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Model with two

Regression

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The analysis of covariance

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The population

Different

representation

The general linear model

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January, 2024



Types of linear models

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THE research

The sample

Model with 1

Regressio models

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The populat

The analysis of covariance

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The populati Different

The model in t

The general linear model

Types:

Independent variable	Туре
factor	Anova
f.i. one placebo group and 2	
medication groups; coding 1,2 3	
Continuous	Regression
f.i dose or weight	_
Both grouping and continuous	Analysis of covariance
f.i one grouping variable medicine	-
and a variable dose	
Extensions with grouping and continuous (interaction)	General linear model

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Model with to

Regression models

models

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The cample

The analysis of covariance model

The da

The population

Different

representation

sample

The general linear model

Anova models

The research

The research

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The research

The cample

Model with to factors

models

The research

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The analysis of covariance

The da

The population

Different

The model in

The general linear model

Placebo	Treatment
87	86.5
86.5	87
89	85
88.5	86
87.5	85
88	83

observations: y_{ij} , the first index stands for the group and the second for the observation number within the group. So y_{25} is the fifth observation from the second group. The group means are denoted with \bar{y}_i and the overall mean with \bar{y}

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The research

The population

Model with tw

factors

Regression models

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The population

The analysis of covariance

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The population

Different

The model in the

The general linear model

The population

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The population

The sample

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The analysis o covariance model

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The model in

The general linear model

The population is the population we would have had if the experiment from the sample was done in the whole population. It's a theoretical construct.

The overall mean in the population is denoted by μ . The population mean of the first group is μ_1 and that of the second group is μ_2 . In general the mean of the i^{th} group is μ_i . The variance in each group is σ^2 . The observations are normally distributed.

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The population

The sample Model with to

Regressi

models

The popul

The sample

The analysis covariance model

The data

The populat

representatio

The model in sample

The general

We want to know if the group means differ from each other. Let's look at 2 situations:

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The research
The population

Model with t

Regressio

models

The research

The sample

The analysis o covariance

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The population

Different

The model in the

The general linear model

1 The group means are approximately the same : $\mu_1 \approx \mu_2$. The two group means are close to each other so they are close to the overall mean. The difference between the group means and the overall mean is small so the deviation $(\mu_i - \mu)$ is small. In this case the best summary of the data is the general mean μ . Some of the observations will be above μ and some will be below μ . How much an observation is above or below the mean is called a residual denoted with ϵ_{ii} . Now a model for the observations in this case is : observation = best summary + residual or $y_{ii} = \mu + \epsilon_{ii}$.

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The population

The sample

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Regression

models
The research

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The analysis of covariance

The data

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The model in 1

The general linear model

The group means are not equal so they will be far apart. So they don't look like the overall mean. The deviation $(\mu_i - \mu)$ is large (positive or negative). In this case the best summary of the data are the group means μ_i . Also here the observation will be above or below its own group mean. How much this is, is called the residual. Thus a model in this case can be $y_{ij} = \mu_i + \epsilon_{ij}$.

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The population

Model with to

Regression models

The research

The sample

The analysis of covariance model

The da

The populat

Different

The model in t

The general linear model

These two models can be written in one line, using that the deviations $(\mu_i - \mu)$, which are called group effects, will show whether or not there are differences between the groups:

$$y_{ij} = \mu + (\mu_i - \mu) + \epsilon_{ij}$$

$$\epsilon_{ij} = y_{ij} - \mu - (\mu_i - \mu) = y_{ij} - \mu_i$$

The anova model in the population.

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The sample

Model with to factors

Regression

The received

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The analysis of

covariance model

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The populat

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The general linear model

In short:

The linear model for the anova case is

$$y_{ij} = \mu + (\mu_i - \mu) + \epsilon_{ij}$$

were the y_{ij} are normally distributed with mean μ_i and variance σ^2

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The sample

Model with

factors

Regression

models

The population

The sample

The analysis of covariance

The dat

The population

Different

The model in the

The general linear model

The sample

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The research

The populat

The sample

Model with t factors

Regressio models

The receive

The sample

The analysis o covariance model

The data

The population

The model in sample

The general linear model

Estimate the model: Replace the population means in the model by the sample means

$$y_{ij} = \bar{y} + (\bar{y}_i - \bar{y}) + e_{ij}$$

were $e_{ij} = y_{ij} - \bar{y}_i$.

