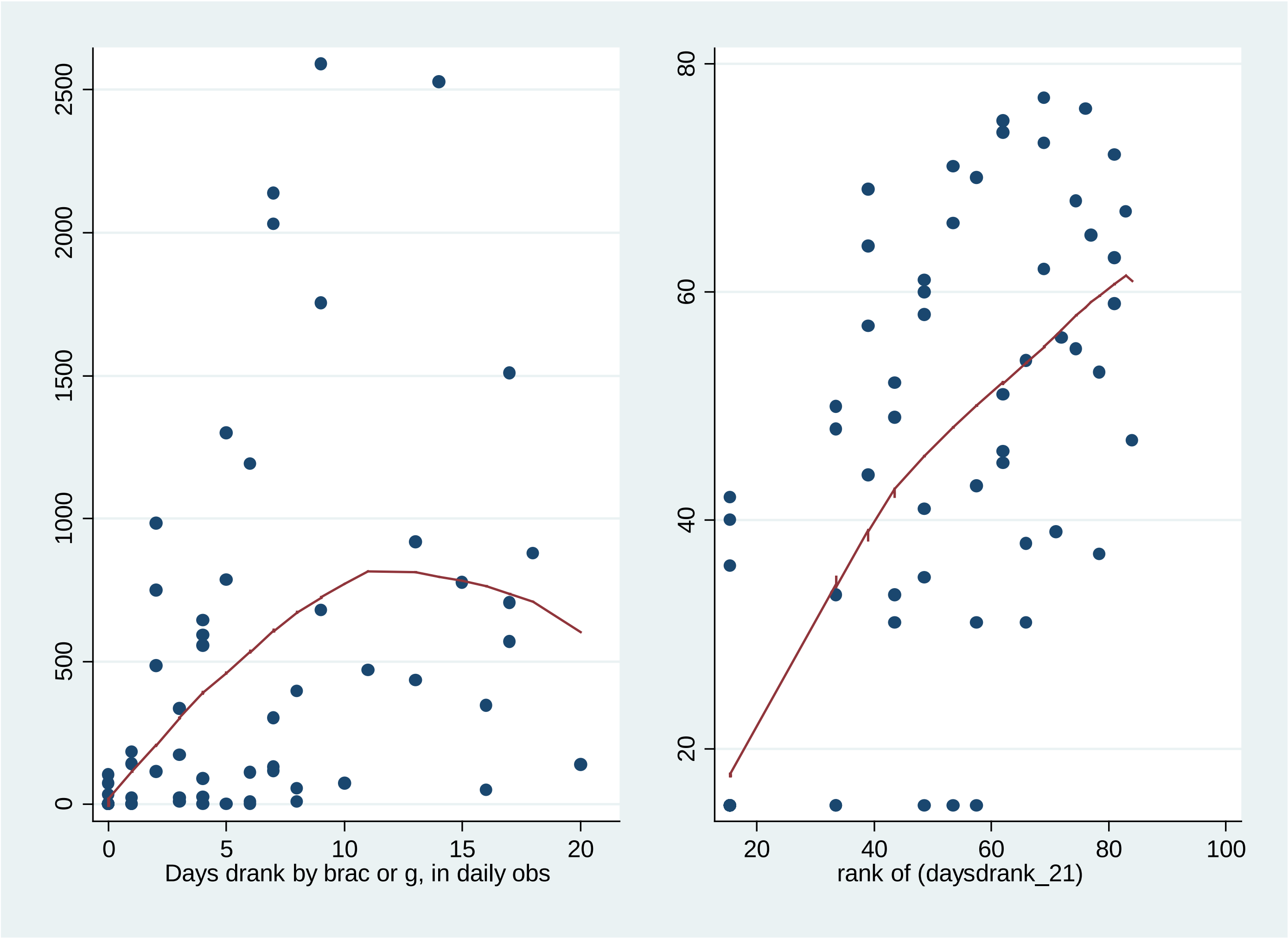
Pearson vs. Spearman

	Pearson	**Spearman**
Sensitivity to outliers	more sensitive	less sensitive
Can be used with ordinal data	no	yes
Assumes data are from a normal distribution	yes	no
Detects non-linear relationship	no	yes

Biomarker and alcohol consumption



Biomarker of alcohol consumption vs. days drinking (raw data vs. ranks)



Pearson and Spearman correlations

```
. pwcorr peth21_18and16 daysdrank_21, obs sig

             | peth2~16 days~_21
-------------+------------------
peth21_18~16 |   1.0000 
             |
             |       77
             |
daysdrank_21 |   0.4717   1.0000 
             |   0.0000
             |       77       85
             |
-----------------------------------
. spearman peth21_18and16 daysdrank_21

 Number of obs =      77
Spearman's rho =       0.7413

Test of Ho: peth21_18and16 and daysdrank_21 are independent
    Prob > |t| =       0.0000
```

