Hypothesis tests for multiple responses regression: effect of probiotics on addiction and binge eating disorder

ARTICLE HISTORY
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Supplementary material

1. Common hypotheses

Let $\boldsymbol{\theta^*}$ be a $h \times 1$ vector of parameters with the exception of correlation parameters, i.e. $\boldsymbol{\theta^*}$ refers only to regression, dispersion or power parameters. The parameter estimates of $\boldsymbol{\theta^*}$ are given by $\hat{\boldsymbol{\theta}}^*$. Similarly, let J^{*-1} be the $h \times h$ inverse of the Godambe information matrix excluding the correlation parameters. Let $\boldsymbol{L}$ be a $s \times h$ matrix specifying the hypotheses to be tested and $\boldsymbol{c}$ be a $s \times 1$ vector with values under the null hypothesis, where s denotes the number of constraints; the hypotheses to be tested can be written as:

$$H_0 : \boldsymbol{L\theta^*} = \boldsymbol{c} \ vs \ H_1 : \boldsymbol{L\theta^*} \neq \boldsymbol{c}. \tag{1}$$

In this way, the Wald test statistic to verify the validity of a hypothesis about parameters of a McGLM is given by:

$$W = (\boldsymbol{L}\hat{\boldsymbol{\theta}}^* - \boldsymbol{c})^T \ (\boldsymbol{L} \ \boldsymbol{J^{*-1}} \ \boldsymbol{L^T})^{-1} \ (\boldsymbol{L}\hat{\boldsymbol{\theta}}^* - \boldsymbol{c}),$$

where $W \sim \chi^2_s$, that is, regardless of the number of parameters in the hypotheses, the test statistic W is a single value that asymptotically follows the χ^2 distribution with degrees of freedom given by the number of constraints, that is, the number of rows in the matrix $\boldsymbol{L}$, denoted by s. Some points must be taken into account about the statement $W \sim \chi^2_s$: it's only holds under the null hypothesis; for non-Gaussian data, the statement only holds asymptotically as sample size tends to infinity; and the statement only holds if the matrix $\boldsymbol{L}$ has rank s.

In general, each column of the matrix $\boldsymbol{L}$ corresponds to one of the h parameters of $\boldsymbol{\theta^*}$ and each row to a constraint. Its construction basically consists of filling the matrix with 0, 1 and eventually -1 in such a way that the product $\boldsymbol{L\theta^*}$ correctly represents the hypotheses of interest. The correct specification of $\boldsymbol{L}$ allows us testing any parameter individually or even formulating hypotheses for several parameters.

In a practical context, after obtaining the estimates of the model parameters, we may be interested in three types of hypotheses: (i) interest in assessing whether there is evidence that allows us to state that only a single parameter is equal to a postulated value; (ii) interest in assessing whether there is evidence to state that a set of parameters is equal to a postulated vector of values; (iii) interest in knowing if the difference between the effects of two variables is equal to 0, that is, if the effect of the variables on the response is the same.

For the purposes of illustrating the types of hypotheses mentioned in the article, consider the situation in which you want to investigate whether a numeric variable X_1 has an effect on two response variables, denoted by Y_1 and Y_2. For this task, consider that a sample with N observations was collected and for each observation the values of X_1, Y_1 and Y_2 were recorded. Based on the collected data, a bivariate McGLM was fitted, with a linear predictor given by:

$$g_r(\mu_r) = \beta_{r0} + \beta_{r1}X_1, r = 1, 2, \tag{2}$$

where the index r denotes the response variable, r = 1,2; β_{r0} represents the intercept; β_{r1} a regression parameter associated with a variable X_1. We assume that each response has only one dispersion parameter τ_{r0} and that the power parameters have been fixed. Therefore, it is a problem in which there are two response variables and only one explanatory variable. We assume that the observations under study are independent, so $Z_0 = I$.

In this scenario, questions of interest could be: is there an effect of the variable X_1 on only one of the responses? Is it possible that the variable X_1 has an effect on both responses at the same time? Is it possible that the effect of the variable is the same for both responses? All these questions can be answered by testing hypotheses on the model parameters and specified using Equation 1. In the next subsections, we present the elements necessary to conduct each test.