Now write this model in terms of **deviations**:

$$y_{ij} - \bar{y} = (\bar{y}_i - \bar{y}) + e_{ij}$$

 $(y_{ij} - \bar{y})$ It is called the total deviation. $(\bar{y}_i - \bar{y})$ the between groups deviations. $e_{ij} = (y_{ij} - \bar{y}_i)$ are the residual deviations (the within group deviation)

Total deviation = between groups deviation + residual deviation

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The research

The population

The sample

Model with tw factors

Regressio models

The researc

The sample

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The da

The population

The model in th

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Now square the deviations and sum over all observations:

$$\sum_{\it all~observations} (y_{ij} - ar{y})^2 = \sum_{\it all~observations} (ar{y}_i - ar{y})^2 + \sum_{\it all~observations} e_{ij}^2$$

The deviations squared and summed are called **sums of squares**.

The total deviation squared and summed is called the **total sum** of squares SS_{Total} .

The between group deviations squared and summed is called the between groups sum of squares or shortly the sum of squares for the groups SS_{Group} .

The sum of the squared residuals is called the **residual sum of squares** SS_{Res} .

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The analysis o covariance model

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The model in the sample

The general linear model

Then

 $SS_{Total} = SS_{Group} + SS_{Res}$

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Model with to

Regression models

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The analysis o covariance

The data

The populatio

The model in t

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The general linear model

Sums of squares are based on a number of informative observations called **degrees of freedom**.

The total sums of squares has $df_{total} = n - 1$ degrees of freedom.

Divide the total sum of squares by this degrees of freedom to obtain the variance of the 12 observations.

The group sum of squares only contain the group means so the degrees of freedom is $df_{Group} = number\ of\ groups - 1$.

The degrees of freedom for the residual sum of squares is what is left: $df_{res} = df_{Total} - df_{group}$.

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The research

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Regression

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The research

The sample

The analysis of covariance

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The model in sample

The general linear model

Divide the sums of squares by there degrees of freedom to get the variances also called **mean sum of squares (MS)**: MS_{Total} , MS_{Group} and MS_{res} . (These don't add up!)

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The analysis of covariance

The da

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No differences between the groups so $\mu_1=\mu_2$ The variance within the groups is the same as the variance between the groups or $F=\frac{MS_{Group}}{MS_{res}}\approx 1$.

If the group means are unequal then the variance between the groups will be much larger than the variance within the groups.

 $H_0: \mu_1 = \mu_2$ against $H_1: \mu_1 \neq \mu_2$ one can use the result that F has a so called Fisher distribution with df_{group} and df_{res} degrees of freedom. One can use this to calculate p-values.

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The research

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Regression

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The analysis o covariance

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The general lines of the analysis are:

- Write down the model in the population:
 - $y_{ij} = \mu + (\mu_i \mu) + \epsilon_{ij}$
- 2 Estimate the model in the sample: $y_{ij} = \bar{y} + (\bar{y}_i \bar{y}) + e_{ij}$
- 3 Write the model in terms of deviations:

$$y_{ij}-\bar{y}=(\bar{y}_i-\bar{y})+e_{ij}$$

- 4 Square the deviations and sum over all observations to get the sum of squares: $SS_{Total} = SS_{Group} + SS_{Res}$
- 5 Divide the sum of squares by there degrees of freedom to get MS_{Total} , MS_{Group} and MS_{res} . See howmany times larger the between group variance is as compared to the residual variance (F).

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Regressio models

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The analysis of covariance model

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The general linear model

Put everything in a table (anova-table)

Name	SS	df	MS	F
groups	SS_{group}	df _{group}	MS_{group}	$\frac{MS_{Group}}{MS_{res}}$
Residual	SS_{res}	df_{res}	MS_{res}	763
Total	SS_{total}	df_{Total}		

In the blood pressure example the anova table is:

Name	SS	df	MS	F
Treatment	16.331	1	16.331	11.2
Residual	14.583	10	1.458	
Total	30.914	11		

The variance between groups is about 11 times larger as the residual. This can only be if there is a systematic difference between the groups. (The p-value is 0.0074)

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Suppose the first 3 observations were from individuals who got dose 1 and the last 3 are from individuals who got dose 2. The same goes for the treatment group. In that case we have a two factor experiment, one factor is treatment with 2 levels, placebo and treatment and the other factor is dose with two levels dose 1 and dose 2.