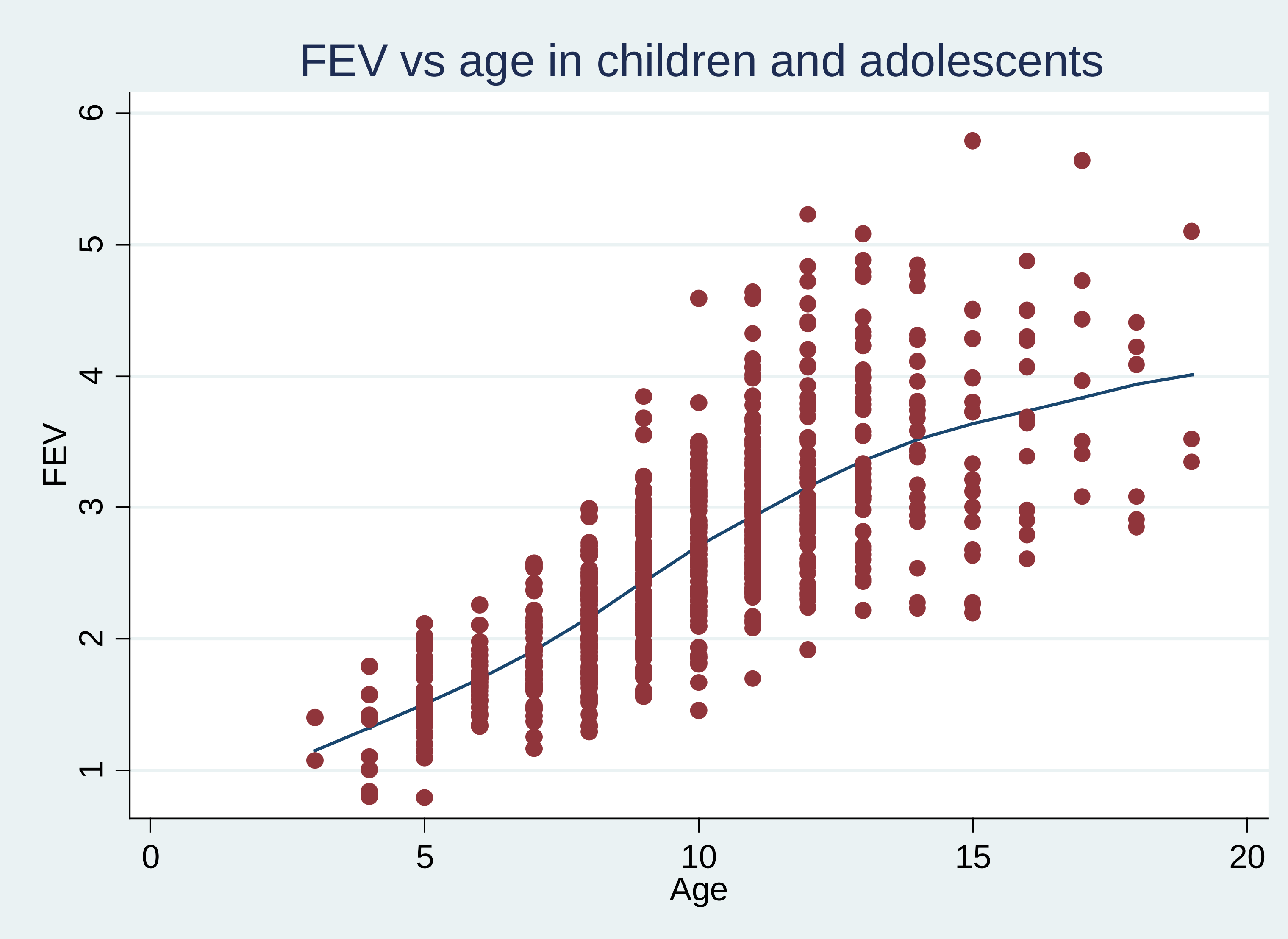
Simple linear regression

- Correlation allows us to quantify a linear relationship between two variables
- Regression allows us to additionally estimate how a change in a random variable X corresponds to a change in random variable Y

Forced expiratory volume (FEV)

- Studies in the 1970’s of children and adolescent’s pulmonary function, examining their own smoking and secondhand smoke
- FEV is the amount of air expelled in the first second of exhalation; forced expiratory volume
- The data are cross-sectional data from a larger prospective study

- Tager, I., Weiss, S., Munoz, A., Rosner, B., and Speizer, F. (1983), “Longitudinal Study of the Effects of Maternal Smoking on Pulmonary Function,” *New England Journal of Medicine*, 309(12), 699-703.
- Tager, I., Weiss, S., Rosner, B., and Speizer, F. (1979), "Effect of Parental Cigarette Smoking on the Pulmonary Function of Children," *American Journal of Epidemiology*, 110(1), 15-26.



