BMEG 802 – Advanced Biomedical Experimental Design and Analysis

Regression

Joshua G. A. Cashaback, PhD

Recap

- Effect Size
- Power
  - Parametric
  - Numerical

Learning Objectives

- Regression
  - Bivariate
    - Linear (Derivation)
    - Nonlinear
  - Multiple Regression
- Correlation
  - Pearson's r
  - Spearman's ρ

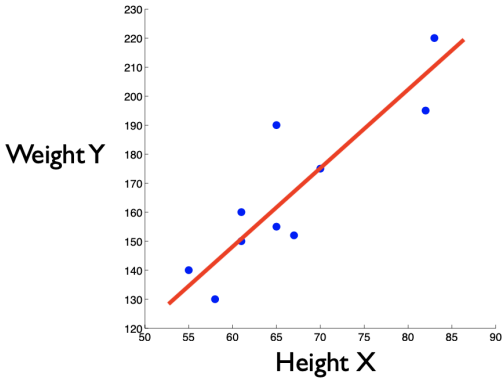
BIVARIATE LINEAR REGRESSION

Regression - Bivariate

$$\hat{y}_i = B_0 + B_1 \cdot x_i$$

- want to predict $\hat{y}_i$ (e.g., height) based on x_i (e.g., weight).
  - equation of a line
    - B_1 (slope), B_1 (intercept)
  - X,Y continuous
  - relationship between X and Y

Regression - Bivariate



Height (X)	Weight (Y)
55	140
61	150
67	152
83	220
65	190
82	195
70	175
58	130
65	155
61	160

Line of best fit: $B_0 = -7.2$, $B_1 = 2.6$

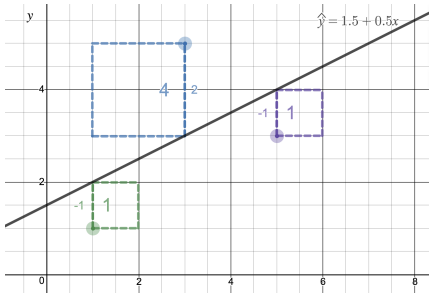
- least squares
- what do squares have to do with this???

Bivariate Regression - Least Squares

Optimization problem:

$$min(y_i - \hat{y}_i)^2$$

where $\hat{y}_i$ and y_i are respectively the predicted and actual y values.



We find B_1 (slope), B_0 (intercept) that minimize the squared differences!

Least Squares Derivation

remember, $\hat{y}_i = B_0 + B_1 \cdot x_i$ and we want to $min(y_i - \hat{y}_i)^2$

$$(y_i - \hat{y}_i)^2 = (y_i - (B_0 + B_1 \cdot x_i))^2$$
$$(y_i - \hat{y}_i)^2 = (y_i - B_0 - B_1 \cdot x_i)^2$$

In particular, we minimum the sum of squares

$$\sum_{i=1}^{n} (y_i - \hat{y}_i)^2 = \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i)^2$$

$$SS = \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i)^2$$

$$\frac{\partial SS}{\partial B_0} = 0$$
$$\frac{\partial SS}{\partial B_1} = 0$$

Results in two equations with two unknowns.

Least Squares Derivation - Intercept

$$\frac{\partial}{\partial B_0} \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i)^2 = 0$$

We can move the sum outside:

$$\sum_{i=1}^{n} \frac{\partial}{\partial B_0} (y_i - B_0 - B_1 \cdot x_i)^2 = 0$$

Taking the derivative (note the chain rule):

$$\sum_{i=1}^{n} 2(y_i - B_0 - B_1 \cdot x_i)(-1) = 0$$

Rearranging,

$$-2 \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i) = 0$$

Least Squares Derivation - Slope

$$\frac{\partial}{\partial B_1} \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i)^2 = 0$$

$$\sum_{i=1}^{n} \frac{\partial}{\partial B_0} (y_i - B_0 - B_1 \cdot x_i)^2 = 0$$

$$\sum_{i=1}^{n} 2(y_i - B_0 - B_1 \cdot x_i)(-x_i) = 0$$

$$-2 \sum_{i=1}^{n} (y_i - B_0 - B_1 \cdot x_i)(x_i) = 0$$

Two equations and two unknowns

Least Squares Derivation - Tip Interlude

$$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i;$$

Thus,

$$\sum_{i=1}^{n} x_i = n\bar{x}$$

Similarly,

$$\sum_{i=1}^{n} y_i = n\bar{y}$$

When summing a constant you can multiply by n. For example,

$$\sum_{i=1}^{n} \bar{x} = n\bar{x}$$

Least Squares Derivation - Tip Interlude Cont'd

$$\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y}) = \sum_{i=1}^{n} x_i \cdot y_i - \sum_{i=1}^{n} x_i \cdot \bar{y} - \sum_{i=1}^{n} y_i \cdot \bar{x} + \sum_{i=1}^{n} \bar{x} \cdot \bar{y} \tag{1}$$

