



STATS – Modelação Estatística
PhD Programme in Health Data Science

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Multiple linear regression is an extension of the simple linear regression model to several covariates

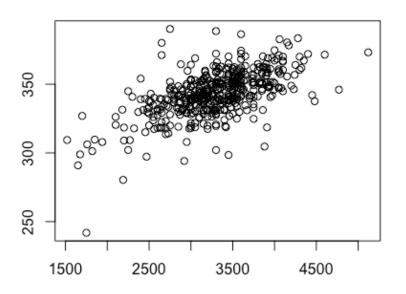
$$y_i = \beta_0 + \beta_1 x_{1i} + \dots + \beta_k x_{ki} + \epsilon_i, \epsilon_i \sim N(0, \sigma^2)$$

$$\mu_{y_i|x_{1i},x_{2i},...,x_{ki}} = \beta_0 + \beta_1 x_{1i} + \dots + \beta_k x_{ki}$$



on

Is the newborn weight related to head circumference?



```
> regressao <- lm(alcohol$ofc~alcohol$birthwt, data=alcohol)</pre>
> summary(regressao)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt, data = alcohol)
Residuals:
    Min
             10 Median
                                    Max
-72.016 -7.760
                 1.330
                          7.688 57.259
Coefficients:
                 Estimate Std. Error t value Pr(>|t|)
(Intercept)
                2.805e+02 4.015e+00
alcohol$birthwt 1.905e-02 1.209e-03
                                       15.76
Signif. codes:
                  '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 13.54 on 452 degrees of freedom
Multiple R-squared: 0.3546, Adjusted R-squared: 0.3532
```

F-statistic: 248.4 on 1 and 452 DF, p-value: < 2.2e-16





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> regressao <- lm(alcohol$ofc~alcohol$birthwt, data=alcohol)</pre>
> summary(regressao)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt, data = alcohol)
Residuals:
            10 Median
   Min
                            3Q
                                   Max
-72.016 -7.760 1.330 7.688 57.259
Coefficients:
                Estimate Std. Error t value Pr(>|t|)
(Intercept)
               2.805e+02 4.015e+00 69.88 <2e-16 ***
alcohol$birthwt 1.905e-02 1.209e-03 15.76 <2e-16 ***
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 13.54 on 452 degrees of freedom
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1

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> summary(regressao)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt, data = alcohol)
Residuals:
            10 Median
    Min
                            30
                                   Max
-72.016 -7.760 1.330 7.688 57.259
Coefficients:
                Estimate Std. Error t value Pr(>|t|)
               2.805e+02 4.015e+00
(Intercept)
                                      69.88
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```

```
Head circumference increases by an average of 0.019 mm for each gram of increase in baby weight.
```





Is the newborn weight related to head circumference?

Head circumference increases by an average of 0.019 mm for each gram of increase in baby weight.

And if we adjust for gestational age, newborn weight mantain the same relation with head circumference?





And if we adjust for gestational age, newborn weight mantain the same relation with head circumference?

```
> regressao2 <- lm(alcohol$ofc~alcohol$birthwt + alcohol$gestlmp, data=alcohol)</pre>
> summary(regressao2)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt + alcohol$gestlmp,
   data = alcohol)
Residuals:
    Min
            10 Median
-72.079 -8.251 1.346
                        7.632 54.835
Coefficients:
                 Estimate Std. Error t value Pr(>|t|)
               2.484e+02 1.486e+01 16.716
(Intercept)
                                              <2e-16 ***
alcohol$birthwt 1.767e-02 1.367e-03 12.922
                                              <2e-16 ***
alcohol$gestlmp 9.374e-01 4.169e-01 2.248
                                               0.025 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 13.53 on 447 degrees of freedom
  (4 observations deleted due to missingness)
Multiple R-squared: 0.3591,
                               Adjusted R-squared: 0.3563
F-statistic: 125.3 on 2 and 447 DF, p-value: < 2.2e-16
```

The effect of both variables becomes significant for a level of significance of 0.05.



```
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```

```
> regressao2 <- lm(alcohol$ofc~alcohol$birthwt + alcohol$gestlmp, data=alcohol)</pre>
> summary(regressao2)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt + alcohol$gestlmp,
    data = alcohol)
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                         7.632 54.835
Coefficients:
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alcohol$birthwt 1.767e-02 1.367e-03 12.922
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                                               0.025 *
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Residual standard error: 13.53 on 447 degrees of freedom
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Multiple R-squared: 0.3591, Adjusted R-squared: 0.3563
F-statistic: 125.3 on 2 and 447 DF, p-value: < 2.2e-16
```

For babies of the same gestational age (fixing the gestational age) the head circumference increases on average 0.018 mm for each gram of baby weight gain.







As in the simple linear regression model we can ask how much variation of y (here head circunference) can be explained by the model (now with 2 variables).

The answer is 36%.

$$\frac{44928 + 925}{44928 + 925 + 81821} = \frac{45853}{127674} = 0,359$$

