Continuous data: linear Models

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Types:

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

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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 $\bar{y}$

The population

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 ith group is μ_i. The variance in each group is σ^2. The observations are normally distributed.

The population: a model for the data generating process

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

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_{ij}. Now a model for the observations in this case is : observation = best summary + residual or $y_{ij} = \mu + \epsilon_{ij}$.

2. 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 $y_{ij} = \mu_i + \epsilon_{ij}$.

The anova model in the population.

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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:

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

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

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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 anova model in the sample

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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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Now square the deviations and sum over all observations:

$$\sum_{\text{all observations}} (y_{ij} - \bar{y})^2 = \sum_{\text{all observations}} (\bar{y}_i - \bar{y})^2 + \sum_{\text{all observations}} e_{ij}^2$$

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}.

Then

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

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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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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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 general lines of the analysis are:

1. 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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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}	
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)

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

Model with two factors

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An observation can be represented by y_{ijk}. This is the kth 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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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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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}	
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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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.

The population

The regression model in the population.

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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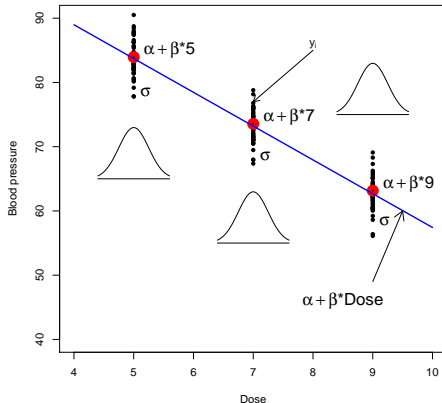The model in the sample

The general linear model

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

The regression model in the population.

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

The sample

The regression model in the sample

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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}.

$$SS_{res} = \sum_i [y_i - (a + bx_i)]^2$$

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

The regression model in the sample

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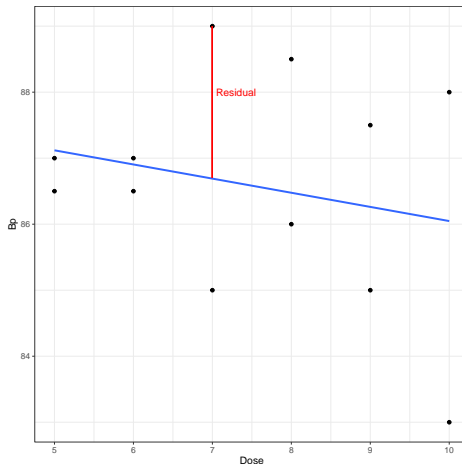sample

The general
linear model

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

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:

$$y_i = a + bx_i + e_i$$

The regression model in the sample

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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The **degrees of freedom** for the **total sums of squares** is $n - 1$

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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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.

The regression model in the sample

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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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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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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The population

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

Different representation

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.

Different representation of the 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 model then is

$$y_{ij} = \alpha_0 + \alpha_1 gr2_{ij} + \alpha_2 gr3_{ij} + \alpha_3 gr4_{ij} + \epsilon_{ij}$$

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.

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

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

The sample

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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**.

The general linear model

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:

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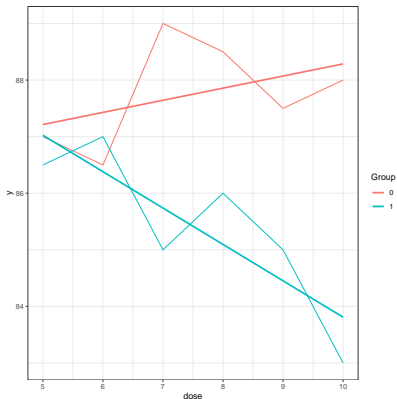The model in the
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The general linear model

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

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**.

The general linear model in the population

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:

$$y_{ij} = \alpha_0 + \alpha_1 group_{ij} + \beta_1 x_{ij} + \beta_2 group_{ij} \times x_{ij} + \epsilon_{ij}$$

An extra slope only when group equals 1.

The general linear model

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

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.

The general linear model

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Name	SS	df	MS	F
group	SS_{group}	df_{group}	MS_{group}	$\frac{MS_{group}}{MS_{res}}$
x	SS_{regres}	df_{regres}	MS_{regres}	$\frac{MS_{regres}}{MS_{res}}$
group*x	$SS_{interaction}$	$df_{interaction}$	$MS_{interaction}$	$\frac{MS_{interaction}}{MS_{res}}$
Residual	SS_{res}	df_{res}	MS_{res}	
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 inter action.

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.

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:

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```
##
## Call:
## glm(formula = y ~ factor(group) + dose + factor(group):dose,
##     data = bp)
##
## Deviance Residuals:
##     Min      1Q  Median      3Q     Max
## -0.9286 -0.6131 -0.2500  0.6250  1.3571
##
## 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
```

$y_{ij} = a_0 + a_1 group_{ij} + b_1 x_{ij} + b_2 group_{ij} \times x_{ij} + \epsilon_{ij}$ $a_0 = 86.1429$, $a_1 = 4.0952$, $b_1 = 0.2143$, $b_2 = -0.8571$

Model group 1: $y_{1j} = 86.1429 + 0.2143\ dose_{1j}$ and Model group 2:

$y_{2j} = (86.1429 + 4.0952) + (0.2143 - 0.8571)\ dose_{2j} = 90.2381 - 0.6429\ dose_{2j}$

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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)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -0.9286  -0.6131  -0.2500   0.6250   1.3571
##
## 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
## factor(group)1:dose  -0.6429     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
## AIC: 36.785
##
```