$$= \sum_{i=1}^{n} x_i \cdot y_i - \sum_{i=1}^{n} x_i \cdot \bar{y} - \sum_{i=1}^{n} y_i \cdot \bar{x} + \sum_{i=1}^{n} \bar{x} \cdot \bar{y} \tag{2}$$

$$= \sum_{i=1}^{n} x_i \cdot y_i - n \cdot \bar{x} \cdot \bar{y} - n \cdot \bar{x} \cdot \bar{y} + n \cdot \bar{x} \cdot \bar{y} \tag{3}$$

$$= \sum_{i=1}^{n} x_i \cdot y_i - n \cdot \bar{x} \cdot \bar{y} \tag{4}$$

Least Squares Derivation - Tip Interlude Cont'd

$$\sum_{i=1}^{n}(x_i - \bar{x})^2 = \sum_{i=1}^{n}(x_i^2 - 2 \cdot x_i \cdot \bar{x} + \bar{x}^2) \tag{5}$$

$$= \sum_{i=1}^{n} x_i^2 - 2 \cdot \bar{x} \sum_{i=1}^{n} \cdot x_i + \sum_{i=1}^{n} \bar{x}^2 \tag{6}$$

$$= \sum_{i=1}^{n} x_i^2 - 2 \cdot \bar{x} \cdot n \cdot \bar{x} + n\bar{x}^2 \tag{7}$$

$$= \sum_{i=1}^{n} x_i^2 - n\bar{x}^2 \tag{8}$$

Least Squares Derivation - Intercept

Let's do some algebra on our previous equation:

$$-2\sum_{i=1}^{n}(y_i - B_0 - B_1 \cdot x_i) = 0$$

Divide both sides by -2,

$$\sum_{i=1}^{n}(y_i - B_0 - B_1 \cdot x_i) = 0$$

$$\sum_{i=1}^{n} y_i - \sum_{i=1}^{n} B_0 - B_1 \cdot \sum_{i=1}^{n} x_i = 0$$

$$n \cdot \bar{y} - n \cdot B_0 - B_1 \cdot n \cdot \bar{x} = 0$$

$$\bar{y} - B_0 - B_1 \cdot \bar{x} = 0$$

$$B_0 = \bar{y} - B_1 \cdot \bar{x}$$

Least Squares Derivation - Slope

$$-2\sum_{i=1}^{n}(y_i - B_0 - B_1 \cdot x_i)(x_i) = 0$$

$$\sum_{i=1}^{n}(x_i \cdot y_i - B_0 \cdot x_i - B_1 \cdot x_i^2) = 0$$

$$\sum_{i=1}^{n} x_i \cdot y_i - B_0 \sum_{i=1}^{n} x_i - B_1 \sum_{i=1}^{n} x_i^2 = 0$$

$$\sum_{i=1}^{n} x_i \cdot y_i - B_0 \sum_{i=1}^{n} x_i - B_1 \sum_{i=1}^{n} x_i^2 = 0$$

Substitute in B_0

$$\sum_{i=1}^{n} x_i \cdot y_i - (\bar{y} - B_1 \cdot \bar{x})n \cdot \bar{x} - B_1 \sum_{i=1}^{n} x_i^2 = 0$$

Least Squares Derivation - Slope Cont'd

$$\sum_{i=1}^{n} x_i \cdot y_i - (\bar{y} - B_1 \cdot \bar{x}) n \cdot \bar{x} - B_1 \sum_{i=1}^{n} x_i^2 = 0$$

$$\sum_{i=1}^{n} x_i \cdot y_i - n \cdot \bar{x} \cdot \bar{y} + n \cdot B_1 \cdot \bar{x}^2 - B_1 \sum_{i=1}^{n} x_i^2 = 0$$

$$\sum_{i=1}^{n} x_i \cdot y_i - n \cdot \bar{x} \cdot \bar{y} = B_1 \sum_{i=1}^{n} x_i^2 - n \cdot B_1 \cdot \bar{x}^2$$

$$\sum_{i=1}^{n} (x_i - \bar{x})(y_i - \bar{y}) = B_1 \sum_{i=1}^{n} (x_i - \bar{x})^2$$

$$B_1 = \frac{\sum_{i=1}^{n} (x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^{n} (x_i - \bar{x})^2}$$