1.1. Example 1: hypothesis for a single parameter

Let's consider the simplest type of hypothesis to test: a hypothesis about a single parameter. We are interested in to evaluate whether there is an effect of the variable X_1 only on the first response. The hypothesis can be written as follows:

$$H_0 : \beta_{11} = 0 \; vs \; H_1 : \beta_{11} \neq 0. \tag{3}$$

The same hypothesis can be rewritten in the most convenient notation for applying the Wald test statistic, as in Equation 1 where:

- $\boldsymbol{\theta^{*T}} = \begin{bmatrix}\beta_{10} \; \beta_{11} \; \beta_{20} \; \beta_{21} \; \tau_{11} \; \tau_{21}\end{bmatrix}$.
- $\boldsymbol{L} = \begin{bmatrix}0 & 1 & 0 & 0 & 0 & 0\end{bmatrix}$.
- $\boldsymbol{c} = \begin{bmatrix}0\end{bmatrix}$.

Note that the vector $\boldsymbol{\theta^*}$ has six elements, therefore the matrix $\boldsymbol{L}$ contains six columns (one for each element) and one row, because only a single parameter is being tested. This single line is composed of zeros, except for the column referring to the parameter of interest, which receives 1. It is simple to verify that the product $\boldsymbol{L\theta^*}$ represents the hypothesis of interest initially postulated in Equation 3. Thus, the asymptotic distribution of the test is χ^2_1.

1.2. Example 2: hypothesis for multiple parameters

Let's consider now we are interested in to assess whether there is sufficient evidence to state that there is an effect of the explanatory variable X_1 on both responses simultaneously. In this case, we have to test 2 parameters: β_{11}, which associates X_1 with the first response and β_{21}, which associates X_1 with the second response. We can write the hypothesis as follows:

$$H_0 : \beta_{r1} = 0 \; vs \; H_1 : \beta_{r1} \neq 0, \tag{4}$$

or, equivalently:

$$H_0 : \begin{pmatrix} \beta_{11} \\ \beta_{21} \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix} \; vs \; H_1 : \begin{pmatrix} \beta_{11} \\ \beta_{21} \end{pmatrix} \neq \begin{pmatrix} 0 \\ 0 \end{pmatrix}.$$

Hypotheses in the form of Equation 1 have the following elements:

- $\boldsymbol{\theta^{*T}} = \begin{bmatrix} \beta_{10} \; \beta_{11} \; \beta_{20} \; \beta_{21} \; \tau_{11} \; \tau_{21} \end{bmatrix}$.
- $\boldsymbol{L} = \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix}$.
- $\boldsymbol{c} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$.

The vector $\boldsymbol{\theta^*}$ remains with six elements and the matrix $\boldsymbol{L}$ with six columns. In this case, we are testing two parameters, so the matrix $\boldsymbol{L}$ has two rows. Again, these lines are composed of zeros, except in the columns referring to the parameter of interest. It is simple to verify that the product $\boldsymbol{L\theta^*}$ represents the hypothesis of interest initially postulated in Equation 4. Thus, the asymptotic distribution of the test is χ^2_2.

1.3. Example 3: hypothesis of equality of parameters

In this case, we are interested in to testing whether the effect of the variable X_1 is the same for both responses. Thus, we form a hypothesis of equality between the parameters or, in other words, if the difference of the effects is null:

$$H_0 : \beta_{11} - \beta_{21} = 0 \; vs \; H_1 : \beta_{11} - \beta_{21} \neq 0, \tag{5}$$

in the notation of Equation 1 the elements of the hypotheses are:

- $\boldsymbol{\theta^{*T}} = \begin{bmatrix} \beta_{10} \; \beta_{11} \; \beta_{20} \; \beta_{21} \; \tau_{11} \; \tau_{21} \end{bmatrix}$.
- $\boldsymbol{L} = \begin{bmatrix} 0 & 1 & 0 & -1 & 0 & 0 \end{bmatrix}$.
- $\boldsymbol{c} = \begin{bmatrix} 0 \end{bmatrix}$.