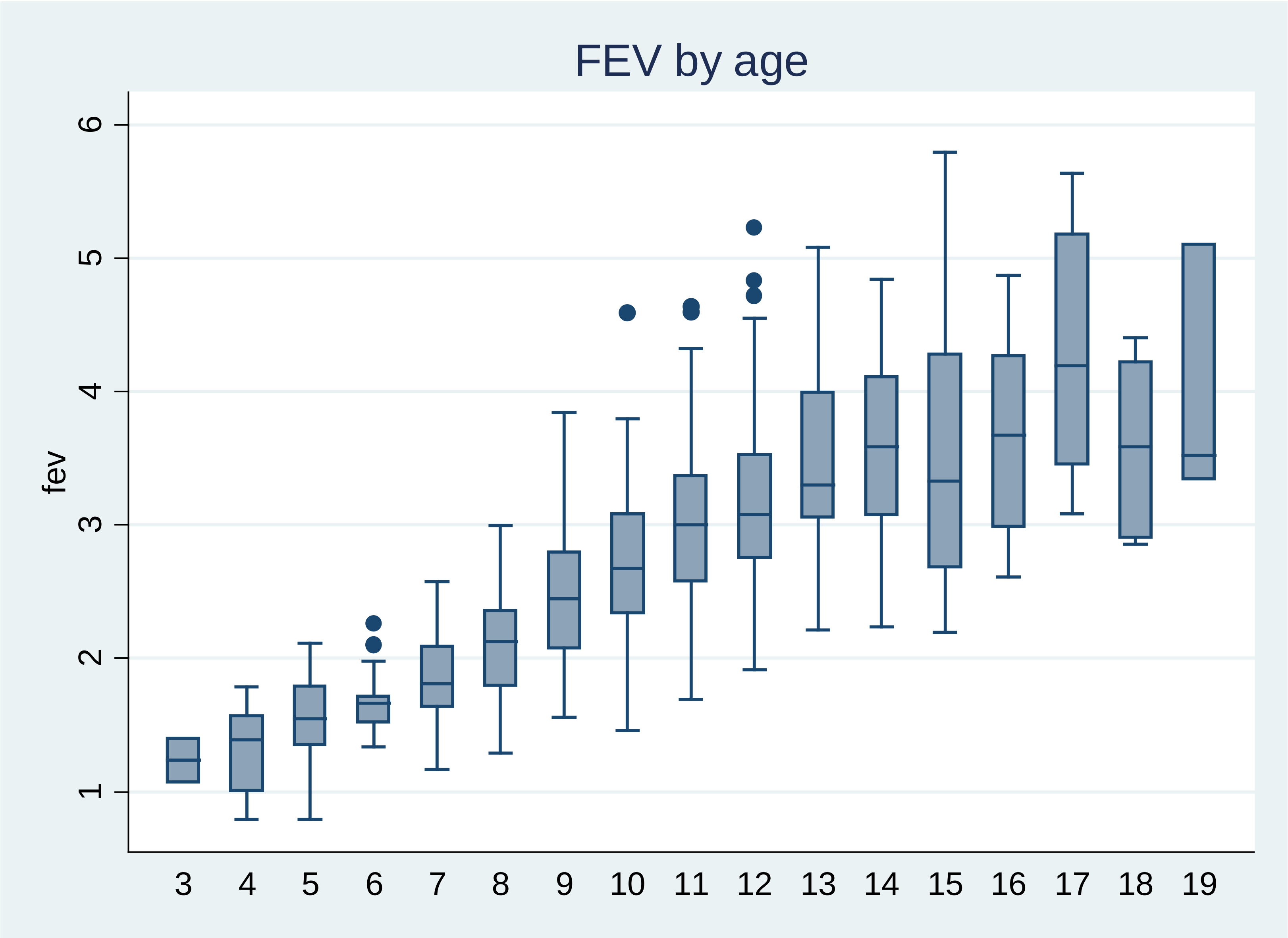

```
twoway (lowess fev age, bwidth(0.8)) (scatter fev age,
sort), ytitle(FEV) xtitle(Age)  legend(off) title(FEV vs
age in children and adolescents)
```