Derivation Summary

$$B_1 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^{n}(x_i - \bar{x})^2}$$

$$B_0 = \bar{y} - B_1 \cdot \bar{x}$$

Calculate B's

Height weight example.

```
weight = c(55,61,67,83,65,82,70,58,65,61)
height = c(140,150,152,220,190,195,175,130,155,160)
B1 = sum((weight - mean(weight)) * (height - mean(height))) / sum((weight -
B0 = mean(height) - B1 * mean(weight)
B0
```

```
## [1] -7.17693
```

```
B1
```

```
## [1] 2.606851
```

Bivariate Prediction

We can now predict height based on weight

```
weight_bob = 80
height_bob = B0 + B1 * weight_bob
height_bob
```

```
## [1] 201.3711
```

- Assumes residuals are normally distributed (plot residuals $(y_i - \hat{y}_i)$
  - flat line with equal noise throughout range of x-values
- Cannot extrapolate
- Least squares sensitive to outliers (robust = absolute deviations)
- Make sure to plot data to see if linear relationship holds

Bivariate - Standard Error of Estimate

$$SE = \sqrt{\frac{\sum_i^n (y_i - \hat{y})^2}{N - 2}}$$

- Quality of the fit
- N = number of pairs of data
  - N-2 = degrees of freedom (lose two because we have two parameters, B_1, B_0)

```
SE = sqrt(sum((height - (B0 + B1 * weight))^2) / (length(weight) - 2))
SE
```

```
## [1] 14.11408
```

Correlation Coefficent (r)

Pearson correlation coefficient (r) is the covariance of the two variables divided by the product of their standard deviations.

- metric for goodness of fit

$$r_{xy} = \frac{\sum_{i=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \bar{x})^2}\sqrt{\sum_{i=1}^{n}(y_i - \bar{y})^2}}$$

- range [-1,1]

- 0 = no relationship
- 1 = perfect positive correlation
- -1 = perfect negative correlation

Correlation Coefficent (r)

```
r = sum((weight - mean(weight)) * (height - mean(height))) / (sqrt(sum((wei
r
```

```
## [1] 0.8786421
```

OR

```
cor(height, weight)
```

```
## [1] 0.8786421
```

Coefficent of Determination (r)

r^2 (square correlation coefficient)

- amount of variance explained
- another way to measure quality of fit
- range [0,1]
  - 0 = no relationship
  - 1 = perfect correlation (explains 100% of the relationship)

```
rsquared = cor(weight,height)^2
rsquared
```

```
## [1] 0.772012
```

Bivariate Regression - Significance Test

H0: (population) r $= 0$;

H1: (population) r not equal to 0 (two-tailed)

H1: (population) r < 0 (or > 0) : one-tailed

Sampling distribution of r

- IF we were to randomly draw two samples from two populations that were not correlated at all, what proportion of the time would we get a value of r as as extreme as we observe?
- if p $< .05$ we reject H0

Bivariate Regression - Significance Test Cont'd

F-Distribution (Fisher-Snedecor):

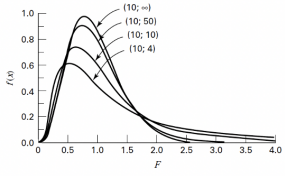
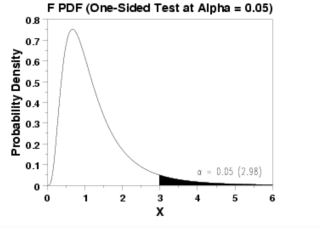


FIGURE 6.10.1 The F distribution for various degrees of freedom. (From *Documenta Geigy, Scientific Tables*, Seventh Edition, 1970. Courtesy of Ciba-Geigy Limited, Basel, Switzerland.)