	Placebo Treatment	
dose 1	87	86.5
	86.5	87
	89	85
dose 2	88.5	86
	87.5	85
	88	83

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The research

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The analysis of covariance model

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An observation can be represented by y_{ijk} . This is the k^{th} observation from treatment i and dose j.

Treatment groups means are μ_i Dose groups group they are μ_j .

The treatment effects are then $\mu_i - \mu$ dose effects are $\mu_j - \mu$.

The analysis causes no extra problems since it goes along the same lines as with one factor:

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Regressio models

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The model in t

The general linear model

1 Write down the model in the population:

$$y_{ijk} = \mu + (\mu_i - \mu) + (\mu_j - \mu) + \epsilon_{ijk}.$$

2 Estimate the model in the sample:

$$y_{ijk} = \bar{y} + (\bar{y}_i - \bar{y}) + (\bar{y}_j - \bar{y}) + \epsilon_{ijk}$$

3 Write the model in terms of deviations:

$$y_{ijk} - \bar{y} = (\bar{y}_i - \bar{y}) + (\bar{y}_j - \bar{y}) + e_{ijk}$$

- 4 Square the deviations and sum over all observations to get the sum of squares: $SS_{Total} = SS_{treatment} + SS_{dose} + SS_{Res}$
- 5 Divide the sum of squares by there degrees of freedom to get MS_{Total} , $MS_{treatment}$, MS_{dose} and MS_{res} .

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Anova models

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Model with two factors

Regression models

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Put everything in a table (anova-table)

Name	SS	df	MS	F
treatment	$SS_{treatment}$	$df_{treatment}$	$MS_{treatment}$	$\frac{MS_{treatment}}{MS_{res}}$
dose	SS_{dose}	df _{dose}	MS_{dose}	$\frac{MS_{dose}}{MS_{res}}$
Residual	SS_{res}	df _{res}	MS_{res}	111-763
Total	SS_{total}	df_{Total}		

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To test whether or not there are differences between then dose groups use the result that $F = \frac{MS_{dose}}{MS_{res}}$ has a Fisher distribution with df_{dose} and df_{res} degrees of freedom.

To test whether or not there are differences between then treatment groups use the result that $F = \frac{MS_{treatment}}{MS_{res}}$ has a Fisher distribution with $df_{treatment}$ and df_{res} degrees of freedom.

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Regression models

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Anova models

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The general linear model

Dose	Blood pressure
5	87;86.5
6	86.5;87
7	89;85
8	88.5;86
9	87.5;85
10	88;83

We can make a scatter plot of this. The dose is on the x-axis and the blood pressure is on the y-axis.

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Regression models

The research

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The general linear model

The population

The regression model in the population.

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Anova models

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The analysis of covariance model

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The population is again the group of persons from which the sample was taken. But also here: it's a theoretical population.

The general form of a straight line is

$$\alpha + \beta x$$

y is the **dependent variable** and x is the **independent one**.

 α s the **intercept** of the line. β is the **regression coefficient** or **the slope**.

The regression model in the population.

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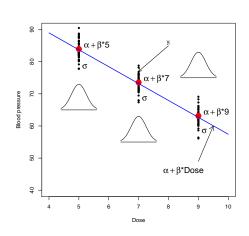


Figure 1: A population model for the relation between dose and blood pressure.

The regression model in the population.

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The linear model for the regression case is

$$y_i = \alpha + \beta x_i + \epsilon_i$$

where the y_i are normally distributed with mean $\alpha + \beta x_i$ and variance σ^2

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Continuous data: linear Models

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The general linear model

The sample values for α and β are a, the sample intercept, and b the sample slope. It are those values that give the **best fitted line** in the sample

A **residual** is given by $y_i - (a + bx_i)$.

This residual squared and summed over all data points is called the **residual sum of squares** SS_{res} .

$$SS_{res} = \sum_{i} \left[y_i - (a + bx_i) \right]^2$$

best fitted line has **smallest residuals** thus has smallest residuals sum of squares.