As there is only one hypothesis, the matrix $\boldsymbol{L}$ has only one row. For the matrix $\boldsymbol{L}$ to be correctly specified in the case of an equality hypothesis, it is necessary to put 1 in the column referring to one parameter, and -1 in the column referring to the other parameter, in such a way that the product $\boldsymbol{L\theta^*}$ represents the hypothesis of interest initially postulated. In this case, the product $\boldsymbol{L\theta^*}$ generates exactly the same hypothesis specified in Equation 5 and the asymptotic distribution of the test is χ^2_1.

1.4. *Example 4: hypothesis about regression or dispersion parameters for responses under the same predictor*

The Equation 2 describes a generic bivariate model. It is important to note that in this example both responses are subject to the same predictor. In practice, when it comes to McGLMs, different predictors can be specified for each response variables. Thus, what was exposed in subsection 1.2 is useful for any case in which there is interest in testing hypotheses about more than one model parameter in the same or in different responses, regardless of the predictors between responses.

However, in cases where the responses have identical linear predictors and the assumptions about the parameters do not change from response to response, an alternative specification of the procedure is to use the Kronecker product as used in [1].

Suppose that, in this example, the hypotheses of interest are still written as in Equation 4. However, as this is a bivariate model with the same predictor for the two responses and the hypothesis of interest are the same for each response and involves only regression coefficients, it is convenient to write the matrix $\boldsymbol{L}$ as the Kronecker product from two matrices: a matrix $\boldsymbol{G}$ and a matrix $\boldsymbol{F}$, that is, $\boldsymbol{L} = \boldsymbol{G} \otimes \boldsymbol{F}$. Thus, the matrix $\boldsymbol{G}$ has dimension $R \times R$ and specifies the hypotheses regarding the responses, whereas the matrix $\boldsymbol{F}$ specifies the hypotheses between variables and has dimension $s' \times h'$, where s' is the number of linear constraints and h' is the total number of coefficients of regression or dispersion of the each response. Therefore, the matrix $\boldsymbol{L}$ has dimension $(s'R \times h)$.

In general, the matrix $\boldsymbol{G}$ is an identity matrix with dimension equal to the number of responses analyzed in the model. Whereas the matrix $\boldsymbol{F}$ is equivalent to a matrix $\boldsymbol{L}$ considering there was only a single response in the model and only regression or dispersion parameters. We use the Kronecker product of these two matrices to ensure that the hypothesis described in the $\boldsymbol{F}$ matrix will be tested on the R model responses.

Thus, considering that this is the case in which the hypotheses can be rewritten by decomposing the $\boldsymbol{L}$ matrix, the test elements are given by:

- $\boldsymbol{\beta^T} = \begin{bmatrix}\beta_{10} \ \beta_{11} \ \beta_{20} \ \beta_{21}\end{bmatrix}$: the regression parameters of the model.
- $\boldsymbol{G} = \begin{bmatrix}1 & 0\\ 0 & 1\end{bmatrix}$: identity matrix with dimension given by the number of responses.
- $\boldsymbol{F} = \begin{bmatrix}0 & 1\end{bmatrix}$: equivalent to a $\boldsymbol{L}$ for a single response.
- $\boldsymbol{L} = \boldsymbol{G} \otimes \boldsymbol{F} = \begin{bmatrix}0 & 1 & 0 & 0\\ 0 & 0 & 0 & 1\end{bmatrix}$: matrix specifying the hypotheses on all responses.
- $\boldsymbol{c} = \begin{bmatrix}0\\ 0\end{bmatrix}$: vector of values under the null hypothesis.

Thus, the product $\boldsymbol{L\beta}$ represents the initially postulated hypothesis of interest. In this case, the asymptotic distribution of the test is χ^2_2. The procedure is easily generalized when there is interest in evaluating a hypothesis about the dispersion parameters and this specification is quite convenient for generating analysis of variance tables.

2. ANOVA and MANOVA via Wald test

Based on Wald test for McGLMs, we can run different procedures for generating ANOVA and MANOVA tables for regression parameters. We used the nomenclature types I, II and III. In addition, we also aim to propose a procedure similar to ANOVA and MANOVA to evaluate the dispersion parameters of a given model. In the case of ANOVAs, a table is generated for each response variable. For MANOVAs only one table is generated, therefore, in order to be able to perform MANOVAs, the model responses must be subject to the same linear predictor.