Correlation

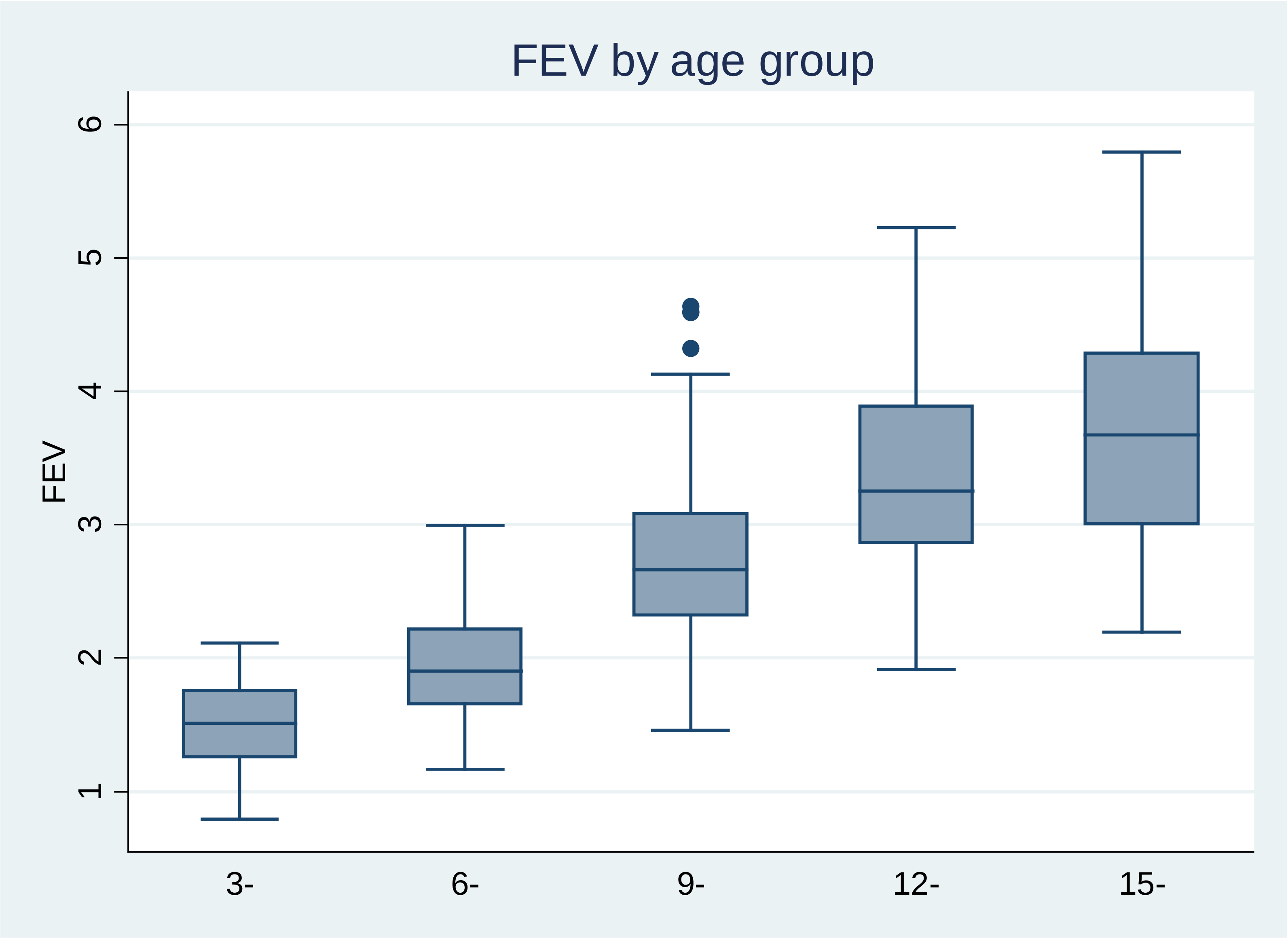
```
. pwcorr fev age, sig obs

             |      fev      age
-------------+------------------
         fev |   1.0000
             |
             |      654
             |
         age |   0.7565   1.0000
             |   0.0000
             |      654      654
             |


. spearman fev age

 Number of obs =     654
Spearman's rho =       0.7984

Test of Ho: fev and age are independent
    Prob > |t| =       0.0000
```

Concept of $\mu_{y|x}$ and $\sigma_{y|x}$

- Consider variables X and Y that are thought to be related
- You want to know how a difference in X translates to a difference in Y
- Plot X versus Y, but instead of using all values of X, categorize X into several categories
- What you get would look like a boxplot of Y by the grouped values of X
- Each of the groups of X has a mean of Y $\mu_{y|x}$ and a standard deviation $\sigma_{y|x}$




```
graph box fev, over(age) title(FEV by age)
```




```
egen agecat = cut(age), at(0,3,6,9,12,15,20) label
graph box fev, over(agecat) title(FEV by age group) ytitle(FEV)
```