The regression model in the sample

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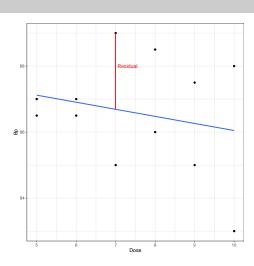


Figure 2: A population model for the relation between dose and blood pressure.

The regression model in the sample

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The analysis of covariance

The da

The populati

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The model in

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The general linear model

a and b can be calculated as :

$$b = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sum (x_i - \bar{x})^2}$$

$$a = \bar{y} - b\bar{x}$$

If a and b are calculated as above then the residual sum of squares is smallest.

That is why these estimates are called **least square estimates**.

The estimated regression model now is:

$$y_i = a + bx_i + e_i$$

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The analysis of covariance model

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The general linear model

Now, plug in $a = \bar{y} - b\bar{x}$ and write in terms of deviations:

$$y_i = \bar{y} - b\bar{x} + bx_i + e_i = \bar{y} + b(x_i - \bar{x}) + e_i$$

so

$$y_i - \bar{y} = b(x_i - \bar{x}) + e_i$$

which shows that:

Total deviation = regression deviation + residual deviation square the deviations and sum to get:

$$\sum_{i} (y_i - \bar{y})^2 = b^2 \sum_{i} (x_i - \bar{x})^2 + \sum_{i} e_i^2$$

SO

$$SS_{Total} = SS_{regres} + SS_{Res}$$

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Model with to

Regression models

The research

The sample

The analysis of covariance model

The data

representation

The model in th sample

The general linear model

The degrees of freedom for the total sums of squares $\sin n - 1$

The degrees of freedom for the regression sum of squares is 1

The degrees of freedom for the the residual sum of squares is what is left thus n-2.

Divide the sum of squares by the degrees of freedom to get the variance or the mean sum of squares: MS_{total} , MS_{regres} and MS_{res} .

Then put everything in a table, the anova table

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Anova models

The research

The population

The sample

Model with t

Regression models

The research

The sample

The analysis of covariance

The da

The populati

representat

The model in sample

The general linear model

The F – value can be calculated as $F = \frac{MS_{regres}}{MS_{res}}$

Can be used to test the hypothesis $H_0: \beta = 0$ against $H_1: \beta \neq 0$.

If this value is much larger then 1 this means that the data is best described with the regression line. If the F-value is approximately 1 then the data does not show a linear relationship and the data can just as well be summarized by calculating the mean.

To calculate a p-value use the result that F has a Fisher distribution with 1 and n-2 degrees of freedom.

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The research

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The sample

Model with to factors

Regression models

The researc

The sample

The analysis of covariance model

The populati

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The model in t sample

The general linear model

The general lines of the analysis are the same as in the anova case:

- **1** Write down the model in the population: $y_i = \alpha + \beta x_i + \epsilon_i$
- 2 Estimate the model in the sample: $y_i = a + bx_i + e_i$
- 3 Write the model in terms of deviations:

$$y_i - \bar{y} = b(x_i - \bar{x}) + e_i$$

- 4 Square the deviations and sum over all observations to get the sum of squares: $\sum_{i}(y_{i}-\bar{y})^{2}=b^{2}\sum_{i}(x_{i}-\bar{x})^{2}+\sum_{i}e_{i}^{2}$ so $SS_{Total}=SS_{regres}+SS_{Res}$
- 5 Divide the sum of squares by there degrees of freedom to get MS_{Total} , MS_{regres} and MS_{res} . See how many times larger the regression variance is as compared to the residual variance (F)

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The research

The population

The sample

Model with to factors

Regression models

The research

The sample

The analysis o covariance

The dat

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The model in the sample

The general linear model

Put everything in a table (anova-table)

Name	SS	df	MS	F
Regression	SS_{regres}	df _{regres}	MS_{regres}	$\frac{MS_{regres}}{MS_{res}}$
Residual	SS_{res}	df _{res}	MS_{res}	
Total	SS_{total}	df_{Total}		

In the blood pressure example the anova table is:

Name	SS	df	MS	F
regression	1.6	1	1.6	0.58
Residual	29.3	10	2.9	
Total	30.9	11		

So there is no evidence that the dose is linear related to the blood pressure.