```
> anova(regressao2)
```

Analysis of Variance Table

Response: alcohol\$ofc

```
Df Sum Sq Mean Sq F value Pr(>F)
              1 44928 44928 245.4500 < 2e-16 ***
alcohol$birthwt
alcohol$gestlmp 1 925 925 5.0556 0.02503 *
Residuals
        447 81821
                       183
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

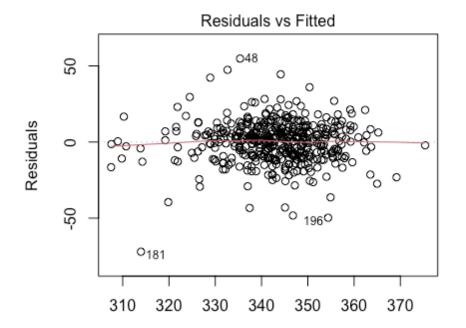






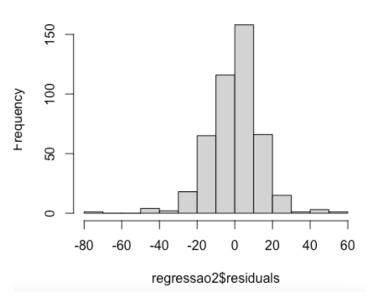
To check the assumptions of the model we can analyze the residuals as we did in the regression simple linear.

> plot(regressao2, 1)



> hist(regressao2\$residuals)

Histogram of regressao2\$residuals









And if we consider the same example but with a categorical covariate:

Sex (0=female; 1=male)

$$HC_i = \beta_0 + \beta_1 * bweight_i + \beta_2 * sex_i + \epsilon_i$$

For girls:

$$HC_i = \beta_0 + \beta_1 * bweight_i + \epsilon_i$$

For boys:

$$HC_i = (\beta_0 + \beta_2) + \beta_1 * bweight_i + \epsilon_i$$





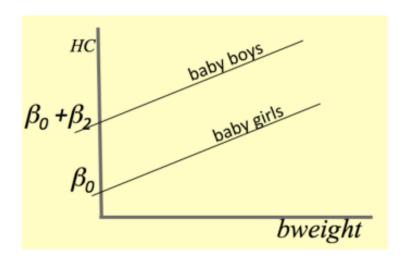
For girls:

$$HC_i = \beta_0 + \beta_1 * bweight_i + \epsilon_i$$

For boys:

$$HC_i = (\beta_0 + \beta_2) + \beta_1 * bweight_i + \epsilon_i$$

Each equation corresponds to a line with the same slope but with different intercepts

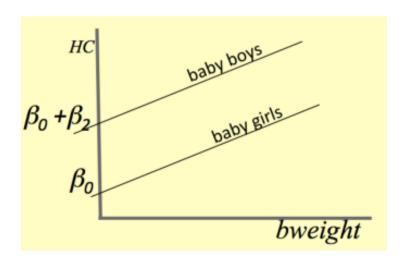








Girls have, on average, a constant head circumference difference to boys, but the effect of baby weight on head circumference is the same for both sexes.





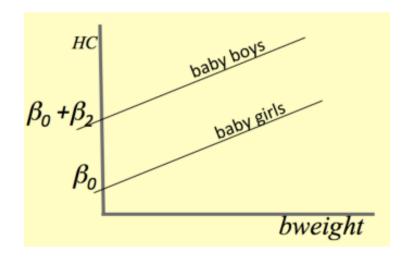




Girls have, on average, a constant head circumference difference to boys, but the effect of baby weight on head circumference is the same for both sexes.

BUT

we forced it when we chose this model



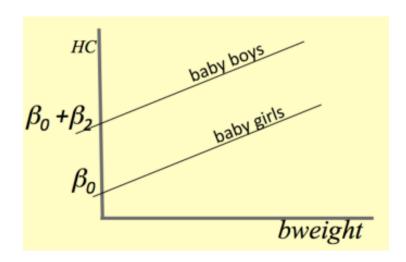






Girls have, on average, a constant head circumference difference to boys, but the effect of baby weight on head circumference is the same for both sexes.