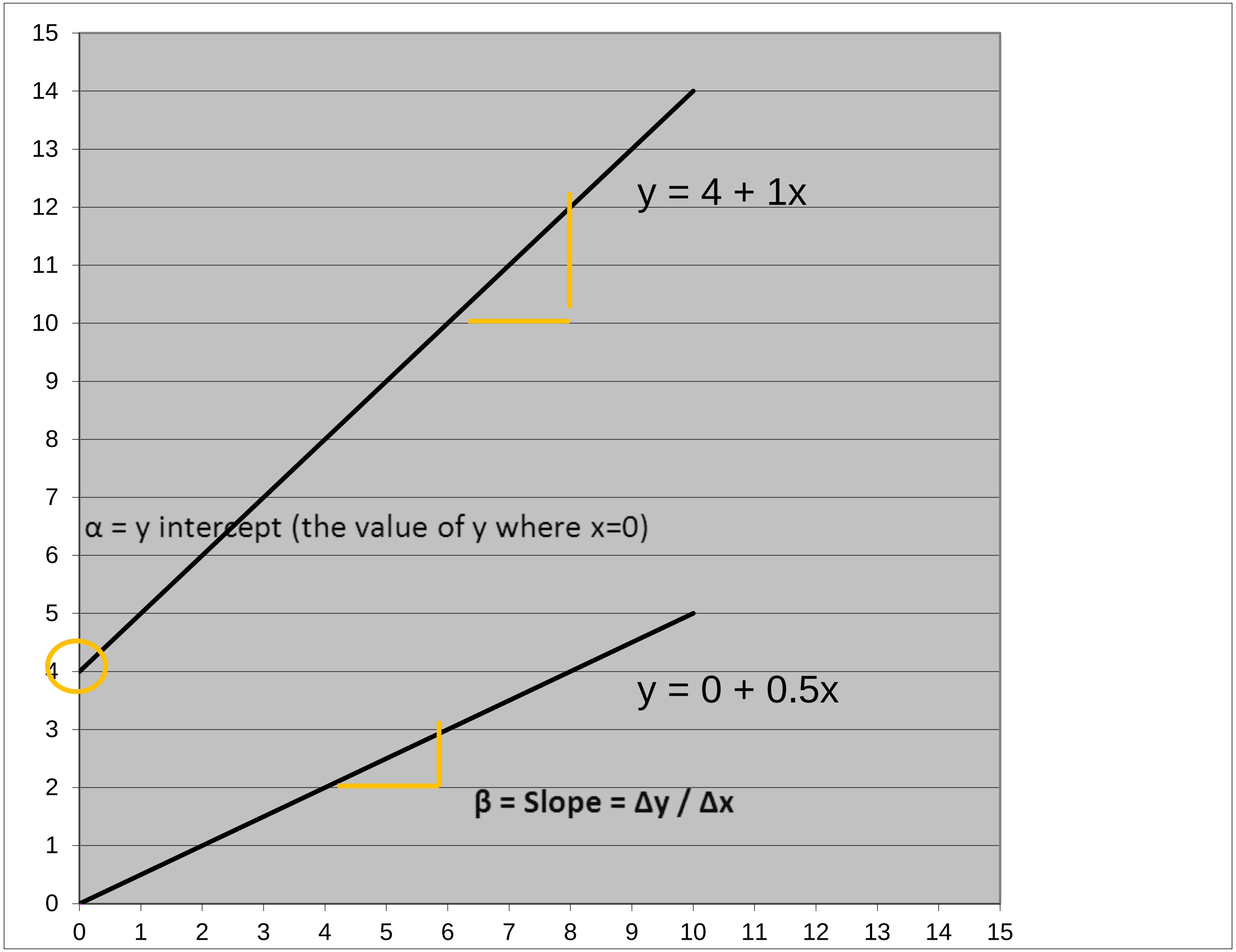
```
. tabstat fev, by(agecat) s(n min median max mean sd)

Summary for variables: fev
     by categories of: agecat

agecat |         N       min       p50       max      mean        sd
-------+------------------------------------------------------------
    3- |        39      .791     1.514     2.115  1.472385  .3346982
    6- |       176     1.165     1.901     2.993  1.943727  .3885005
    9- |       265     1.458     2.665     4.637   2.71723  .5866867
   12- |       125     1.916     3.255     5.224  3.384576  .7326963
   15- |        49     2.198     3.674     5.793  3.710143  .8818795
-------+------------------------------------------------------------
 Total |       654      .791    2.5475     5.793   2.63678  .8670591
--------------------------------------------------------------------
```

Simple linear regression

- The method allows us to investigate the effect of a difference in the *explanatory* variable on the *response* variable.
- Equivalent terms:
  - Response variable, dependent variable, outcome variable, Y
  - Explanatory variable, independent variable, predictor variable, correlate, X
- Here it matters which variable is X and which variable is Y
- Y is the variable that you want to predict, or better understand with X