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The research

The sample

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The analysis of covariance model

The data

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The general linear model

The analysis of covariance model

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Placebo		Treatment	
dose	blood pressure	dose	blood pressure
5	87	5	86.5
6	86.5	6	87
7	89	7	85
8	88.5	8	86
9	87.5	9	85
10	88	10	83

Think carefully about what to take as a covariate. The covariate may not be influenced by the treatment.

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Regression

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Anova models

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Model with to factors

Regression models

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The general linear model

The population is again the group of persons from which the sample was taken. But also here: it's a theoretical one.

The model is

$$y_{ij} = \alpha_i + \beta x_{ij} + \epsilon_{ij} = \alpha + (\alpha_i - \alpha) + \beta x_{ij} + \epsilon_{ij}$$

In group 1 this becomes: $y_{1j} = \alpha_1 + \beta x_{1j} + \epsilon_{1j}$

In group 2 this is: $y_{2j} = \alpha_2 + \beta x_{2j} + \epsilon_{2j}$.

The linear model for the ancova case is $y_{ij} = \alpha_i + \beta x_{ij} + \epsilon_{ij}$, y_i normally distributed with mean $\alpha_i + \beta x_{ij}$ and variance σ^2

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Anova models

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Model with two

Regression

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The population

Different

representation

sample

The general linear model

Different representation

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The research

The sample

Model with to factors

Regression models

The research

The sample

The analysis of covariance model

The da

The populat

The model in t

The model in t sample

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Consider the situation were there are only two groups and no covariates. Use a column with zero's and one's. So this column is a group 2 (treatment) **indicator**.

Call this column group and write the anova model as:

$$y_{ij} = \alpha_0 + \alpha_1 group_{ij} + \epsilon_{ij}$$

For the observations of group 1 this is $y_{1j} = \alpha_0 + \epsilon_{1j}$ so α_0 is the mean of group 1.

For group 2 the model is $y_{2j} = \alpha_0 + \alpha_1 + \epsilon_{2j}$. The mean of the model for group 2 minus the mean of the model for group 1 is $\alpha_0 + \alpha_1 - \alpha_0 = \alpha_1$. So α_1 is the difference in group means.

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The research

701

The sample

Model with to factors

Regression

The research

The sample

The analysis of covariance model

The da

The populatio

Different

The model in th

The general linear model

If there are f.i. 4 groups we need 3 group indicator variables: one indicating group 2, one indicating group 3 and one indicating group 4.

Group	gr2	gr3	gr4
1	0	0	0
2	1	0	0
3	0	1	0
4	0	0	1

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The researc

The sample

Model with tw factors

Regression models

The populat

The analysis of covariance

The da

The populati

The model in

The model in t

The general linear model

The model then is

$$y_{ij} = \alpha_0 + \alpha_1 gr 2_{ij} + \alpha_2 gr 3_{ij} + \alpha_3 gr 4_{ij} + \epsilon_{ij}$$

For group 1 the mean is α_0 , for group 2 that is $\alpha_0 + \alpha_1$ so α_1 is the difference in means between group 1 and 2. For group 3 the mean is $\alpha_0 + \alpha_2$ so α_2 is the difference in group means between group 3 and 1.

With 4 groups you need 3 such group indicating variables. Each variable has a 1 indicating its own group. The group that is not indicated (group 1 here) is the one with which the comparison is made.

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The reses

The sample

Model with to

Regression models

The research

The samp

The analysis of covariance model

The d

The population

Different representation

The model in the

The general linear model

The ancova model can now be written as:

$$y_{ij} = \alpha_0 + \alpha_1 group_{ij} + \beta x_{ij} + \epsilon_{ij}$$

For group 1 this is $y_{ij} = \alpha_0 + \beta x_{ij} + \epsilon_{ij}$, α_0 is the intercept in group 1.

For group 2 the model is $y_{ij} = \alpha_0 + \alpha_1 + \beta x_{ij} + \epsilon_{ij}$. So $\alpha_0 + \alpha_1$ is the intercept in group 1, thus α_1 is the difference in intercept.

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The research

The population

The sample

Model with two

Tactors

Regression models

The resear

The population

The sample

The analysis of covariance

The dat

The population

Different representation

The model in the sample

The general linear model

The model in the sample

The sample

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Anova models

The recent

The resear

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Model with t

Regressi

The resear

The sampl

The analysis of covariance

The d

The populat

The model in the

sample

The general linear model

Estimate the model as:

$$y_{ij} = a_0 + a_1 group_{ij} + bx_{ij} + e_{ij}$$

(using least squares)

The a_0 , a_1 and b are estimates of α_0 , α_1 , and β such that the residual sums of squares is smallest.