But, in fact, the effect of the baby's weight on the head circumference may be different in each sex, but the model we choose doesn't allows this difference.





279.86750

2.11979

0.01891

(Intercept)

alcohol\$sex

alcohol\$birthwt

```
> regressao3 <- lm(alcohol$ofc~alcohol$birthwt + alcohol$sex, data=alcohol)
> summary(regressao3)

Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt + alcohol$sex, data = alcohol)

Residuals:
    Min    1Q Median    3Q Max
-73.213 -7.823    0.807    8.069    56.204

Coefficients:
    Estimate Std. Error t value Pr(>|t|)
```

4.02765 69.487

0.00121 15.635

1.27486

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

1.663

<2e-16 ***

<2e-16 ***

0.0971 .

Residual standard error: 13.51 on 451 degrees of freedom Multiple R-squared: 0.3586, Adjusted R-squared: 0.3557 F-statistic: 126.1 on 2 and 451 DF, p-value: < 2.2e-16 Gender is not significant, so we have no evidence of differences between sex in the head circumference, even adjusting for the baby's weight.





If the categorical variable has more than two categories there are two possible approaches.

Mothers' weight can be a categorical variable:

 $0: \le 65 \text{ kg}$

1: between 65 and 75 kg

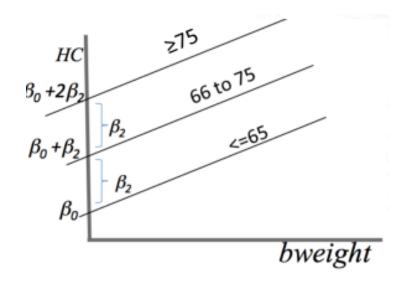
 $2: \geq 75 \text{ kg}$

$$HC_i = \beta_0 + \beta_1 * bweight_i + \beta_2 * mweight_i + \epsilon_i$$

$$HC_{i} = \beta_{0} + \beta_{1}bweight_{i} + \varepsilon_{i} \qquad \qquad \text{For mweight = 0}$$

$$HC_{i} = (\beta_{0} + \beta_{2}) + \beta_{1}bweight_{i} + \varepsilon_{i} \qquad \qquad \text{For mweight = 1}$$

$$HC_{i} = (\beta_{0} + 2\beta_{2}) + \beta_{1}bweight_{i} + \varepsilon_{i} \qquad \qquad \text{For mweight = 2}$$



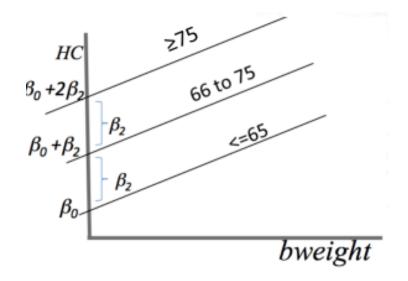






In addition to the lines being parallel (forced by the model) it is also imposed that the difference between the 3rd and 2nd groups is the same as the difference between the 1st and 2nd groups.

$$HC_{i} = \beta_{0} + \beta_{1}bweight_{i} + \varepsilon_{i}$$
 For mweight = 0
$$HC_{i} = (\beta_{0} + \beta_{2}) + \beta_{1}bweight_{i} + \varepsilon_{i}$$
 For mweight = 1
$$HC_{i} = (\beta_{0} + 2\beta_{2}) + \beta_{1}bweight_{i} + \varepsilon_{i}$$
 For mweight = 2









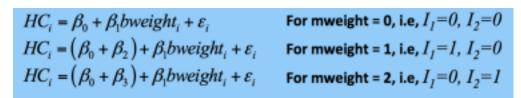
We can allow different differences between the groups.

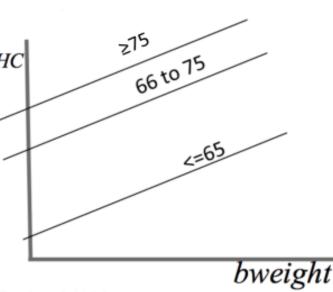
For that we have to create indicator variables (dummy).

$$HC_i = \beta_0 + \beta_1 bweight_i + \beta_2 I_{1i} + \beta_3 I_{2i} + \varepsilon_i$$

$$I_{1i} = \begin{cases} 1 \text{ if mweight}_i = 1 \\ 0 \text{ otherwise} \end{cases} \qquad I_{2i} = \begin{cases} 1 \text{ if mweight}_i = 2 \\ 0 \text{ otherwise} \end{cases}$$