- Compare if regression explains significantly more data with B_1
- p(df_{k-1}, df_{N-k}) - probability of F-statistic
  - k = number of parameters (e.g., k = 2 since B_1, B_0)
  - N = number of pairs

Bivariate Regression - Significance Test Cont'd

F-statistic for Bivariate regression:

$$F = \frac{r^2(N-2)}{1-r^2}$$

```
N = length(weight)
Fstat0 <- (r*r*(N-2)) / (1-(r*r))
# Area under F-Distribution, using pf() function
pval0 <- 1 - pf(Fstat0, 1, N-2) # Fstat, parameters (k - 1), df (N - k)
Fstat0
```

```
## [1] 27.08957
```

```
pval0
```

```
## [1] 0.0008176335
```

Bivariate Regression in R

Linear

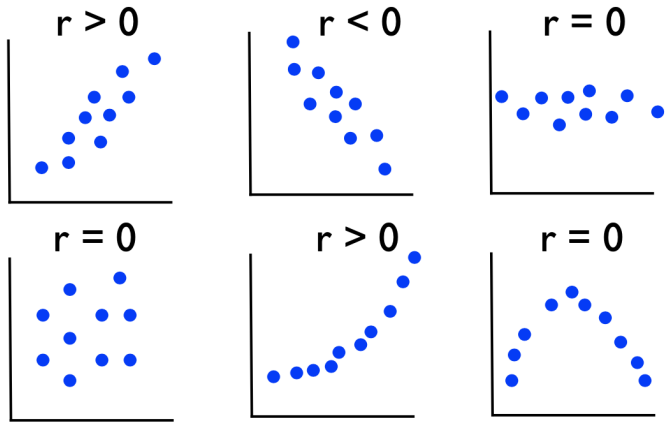
```
m1 <- lm(weight ~ height) # Linear model function!
```

```
summary(m1)
```

```
##
## Call:
## lm(formula = weight ~ height)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -8.6002 -2.9754  0.6787  2.0677  6.9190
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  17.3322     9.6037   1.805 0.108760
## height        0.2962     0.0569   5.205 0.000818 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 4.757 on 8 degrees of freedom
## Multiple R-squared:  0.772,  Adjusted R-squared:  0.7435
## F-statistic: 27.09 on 1 and 8 DF,  p-value: 0.0008176
```

BIVARIATE NONLINEAR REGRESSION

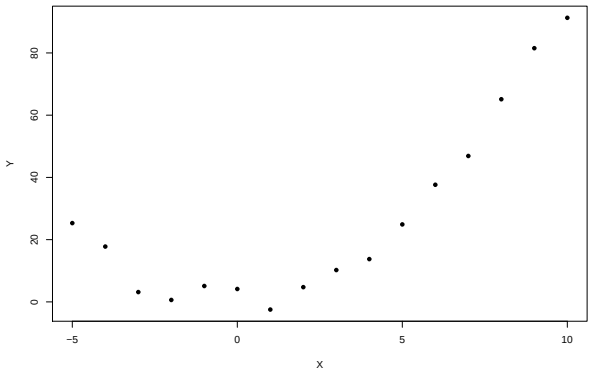
Regression - Nonlinear



remember: *r* measures **linear** correlation

Regression - Nonlinear

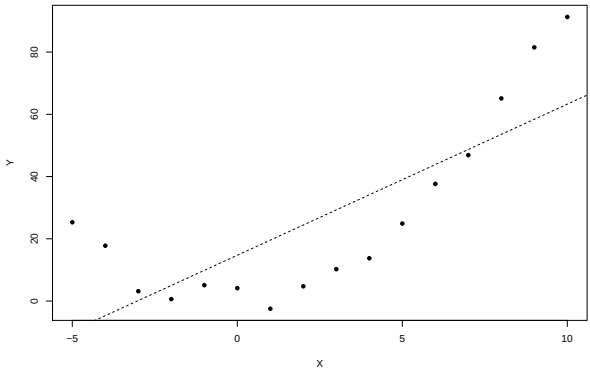
```
X <- c(-5,-4,-3,-2,-1,0,1,2,3,4,5,6,7,8,9,10)
Y <- X^2 + rnorm(16,0,3)
plot(X,Y,pch=16)
```



Regression - Nonlinear

Linear regression would produce:

```
m2 <- lm(Y ~ X)
plot(X,Y,pch=16)
abline(m2, lty=2)
```



Regression - Nonlinear

We can include nonlinear terms: $\hat{y}_i = B_0 + B_1 \cdot x_i^2$

```
Xsquared <- X*X # make a nonlinear variable in R
m0 <- lm(Y ~ Xsquared)
summary(m0)
```