There are now no easy formulas

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The research

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Model with to

Regressio

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The analysis of covariance

The da

The populati

The model in the

sample

The general linear model

N.1		ıc	1.40	
Name	SS	dt	MS	
group	SS_{group}	df _{group}	MS_{group}	$\frac{MS_{group}}{MS_{res}}$
X	SS_{regres}	df_{regres}	MS_{regres}	$\frac{MS_{res}}{MS_{regres}}$
Residual	SS_{res}	df_{res}	MS_{res}	- 763
Total	SS_{total}	df_{Total}		

Here is $df_{group} = number\ of\ groups - 1$ and $df_{res} = n - 1 - 1 - df_{group}$

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The research

The population

Model with to

Regressio

models

The popula

The analysis of covariance

The data
The populati

The model in the sample

The general linear model

To test the hypothesis: $H_0: \beta=0$ versus $H_1: \beta\neq 0$ use the result that $F=\frac{MS_{regres}}{MS_{res}}$ has a Fisher distribution with 1 and df_{res} degrees of freedom.

To test the hypothesis: $H_0: \alpha_1=0$ versus $H_1: \alpha_1\neq 0$ use the result that $F=\frac{MS_{group}}{MS_{res}}$ has a Fisher distribution with df_{group} and df_{res} degrees of freedom.

If this last null hypothesis can not be rejected, one might just as well take the model with $\alpha_1 = 0$. One then gets the ordinary regression model.

So these hypothesis test whether or not the intercepts in both groups are the same.

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The research

The population

The sample

Model with two

Regressi

models

The resear

The population

The analysis

model

The dat

The population

Different

representation

The model in the sample

The general linear model

The general linear model

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The resea

The sample

Model with to factors

Regressio models

The research

The sample

The analysis of covariance model

The da

The populat

The model in

sample

In this previous model the 2 groups have the same regression coefficient.

They differ only in intercepts.

This means that the lines are parallel.

This is not always justified. Let's look at the example:

The general linear model

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The research

The sample

Model with 1

D......

models

The resea

The sampl

covariance

The da

The populati

Different

The model in th

The general

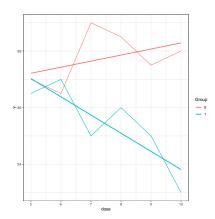


Figure 3: The relation between dose and blood pressure for the two groups.

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The research

The sample

Model with two

Regression models

The recearch

The popular

The analysis of covariance model

The data

Different

The model in

The general linear model

In the placebo group there is not much happening what ever the dose is. In the treatment group the blood pressure is going down if the dose is increased. So the effect of the dose depends on the group.

This is called an **interaction effect**.

Interaction effect: The effect of one independent variable on the dependent variable, depends on the outcome of an other independent variable.

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The research

771

The sample

Model with to factors

Regression models

The recent

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The analysis o

The d

The populat

Different

The model in the sample

The general linear model

An interaction effect is denoted by a product: a group times dose effect.

This is because one can model the interaction effect by multiplying the two independent variables and put this product in the model:

$$y_{ij} = \alpha_0 + \alpha_1 \operatorname{group}_{ij} + \beta_1 x_{ij} + \beta_2 \operatorname{group}_{ij} \times x_{ij} + \epsilon_{ij}$$

An extra slope only when group equals 1.

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The researc

The researc

The sample

Model with to factors

Regression models

The resear

he sample

The analysis of covariance model

The d

The popular

The model in

The general

In group 1 this model is: $y_{ij} = \alpha_0 + \beta_1 x_{ij} + \epsilon_{ij}$

The intercept here is α_0 and the regression coefficient is β_1 .

In group 2 the model is

$$y_{ii} = \alpha_0 + \alpha_1 + \beta_1 x_{ii} + \beta_2 x_{ii} + \epsilon_{ii} = (\alpha_0 + \alpha_1) + (\beta_1 + \beta_2) x_{ii} + \epsilon_{ii}$$

The intercept here is $(\alpha_0 + \alpha_1)$ and the regresion coefficient is $(\beta_1 + \beta_2)$

So this model has 2 different intercepts and 2 different regression coefficients.