Mweight	I_{I}	I_2
0	0	0
1	1	0
2	0	1

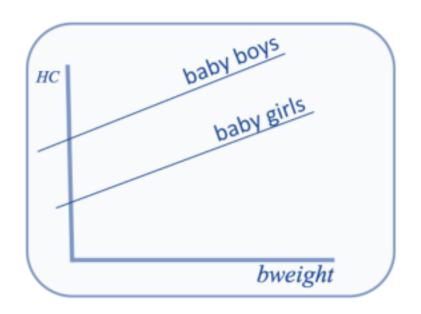


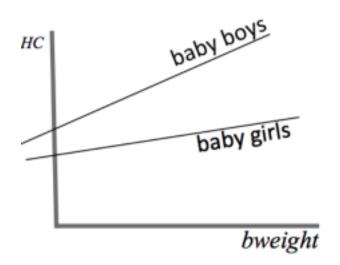




$$HC_i = \beta_0 + \beta_1 * bweight_i + \beta_2 * sex_i + \epsilon_i$$

assumes parallel lines in both sexes





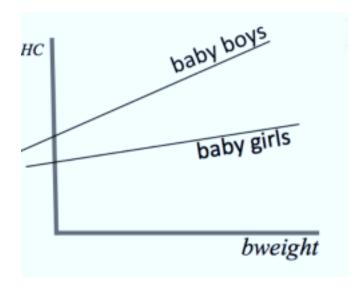




The lines being parallel means that the effect of the weight in head circumference is the same in both sexes.

The increase of 1 gr of weight leads to the same increases in head circumference in boys and in the girls.

If the effect of newborn weight is different for each sex we say that there is a **interaction** between weight and gender.





HEADS PHO PROGRAMME IN HEALTH DATA SCIENCE

That is, we will have two straight lines with diferente intercepts and slopes.

$$HC_i = \beta_0 + \beta_1 * bweight_i + \beta_2 * sex_i + \beta_3 * bweight_i * sex_i + \epsilon_i$$

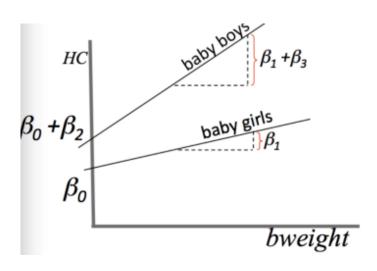
$$HC_i = \beta_0 + \beta_1 * bweight_i + \epsilon_i$$

$$HC_i = \beta_0 + \beta_2 + (\beta_1 + \beta_3) * bweight_i + \epsilon_i$$



$$HC_i = \beta_0 + \beta_1 * bweight_i + \epsilon_i$$

$$HC_i = \beta_0 + \beta_2 + (\beta_1 + \beta_3) * bweight_i + \epsilon_i$$





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```
> regressao3 <- lm(alcohol$ofc~alcohol$birthwt + alcohol$sex + alcohol$sex*alcohol$birthwt, data=alcohol)</pre>
> summary(regressao3)
Call:
lm(formula = alcohol$ofc ~ alcohol$birthwt + alcohol$sex + alcohol$sex *
    alcohol$birthwt, data = alcohol)
Residuals:
    Min
             10 Median
                                   Max
-71.704 -7.749 1.017 8.138 56.747
Coefficients:
                             Estimate Std. Error t value Pr(>|t|)
(Intercept)
                           284.327309 6.175274 46.043
                                                           <2e-16 ***
alcohol$birthwt
                             0.017535 0.001884
                                                   9.305
                                                           <2e-16 ***
alcohol$sex
                            -5.537319 8.136821 -0.681
                                                            0.497
alcohol$birthwt:alcohol$sex 0.002342 0.002458
                                                  0.953
                                                            0.341
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Residual standard error: 13.51 on 450 degrees of freedom
Multiple R-squared: 0.3599,
                              Adjusted R-squared: 0.3556
```

F-statistic: 84.33 on 3 and 450 DF, p-value: < 2.2e-16

The effect of weight on head circumference is 0.018 for girls (sex=0) and 0.018+0.002 for the boys (sex=1). However, this interaction it is not significant(p=0.341).

When we have an interaction in the model, the main effects test no longer has big importance.





If an interaction or covariable effect is non-significant, should we remove it from the model?

It depends...

How do we decide what variables to include or exclude from the model?

Common sense might be the right way to go