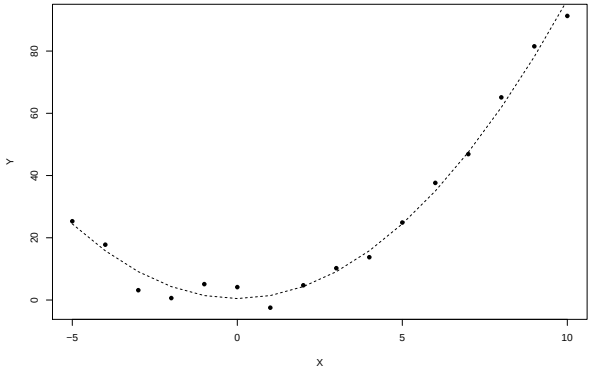
```
##
## Call:
## lm(formula = Y ~ Xsquared)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.9499 -2.4734  0.6495  2.7762  3.6779
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  0.46555    1.13890   0.409    0.689
## Xsquared     0.95968    0.02808  34.171  6.9e-15 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.348 on 14 degrees of freedom
## Multiple R-squared:  0.9882, Adjusted R-squared:  0.9873
## F-statistic:  1168 on 1 and 14 DF,  p-value: 6.9e-15
```

Note: In practice you typically assume linearity a priori (unless you have theoretical reason)

Regression - Nonlinear

Plotting the result:

```
 Xsquared <- X*X # make a nonlinear variable in R
yfit <- predict(m0,data.frame(X=Xsquared)) # predicted y-values from linear model
plot(X,Y,pch=16)
lines(X,yfit,lty=2)
```



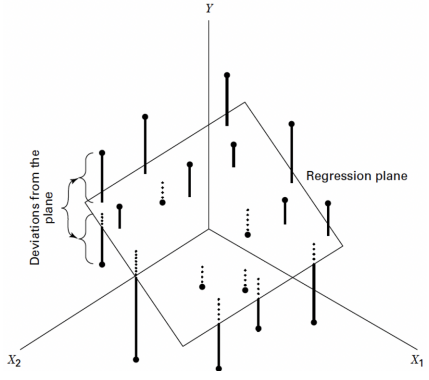
Note: In practice you typically assume linearity a priori (unless you have theoretical reason)

MULTIPLE REGRESSION

Multiple Regression

Same idea as bivariate, but just adding more terms

$$\hat{y}_i = B_0 + B_1 \cdot x_i + B_2 \cdot x_i + ... + B_n \cdot x_i$$



Multiple Regression

TABLE 10.6.1 Bone Toughness and Collagen Network Properties for 29 Femurs

W	P	S
193.6	6.24	30.1
137.5	8.03	22.2
145.4	11.62	25.7
117.0	7.68	28.9
105.4	10.72	27.3
99.9	9.28	33.4
74.0	6.23	26.4
74.4	8.67	17.2
112.8	6.91	15.9
125.4	7.51	12.2
126.5	10.01	30.0
115.9	8.70	24.0
98.8	5.87	22.6
94.3	7.96	18.2
99.9	12.27	11.5
83.3	7.33	23.9
72.8	11.17	11.2
83.5	6.03	15.6
59.0	7.90	10.6
87.2	8.27	24.7
84.4	11.05	25.6
78.1	7.61	18.4
51.9	6.21	13.5
57.1	7.24	12.2
54.7	8.11	14.8
78.6	10.05	8.9
53.7	8.79	14.9
96.0	10.40	10.3
89.0	11.72	15.4

W (Bone Toughness: Force required to fracture bone)

P (Porosity)

S (Tensile Strength)

Multiple Regression

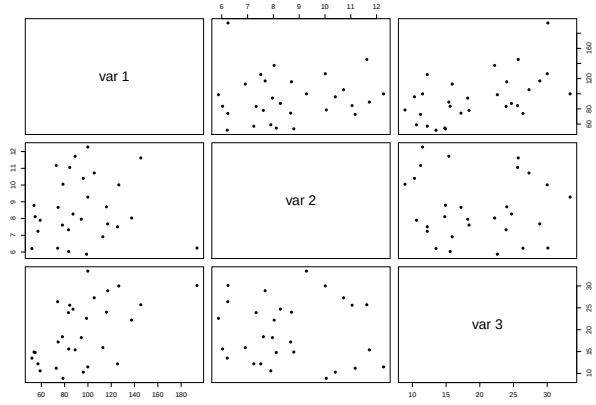
Inputting data (note, you can also have R read in files)

```
W = c(193.6, 137.5, 145.4, 117, 105.4, 99.9, 74, 74.4, 112.8, 125.4, 126.5
P = c(6.24, 8.03, 11.62, 7.68, 10.72, 9.28, 6.23, 8.67, 6.91, 7.51, 10.01,
S = c(30.1, 22.2, 25.7, 28.9, 27.3, 33.4, 26.4, 17.2, 15.9, 12.2, 30., 24.
data0 <- array(c(W,P,S), dim = c(length(W), 3))
```