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The research

The populatio

The sample

Model with to factors

models

The resea

The sample

The analysis of covariance

The da

The populati

The model in t

The general

Name	SS	df	MS	F
group	SS_{group}	df _{group}	MS_{group}	MS _{group} MS _{res} MS _{regres}
×	SS_{regres}	df _{regres}	MS_{regres}	MSrac
group*x	$SS_{interaction}$	df _{interaction}	MS _{interaction}	$\frac{MS_{interaction}}{MS_{res}}$
Residual	SS_{res}	df _{res}	MS_{res}	-763
Total	SS_{total}	df_{Total}		

The degrees of freedom for the interaction effect: multiply the degrees of freedom of the independent variable that make the interaction.

To test wether or not the lines are parallel: H_0 : $\beta_2 = 0$ vs H_1 : $\beta_2 \neq 0$.

One can use the result that $F = \frac{MS_{interaction}}{MS_{res}}$ has a Fisher distribution with $df_{interaction}$ and df_{res} degrees of freedom.

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The resea

The sample

Regression

The research

The sample

The analysis o covariance model

The d

The populat Different

The model in

The general linear model

To estimate the model in the sample one has to estimate what the parameters are and the are called a_0 , a_1 , b_1 , b_2 and then the model becomes

$$y_{ij} = a_0 + a_1 group_{ij} + b_1 x_{ij} + b_2 group_{ij} \times x_{ij} + \epsilon_{ij}$$

The r-output for this model is:

```
Continuous
data: linear
Models
```

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Anova model

```
The research
```

The sample

Model with to

models

The research

The sample

covariance

The data

The populati

representation

The model in th sample

The general linear model

```
## Call:
## glm(formula = y ~ factor(group) + dose + factor(group):dose,
       data = bp)
##
## Coefficients:
                        Estimate Std. Error t value Pr(>|t|)
##
## (Intercept)
                         86 1429
                                       1.6635 51.785 2.14e-11 ***
## factor(group)1
                         4.0952 2.3525 1.741 0.1199
## dose
                           0.2143 0.2163 0.991
                                                       0.3508
## factor(group)1:dose
                         -0.8571
                                       0.3058 -2.803
                                                         0.0231 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.8184524)
##
       Null deviance: 30.9167 on 11 degrees of freedom
## Residual deviance: 6.5476 on 8 degrees of freedom
## AIC: 36.785
##
## Number of Fisher Scoring iterations: 2
y_{ij} = a_0 + a_1 group_{ij} + b_1 x_{ij} + b_2 group_{ij} \times x_{ii} + \epsilon_{ii} a_0 = 86.1429, a_1 = 4.0952, b_1 = 0.2143, b_2 = -0.8571
Model group 1: y_{1i} = 86.1429 + 0.2143 \ dose_{1i} and Model group 2:
y_{2i} = (86.1429 + 4.0952) + (0.2143 - 0.8571) dose_{2i} = 90.2381 - 0.6429 dose_{2i}
```

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Anova models

The research

##

The sample

Model with tw factors

Regressio models

The research
The population

The analysis covariance

model

The populatio

ne model in the mple

The general

nested version of the model: In order to see the dose effect (the slope of the dose) within group 0 and within group 0, one can fit the nested version of this model. If, in general one wants the effect of B only within the A-groups one uses the nested version: A+A:B. That is done below with group and dose:

```
## Call:
## glm(formula = y ~ factor(group) + factor(group):dose, data = bp)
##
## Coefficients:
                       Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                       86.1429
                                   1.6635 51.785 2.14e-11 ***
## factor(group)1
                      4.0952
                                   2.3525
                                            1.741
                                                    0.1199
## factor(group)0:dose 0.2143
                                   0.2163
                                            0.991
                                                    0.3508
                       -0.6429
## factor(group)1:dose
                                   0.2163 - 2.973
                                                    0.0178 *
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## (Dispersion parameter for gaussian family taken to be 0.8184524)
##
       Null deviance: 30.9167 on 11 degrees of freedom
## Residual deviance: 6.5476 on 8 degrees of freedom
## ATC: 36.785
##
## Number of Fisher Scoring iterations: 2
```