The equation of a straight line

$y = \alpha + \beta x$



Simple linear regression

- Population regression equation is defined as

  $$\mu_{y|x} = \alpha + \beta x$$

- This is the equation of a straight line

- α and β are constants and are called the coefficients of the equation

Simple linear regression

- α is the y-intercept of the line y=$\alpha + \beta x$
- α is the mean value of Y when X=0

$$\mu_{y|0} = \alpha + \beta X \quad = \alpha$$

- β is the slope of the line
- β is the change in the mean value of y that corresponds to a one-unit increase in X

- E.g. X=3 vs. X=2

$$\mu_{y|3} - \mu_{y|2} = (\alpha + \beta*3) - (\alpha + \beta*2) = \beta$$

Simple linear regression

- Even if there is a linear relationship between Y and X in theory, there will be some variability in the population

- At each value of X, there is a range of Y values, with a mean $\mu_{y|x}$ and a standard deviation $\sigma_{y|x}$

- We note this by including an error term, ε, in our regression equation

Simple linear regression

- The linear regression equation is $y = \alpha + \beta x + \varepsilon$
- The error, ε, is the distance a sample value y has from the population regression line

$$y = \alpha + \beta x + \varepsilon$$

$$\mu_{y|x} = \alpha + \beta x \quad \textit{(population regression line)}$$

so $y - \mu_{y|x} = \varepsilon$

Simple linear regression

- Assumptions of linear regression
  - X's are measured without error
    - Violations of this cause the coefficients to attenuate toward zero
  - For each value of x, the y's are normally distributed with mean $\mu_{y|x}$ and standard deviation $\sigma_{y|x}$
  - The regression equation is correct $\mu_{y|x} = \alpha + \beta x$

Simple linear regression

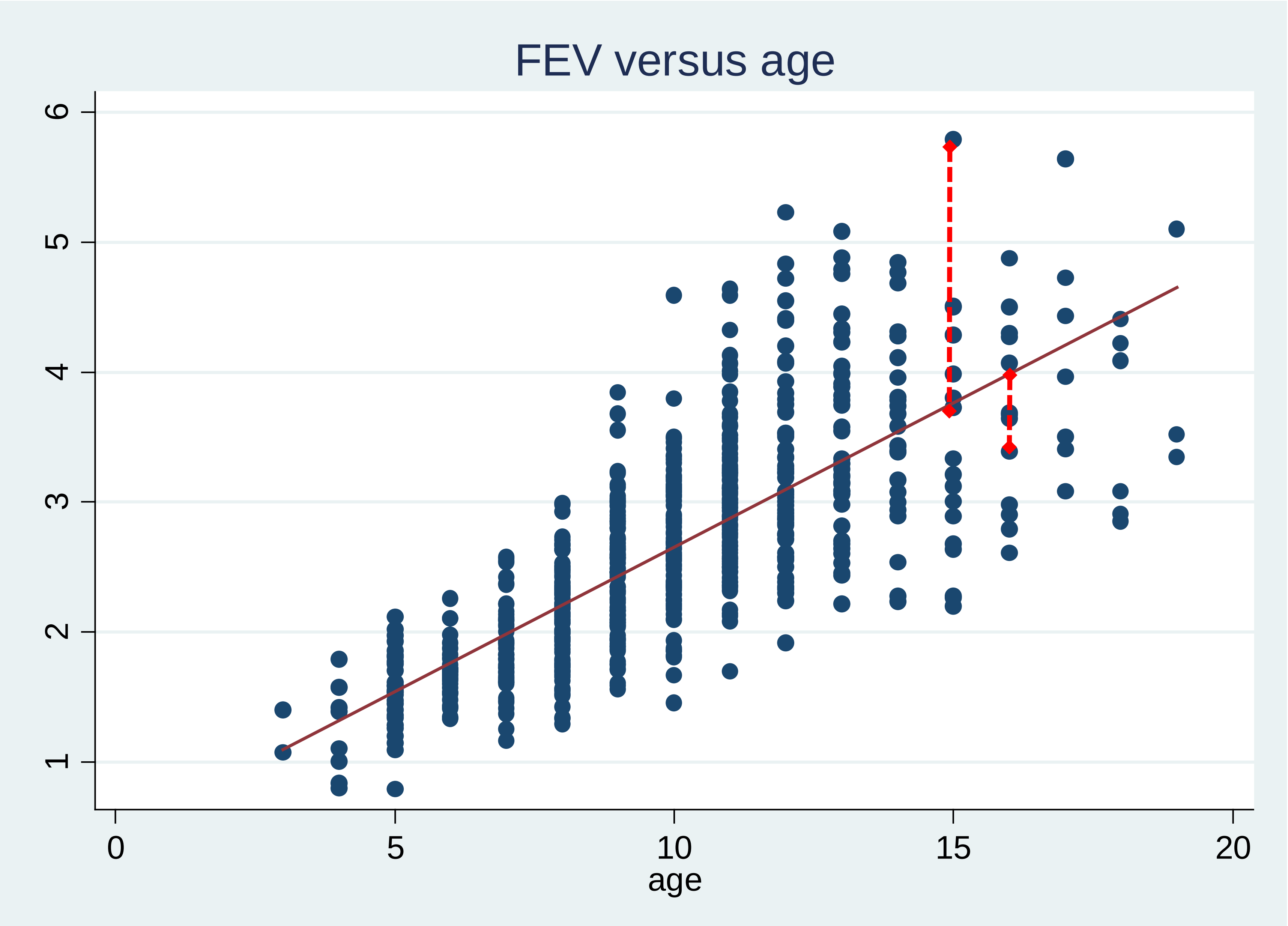
- Assumptions of linear regression (continued)
  - Homoscedasticity – the standard deviation of y at each value of X is constant; $\sigma_{y/x}$ the same for all values of X
    - The opposite of homoscedasticity is heteroscedasticity
    - This is similar to the equal variance issue that we saw in ttests and ANOVA
  - All the y_i ‘s are independent
    - You can’t guess the y value for one person (or observation) based on the outcome of another
- <u>Note that we do not need the X’s to be normally distributed, just the Y’s at each value of X</u>