Multiple Regression

Take a look at the data

```
pairs(data0, pch=16)
```



Multiple Regression - NEED TO CHECK

How correlated are porosity (P, column 2) and strength (S, column 3) to bone toughness (W, column1)

```
r <- cor(data0)
r <- r[1,2:3]
r
```

```
## [1] 0.04331177 0.53547194
```

Multiple Regression - NEED TO FIX

Calculate p-values from the F-distribution

```
N <- nrow(data0) # length of data
# compute F statistic and then p value
F <- ((r^2)*(N-2))/(1-(r^2))
p <- 1-pf(F,1,N-2)
p
```

```
## [1] 0.823468733 0.002758688
```

Multiple Regression

Calculate p-values from the F-distribution

```
m2 <- lm(W ~ S + P)
```

```
summary(m2)
```

```
##
## Call:
## lm(formula = W ~ S + P)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -33.907 -19.594  -0.517  10.159  76.813
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  35.6138    29.1296   1.223  0.23245
## S             2.3960     0.7301   3.282  0.00294 **
## P             1.4509     2.7632   0.525  0.60397
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 27.42 on 26 degrees of freedom
## Multiple R-squared:  0.2942, Adjusted R-squared:  0.2399
## F-statistic: 5.419 on 2 and 26 DF,  p-value: 0.01078
```

Multiple Regression

The coefficients are: P (1.451) and S(2.396)

Stepwise - Multiple Regression

```
m_min <- lm(W ~ 1)
m_all <- lm(W ~ S + P)
mbest <- step(m_min, list(lower=m_min, upper=m_all), direction="both")
```

```
## Start:  AIC=201
## W ~ 1
##
##        Df Sum of Sq   RSS    AIC
## + S     1    7943.8 19761 193.20
## <none>              27705 201.00
## + P     1      52.0 27653 202.94
##
## Step:  AIC=193.2
## W ~ S
##
##        Df Sum of Sq   RSS   AIC
## <none>              19761 193.2
## + P     1     207.4 19554 194.9
## - S     1    7943.8 27705 201.0
```

BIVARIATE NONPARAMETRIC

Nonparametric - Spearman's rank correlation coefficient

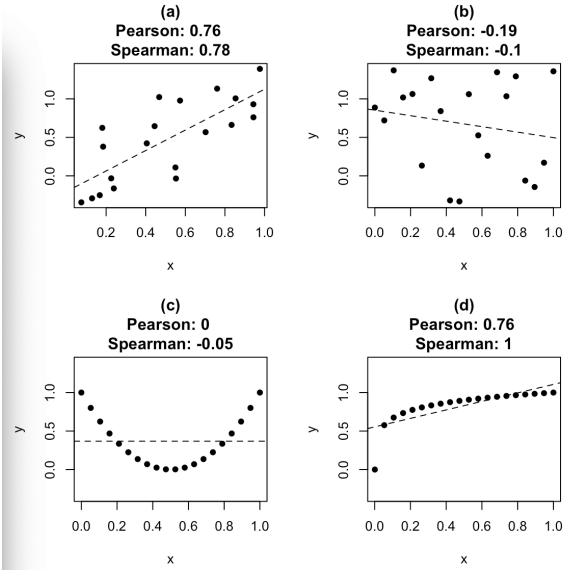
- violations of normality
  - e.g., heteroskedastic
- nonlinear
- less sensitive to outliers
- etc.

Nonparametric - Spearman's

Spearman's rank correlation coefficient (ρ)

- It assesses how well the relationship between two variables can be described using a monotonic (increasing or decreasing) function
- rank order method
- range [-1,+1]

Nonparametric - Spearman's



Nonparametric - Spearman's

IQ, X_i	Hours of TV per week, Y_i	rank x_i	rank y_i	d_i	d_i^2
86	2	1	1	0	0
97	20	2	6	–4	16
99	28	3	8	–5	25
100	27	4	7	–3	9
101	50	5	10	–5	25
103	29	6	9	–3	9
106	7	7	3	4	16
110	17	8	5	3	9
112	6	9	2	7	49
113	12	10	4	6	36

Next Week

Analysis of Variance (ANOVA) - between (one-way)