With the purposes of to illustrate the tests performed by each type of analysis of variance, we consider the situation in which one wants to investigate whether two numeric variables denoted by X_1 and X_2 have an effect on two response variables denoted by Y_1 and Y_2. For this task, we suppose that a sample with N observations was collected and for each observation the values of X_1, X_2, Y_1 and Y_2 were recorded. Based on the collected data, a bivariate model was fitted, with linear predictor given by:

$$g_r(\mu_r) = \beta_{r0} + \beta_{r1}X_1 + \beta_{r2}x_2 + \beta_{r3}X_1X_2.$$

where the index r denotes the response variable, r = 1,2; β_{r0} represents the intercept; β_{r1} a regression parameter associated with the variable X_1, β_{r2} a regression parameter associated with the variable X_2 and β_{r3} a regression parameter associated with the interaction between X_1 and X_2. Assume that the units under study are independent, so each response has only one dispersion parameter τ_{r0} associated with a matrix $Z_0 = I$. Finally, we consider that the power parameters have been fixed.

2.1. ANOVA and MANOVA type I

Our type I analysis of variance proposal for McGLMs performs tests on the regression parameters sequentially. In this scenario, the following tests would be performed:

(1) Tests if all parameters are equal to 0.
(2) Tests if all parameters except intercept are equal to 0.
(3) Tests if all parameters except intercept and parameters referring to X_1 are equal to 0.
(4) Tests if all parameters except intercept and parameters referring to X_1 and X_2 are equal to 0.

Each of these tests would be a row of the analysis of variance table. In the case of ANOVA, one table per response would be generated, in the case of MANOVA a table in which the hypotheses are tested for both responses. This procedure can be called sequential because a variable is added to each line. In general, precisely because of this sequentiality, it is difficult to interpret the effects of variables using type I analysis of variance. On the other hand, type II and III analyzes test hypotheses that are generally of more interest.

2.2. ANOVA and MANOVA type II

Our type II analysis of variance performs tests similar to the last test of the sequential analysis of variance. In a model without interactions what is done is, in each line, testing the complete model against the model without a variable. In this way, the effect of that variable on the complete model becomes better interpretable, that is, the impact on the quality of the model if we removed a certain variable.

If there are interactions in the model, the complete model is tested against the model without the main effect and any interaction effect involving the variable. Considering the previous example, the type II analysis of variance would do the following tests:

(1) Tests if the intercept is equal to 0.
(2) Tests if the parameters referring to X_1 are equal to 0. That is, the impact of removing X_1 from the model is evaluated. In this case, the interaction is removed because it contains X_1.
(3) Tests if the parameters referring to X_2 are equal to 0. That is, the impact of removing X_2 from the model is evaluated. In this case, the interaction is removed because it contains X_2.
(4) Tests if the interaction effect is 0.

Note that, in the lines that we aim to understand the effect of X_1 and X_2, the interaction is also evaluated, as all parameters involving that variable are removed from the model.

2.3. ANOVA and MANOVA type III

Finally, our type III analysis of variance considers the complete model against the model without a certain effect. Considering the previous example, the type III analysis of variance would do the following tests:

(1) Tests if the intercept is equal to 0.
(2) Tests if the main effect parameters referring to X_1 are equal to 0. That is, the impact of withdrawing X_1 on the main effects of the model is evaluated. In this case, unlike type II, nothing is assumed about the interaction parameter, even though it involves X_1.
(3) Tests if the main effect parameters referring to X_2 are equal to 0. That is, the impact of withdrawing X_2 on the main effects of the model is evaluated. In this case, unlike type II, nothing is assumed about the interaction parameter, even though it involves X_2.
(4) Tests if the interaction effect is 0.

Note that in the lines where the effect of X_1 and X_2 is tested, the interaction effect is maintained, unlike what is done in the type II analysis of variance. It is important to note that the type II and III analyzes of variance as proposed in this work generate the same results when applied to models without interaction effects. Furthermore, the procedures can be easily generalized to deal with dispersion parameters.

3. Multiple comparisons test via Wald test

When ANOVA shows a significant effect of a categorical variable, it is usually of interest to assess which of the levels differ from each other. For this, multiple comparison tests are used. In the literature there are several procedures to perform such tests, many of them described in [2].

