Evidence-based Orthodontics

Controlling false positive rates in research and its clinical implications

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Statistical analysis is, in fact, an error analysis. A statistical test does not guarantee reliable results, it only quantifies the probability of error of a given conclusion.¹ While reading the articles of this journal, you will find a p-value. For instance, the article by Garib et al² describes the p-values for a given variable at two different moments: this p-value, also known as false-positive rate,¹ demonstrates the probability of error when asserting that there is a difference before and after expansion.

Every research is subjected to some degree of error, given that we are not investigating an entire population, but only a fraction, a sample. For this reason, when we compare two samples undergoing different treatment procedures with a view to identifying the most efficient therapy, we will always have the chance of having reached a wrong conclusion. Therefore, the lower the p-value is, the smaller the chance of error and, as a result, the more certain we are to assure that treatment “A” is more efficient than “B”.

But, how can we control a false-positive error? Initially, we have to decide on the significance level (α) we expect to establish. In Dentistry, we usually set a significance level not greater than 5% (α = 5%). Nevertheless, should we increase the number of comparisons of a given study, we increase the chances of yielding outcomes that are due just to chance and, as a consequence, finding a false-positive result. The lottery is a good example. The chances of winning are little, less than 5%. However, the more we bet, the higher our chances of winning.

In statistical tests, there is a dramatic increase in false-positive rates, in which the number of comparisons is directly proportional to the number of false-positive results, as shown in Table 1.

Thus, when we make several comparisons using a simple statistical test, we significantly increase the chances of yielding a false-positive result. Table 1 demonstrates that the chances of yielding a false-positive result are of 40% for a study involving 10 comparisons. In these cases, some adjustments are necessary to keep the significance level set at 5%. One of the procedures employed to correct false-positive rates is the Bonferroni correction. It consists of dividing the significance level by the number of comparisons made in a given study.³ Suppose we carried out a comparative analysis of five cephalometric variables between two groups using an independent t-test. By dividing the significance level initially set at 0.05 or 5% by 5, the new level of error will be adjusted to 0.01 or 1%. Thus, differences will be considered significant for a p-value lower than or equal to 0.01. Nevertheless, Bonferroni correction

| # tests | α value | FW α |
|---------|---------|------|
| 1       | 0.05    | 0.05 |
| 3       | 0.05    | 0.14 |
| 6       | 0.05    | 0.26 |
| 10      | 0.05    | 0.4  |
| 15      | 0.05    | 0.54 |

\[ \alpha_C = 1 - (1 - \alpha)^C \]

C = # of comparisons. α₀ stands for error type I (0.05).

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results in a much more inflexible significance level than necessary, thus increasing the chances of yielding a false-negative rate.  

In 1995, Benjamini and Hochberg (BH) suggested another method to counteract false-positive rates when multiple comparisons with univariate statistical analysis are carried out. In this procedure, the researcher has to accept a minor false-positive rate and set this rate before the procedure. Suppose we compared 10 cephalometric measures between two populations A and B. After the number of comparisons is established, we determine the p-value for each analysis and organize these values in ascending order. The value of i = 1 (0.01) will be lower than the p-value, with i = 10 being the highest value. Table 2 shows the p-values in ascending order. After values are properly ranked, we apply the Benjamini-Hochberg formula: \( \left( \frac{i}{m} \right) \cdot Q \) (Q = false-positive acceptance rate; m = total number of comparisons). This formula allows us to correct the p-value and eliminate potential false-positive rates. With a view to obtaining the Q value, we divide the number of comparisons with \( P < 0.05 \) by the number of comparisons with \( P > 0.05 \). Table 3 shows that after finding the Q value and applying the Benjamini-Hochberg formula, we find the corrected p-value for each comparison \( (i = 1, i = 2, \text{etc.}) \). Subsequently, we arrange the data in a table similar to Table 3, including the initial p-value and the p-value corrected by means of the formula. This method allows us to determine which comparisons are significant, in which case only those with a p-value lower than \( \left( \frac{i}{m} \right) \cdot Q \) are significant. Table 3 shows that comparisons 1 and 2 are the only ones with p-value lower than \( \left( \frac{i}{m} \right) \cdot Q \).

In this same example, should we use Bonferroni correction to counteract error type I, comparisons 1 and 2 would probably not be significant, since \( \alpha = 5\% \) divided by the number of comparisons (ten) would result in \( 0.05/10 = 0.005 \). This value would be lower than comparisons 1 and 2 corrected by the BH technique, which demonstrates how strict Bonferroni’s procedure is.

Choosing the wrong statistical test may lead clinicians to jump to conclusions. For instance, a given treatment may be considered the best one as a result of statistical analysis. Thus, statistical analysis is the key to reach more reliable clinical results. Employing more simple statistical procedures, such as the t-test, to carry out multiple comparisons, creates the need to counteract type I error (false-positive). Therefore, it is reasonable to conclude that multiple comparisons require one to carefully choose the test as well as the corrections to be employed.

### Table 2

| Comparisons | P-value |
|-------------|---------|
| i = 1       | 0.01    |
| i = 2       | 0.017   |
| i = 3       | 0.2     |
| i = 4       | 0.22    |
| i = 5       | 0.23    |
| i = 6       | 0.3     |
| i = 7       | 0.35    |
| i = 8       | 0.4     |
| i = 9       | 0.45    |
| i = 10      | 0.5     |

### Table 3

| Comparisons | P-value | \( \left( \frac{i}{m} \right) \cdot Q \) |
|-------------|---------|--------------------------------------|
| i = 1       | 0.01    | 0.025                                |
| i = 2       | 0.017   | 0.005                                |
| i = 3       | 0.2     | 0.075                                |
| i = 4       | 0.22    | 0.1                                 |
| i = 5       | 0.23    | 0.125                                |
| i = 6       | 0.3     | 0.15                                |
| i = 7       | 0.35    | 0.175                                |
| i = 8       | 0.4     | 0.2                                 |
| i = 9       | 0.45    | 0.225                                |
| i = 10      | 0.5     | 0.25                                |

\[ Q = \frac{2}{8} = 0.25. \]

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