Least squares

- We estimate the coefficients of the population regression line (α and β) using our sample of measurements of y and x
- We have a set of data, where the points are (y_i, x_i), and we want to put a line through them
- The distance from a data point (x_i, y_i) to the line at x_i is called the residual, e_i

$$e_i = y_i - \hat{y}_i$$

$\hat{y}_i$ is y-value of the regression line at x_i


FEV versus age
1
2
3
4
5
6
0
5
10
15
20
age

Simple linear regression

- The regression line equation is $\hat{y} = \hat{\alpha} + \hat{\beta}x$
- The "best" line is the one that finds the α and β that minimize the sum of the squared residuals Σe_i^2 (hence the name "least squares")
- We are minimizing the sum of the squares of the residuals, called the error sum of squares or the residual sum of squares

$$\sum_{i=1}^{n} e_i^2 = \sum_{i=1}^{n} (y_i - \hat{y}_i)^2$$

$$= \sum_{i=1}^{n} [y_i - (\hat{\alpha} + \hat{\beta}x_i)]^2$$

Simple linear regression

- The solution to this minimization is

$$\hat{\beta} = \frac{\sum_{i=1}^{n}(x_i - \overline{x})(y_i - \overline{y})}{\sum_{i=1}^{n}(x_i - \overline{x})^2} \quad \text{and} \quad \hat{\alpha} = \overline{y} - \hat{\beta}\overline{x}$$

  – These estimates are calculated directly from the x's and y's

Simple linear regression example: Regression of age on FEV

FEV= $\hat{\alpha} + \beta$ age

regress yvar xvar

```
. regress fev age

      Source |       SS       df       MS              Number of obs =     654
-------------+------------------------------           F(  1,   652) =  872.18
       Model |  280.919154     1  280.919154           Prob > F      =  0.0000
    Residual |  210.000679   652  .322086931           R-squared     =  0.5722
-------------+------------------------------           Adj R-squared =  0.5716
       Total |  490.919833   653  .751791475           Root MSE      =  .56753

------------------------------------------------------------------------------
         fev |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |    .222041   .0075185    29.53   0.000     .2072777    .2368043
       _cons |   .4316481   .0778954     5.54   0.000      .278692    .5846042
------------------------------------------------------------------------------
```

$\hat{\beta}$ = Coef for age

$\hat{\alpha}$ = _cons (short for constant)

Interpretation of the parameter estimates

- The least squares estimate is

  $\hat{y} = 0.432 + 0.222\,x$
- The intercept, 0.432 is the fitted value of y (FEV) for x (age) = 0
- The slope, 0.222 is the change in FEV corresponding to a change of 1 year in age. So a child with age=10 would have an FEV that is (on average) 0.222 higher than someone age 9. And the same for age 7 vs. 6, etc.