Such a situation can be evaluated using the Wald test. By correctly specifying the $\boldsymbol{L}$ matrix, it is possible to evaluate hypotheses about any possible contrast between the levels of a given categorical variable. Therefore, it is possible to use Wald's statistics to perform multiple comparison tests as well.

The procedure is basically based on 3 steps. The first one is to obtain the matrix of linear combinations of the model parameters that result in the fitted means. With this matrix it is possible to generate the matrix of contrasts, given by subtracting each pair of lines from the matrix of linear combinations. Finally, just select the lines of interest from this matrix and use them as the Wald test hypothesis specification matrix, in place of the $\boldsymbol{L}$ matrix.

For example, suppose there is a response variable Y subject to an explanatory variable X of 4 levels: A, B, C and D. Consider, to evaluate the effect of the variable X, a model given by:

$$g(\mu) = \beta_0 + \beta_1[X = B] + \beta_2[X = C] + \beta_3[X = D].$$

In this parameterization, the first level of the categorical variable is used as a reference category and, for the other levels, the change to the reference category is measured; this is called treatment contrast. In this context, β_0 represents the fitted mean of level A, while β_1 represents the difference from A to B, β_2 represents the difference from A to C and β_3 represents the difference from A to D. With this parameterization it is possible to obtain the predicted value for any of the categories in such a way that if the individual belongs to category A, β_0 represents the predicted value; if the individual belongs to category B, $\beta_0 + \beta_1$ represents the predicted value; for category C, $\beta_0+\beta_2$ represents the predicted value, and finally, for category D, $\beta_0+\beta_3$ represents the predicted value.

In matrix terms, these results can be described as

$$\boldsymbol{K_0} = \begin{array}{c} A \\ B \\ C \\ D \end{array} \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix}$$

Note that the product $\boldsymbol{K_0\beta}$ generates the vector of predictions for each level of X. By subtracting the rows from the matrix of linear combinations $\boldsymbol{K_0}$ we generate a matrix of contrasts $\boldsymbol{K_1}$

$$\boldsymbol{K_1} = \begin{array}{c} A-B \\ A-C \\ A-D \\ B-C \\ B-D \\ C-D \end{array} \begin{bmatrix} 0 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & -1 \\ 0 & 1 & -1 & 0 \\ 0 & 1 & 0 & -1 \\ 0 & 0 & 1 & -1 \end{bmatrix}$$

To carry out a test of multiple comparisons, it is enough to select the desired contrasts in the lines of the matrix $\boldsymbol{K_1}$ and use these lines as a matrix for specifying the hypotheses of the Wald test. Finally, due to the amount of hypothesis testing in a multiple comparison procedure, correction of p-values is recommended, we used Bonferroni correction.

To carry out this procedure for McGLMs, we must remember that this is a class of multivariate models. Thus, as in the case of analysis of variance, for tests of multiple comparisons there are two possibilities: tests for a single response and tests for multiple responses.

In practice, if the interest is a multivariate multiple comparison test, there is a need for all responses to be subject to the same linear predictor and it is enough to expand the contrast matrix using the Kronecker product, following an idea similar to that exposed in subsection 1.4. In the case of a multiple comparison test for each response, simply select the vector of estimates and the partition corresponding to the matrix $J_{\boldsymbol{\theta}}^{-1}$ for the specific response and proceed with the test. In this way, it is possible to obtain a simple and useful procedure of multiple comparisons when there is a McGLM with categorical explanatory variables and there is an interest in determining which levels differ from each other.

4. Hypotheses tested in the simulation study

Null hypothesis	β_0	β_1	β_2	β_3
H_{01}	5	0	0	0
H_{02}	4.85	0.05	0.05	0.05
H_{03}	4.7	0.1	0.1	0.1
H_{04}	4.55	0.15	0.15	0.15
H_{05}	4.4	0.2	0.2	0.2
H_{06}	4.25	0.25	0.25	0.25
H_{07}	4.1	0.3	0.3	0.3
H_{08}	3.95	0.35	0.35	0.35
H_{09}	3.8	0.4	0.4	0.4
H_{10}	3.65	0.45	0.45	0.45
H_{11}	3.5	0.5	0.5	0.5
H_{12}	3.35	0.55	0.55	0.55
H_{13}	3.2	0.6	0.6	0.6
H_{14}	3.05	0.65	0.65	0.65
H_{15}	2.9	0.7	0.7	0.7
H_{16}	2.75	0.75	0.75	0.75
H_{17}	2.6	0.8	0.8	0.8
H_{18}	2.45	0.85	0.85	0.85
H_{19}	2.3	0.9	0.9	0.9
H_{20}	2.15	0.95	0.95	0.95

Table 1. Tested hypotheses for regression parameters in models with response following Normal distribution.