Simple linear regression – hypothesis testing

- We want to know if there is a relationship between x and y.
  - If there is no relationship then the value of y does not change with the value of x, and $\beta=0$.
  - Therefore $\beta=0$ is our null hypothesis.
- This is mathematically equivalent to the null hypothesis that the correlation $\rho=0$.
- We can also calculate a 95% confidence interval for β

Inference for regression coefficients

- We want to use the least squares regression line $\hat{y}=\hat{\alpha} + \hat{\beta}x$ to make inference about the population regression line $\mu_{y|x} = \alpha + \beta x$
- If we took repeated samples in which we measured x and y together and calculated the least squares estimates , we would have a distribution for the estimates $\hat{\alpha}$ and $\hat{\beta}$

Inference for regression coefficients

- The standard error of the estimates are

$$se(\hat{\beta}) = \frac{\sigma_{y|x}}{\sqrt{\sum_{i=1}^{n}(x_i - \overline{x})^2}}$$

$$se(\hat{\alpha}) = \sigma_{y|x}\sqrt{\frac{1}{n} + \frac{\overline{x}^2}{\sum_{i=1}^{n}(x_i - \overline{x})^2}}$$

where we estimate $\sigma_{y|x}$ with $s_{y|x}$

and $$s_{y|x} = \sqrt{\frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{n-2}}$$

Inference for regression coefficients

- We can use these to test the null hypothesis H_0: $\beta = \beta_0$ against the alternative H_0: $\beta \neq \beta_0$
- The test statistic for this is $t = \dfrac{\hat{\beta} - \beta_0}{s\hat{e}(\hat{\beta})}$
- And it follows the t distribution with n-2 degrees of freedom under the null hypothesis

Inference for regression coefficients

- When β_0=0 , i.e. testing H_0: β =0 , this is equivalent to testing $\mu_{y|x} = \alpha + 0*x = \alpha$
- This is the same as testing the null hypothesis H_0: ρ=0
- The regression slope and the correlation coefficient are related: $\hat{\beta} = r\left(\frac{s_y}{s_x}\right)$
- 95% confidence intervals for β

$(\beta - t_{n-2,.025}se(\beta) , \beta + t_{n-2,.025}se(\beta))$

Simple linear regression example: Regression of age on FEV

FEV= $\hat{\alpha}$ + β age

```
regress yvar xvar

. regress fev age

      Source |       SS       df       MS              Number of obs =     654
-------------+------------------------------           F(  1,   652) =  872.18
       Model |  280.919154     1  280.919154           Prob > F      =  0.0000
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------------------------------------------------------------------------------
         fev |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |    .222041   .0075185    29.53   0.000     .2072777    .2368043
       _cons |   .4316481   .0778954     5.54   0.000      .278692    .5846042
------------------------------------------------------------------------------
```

R^2

- A summary of the model fit is the coefficient of determination, R^2
- $R^2 = r^2$, i.e. the Pearson correlation coefficient squared
- R^2 ranges from 0 to 1, and measures the proportion of the variability in y that is explained by the regression of y on x

R^2

- $\sigma^2_{y|x} = (1-\rho^2)\sigma^2_y$

  If correlation=0, then $\sigma^2_{y|x} = \sigma^2_y$

  If correlation=1, then $\sigma^2_{y|x} = 0$

- Substituting in sample values and rearranging:

$$R^2 = \frac{s_y^2 - s_{y|x}^2}{s_y^2}$$

- Looking at this formula illustrates how R^2 represents the portion of the variability that is removed by performing the regression on X

Simple linear regression: evaluating the model

$$\text{model sum of squares} = MSS = \sum_{i=1}^{n}(\hat{y}_i - \bar{y})^2$$

```
regress fev age

      Source |       SS       df       MS              Number of obs =     654
-------------+------------------------------           F(  1,   652) =  872.18
       Model |  280.919154     1  280.919154           Prob > F      =  0.0000
    Residual |  210.000679   652  .322086931           R-squared     =  0.5722
-------------+------------------------------           Adj R-squared =  0.5716
       Total |  490.919833   653  .751791475           Root MSE      =  .56753

------------------------------------------------------------------------------
         fev |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |    .222041   .0075185    29.53   0.000     .2072777    .2368043
       _cons |   .4316481   .0778954     5.54   0.000      .278692    .5846042
------------------------------------------------------------------------------
```

$=.7565^2$

$$\text{residual sum of squares} = RSS = \sum_{i=1}^{n}(y_i - \hat{y}_i)^2$$

$$\text{total sum of squares} = TSS = MSS + RSS$$
$$= \sum_{i=1}^{n}(y_i - \bar{y})^2$$

$$R^2 = \frac{TSS - RSS}{TSS} = \frac{MSS}{TSS}$$

- Notation note:
  - Biostat 208 textbook Vittinghoff et al. use slightly different notation
  - The regression line notation we are using is

$$\hat{y} = \hat{\alpha} + \hat{\beta} x$$

Vittinghoff et al. uses

$$\hat{y} = \hat{\beta}_0 + \hat{\beta}_1 x$$

For next time

- Read Pagano and Gauvreau
  - Pagano and Gauvreau Chapter 17-18 (review)
  - Pagano and Gauvreau Chapter 18-19