Null hypothesis	β_0	β_1	β_2	β_3
H_{01}	2.3	0	0	0
H_{02}	2.25	0.017	0.017	0.017
H_{03}	2.2	0.033	0.033	0.033
H_{04}	2.15	0.05	0.05	0.05
H_{05}	2.10	0.067	0.067	0.067
H_{06}	2.05	0.083	0.083	0.083
H_{07}	2	0.1	0.1	0.1
H_{08}	1.95	0.117	0.117	0.117
H_{09}	1.9	0.133	0.133	0.133
H_{10}	1.85	0.15	0.15	0.15
H_{11}	1.8	0.167	0.167	0.167
H_{12}	1.75	0.167	0.167	0.167
H_{13}	1.7	0.2	0.2	0.2
H_{14}	1.65	0.217	0.217	0.217
H_{15}	1.6	0.233	0.233	0.233
H_{16}	1.55	0.25	0.25	0.25
H_{17}	1.5	0.267	0.267	0.267
H_{18}	1.45	0.283	0.283	0.283
H_{19}	1.4	0.3	0.3	0.3
H_{20}	1.35	0.317	0.317	0.317

Table 2. Tested hypotheses for regression parameters in models with response following Poisson distribution.

Null hypothesis	β_0	β_1	β_2	β_3
H_{01}	0.5	0	0	0
H_{02}	0.250	0.083	0.083	0.083
H_{03}	0	0.167	0.167	0.167
H_{04}	-0.25	0.25	0.25	0.25
H_{05}	-0.500	0.333	0.333	0.333
H_{06}	-0.750	0.417	0.417	0.417
H_{07}	-1.0	0.5	0.5	0.5
H_{08}	-1.250	0.583	0.583	0.583
H_{09}	-1.500	0.667	0.667	0.667
H_{10}	-1.75	0.75	0.75	0.75
H_{11}	-2.000	0.833	0.833	0.833
H_{12}	-2.250	0.917	0.917	0.917
H_{13}	-2.5	1.0	1.0	1.0
H_{14}	-2.750	1.083	1.083	1.083
H_{15}	-3.000	1.167	1.167	1.167
H_{16}	-3.25	1.25	1.25	1.25
H_{17}	-3.500	1.333	1.333	1.333
H_{18}	-3.750	1.417	1.417	1.417
H_{19}	-4.0	1.5	1.5	1.5
H_{20}	-4.250	1.583	1.583	1.583

Table 3. Tested hypotheses for regression parameters in models with response following the Bernoulli distribution.

Null hypothesis	β_0	β_1
H_{01}	1	0
H_{02}	0.98	0.02
H_{03}	0.96	0.04
H_{04}	0.94	0.06
H_{05}	0.92	0.08
H_{06}	0.9	0.1
H_{07}	0.88	0.12
H_{08}	0.86	0.14
H_{09}	0.84	0.16
H_{10}	0.82	0.18
H_{11}	0.8	0.2
H_{12}	0.78	0.22
H_{13}	0.76	0.24
H_{14}	0.74	0.26
H_{15}	0.72	0.28
H_{16}	0.7	0.3
H_{17}	0.68	0.32
H_{18}	0.66	0.34
H_{19}	0.64	0.36
H_{20}	0.62	0.38

Table 4. Tested hypotheses for dispersion parameters.

References

[1] W.H. Bonat, R.R. Petterle, P. Balbinot, A. Mansur, and R. Graf, *Modelling multiple outcomes in repeated measures studies: Comparing aesthetic eyelid surgery techniques*, Statistical Modelling (2020), p. 1471082X20943312.

[2] J. Hsu, *Multiple comparisons: theory and methods*, CRC Press, 1996.