Chapter 3
Null-Hypothesis Testing with Graphs

1 General Purpose

Because biological processes are *full* of variations, statistics will give no certainties only chances. What chances? Chances that hypotheses are true/untrue. What hypotheses? For example:

1. our mean effect is not different from a 0 effect,
2. it is really different from a 0 effect,
3. it is worse than a 0 effect,

where 0 effect means that your new treatment or any other intervention doesnot work. Statistics is about estimating such chances/testing such hypotheses. Please note that trials often calculate differences between a test treatment and a control treatment, and, subsequently, test whether this difference is larger than 0. A simple way to reduce a study of two groups of data, and, thus, two means to a single mean and single distribution of data, is to take the difference between the two means and compare it with 0.

In the Chap.2 we explained that the data of a trial can be described in the form of a normal distribution graph with SEMs on the x-axis, and that this method is adequate for testing various statistical hypotheses. We will now focus on a very important hypothesis, the null-hypothesis. What it literally means is: no difference from a 0 effect: the mean value of our sample is not different from the value 0. We will try and make a graph of this null-hypothesis, and then assess whether our result is significantly different from the null-hypothesis.

T.J. Cleophas, A.H. Zwinderman, *Clinical Data Analysis on a Pocket Calculator*,
DOI 10.1007/978-3-319-27104-0_3

2 Schematic Overview of Type of Data File

Outcome
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3 Primary Scientific Question

Is the result of our study significant different from the null-hypothesis?

4 Data Example

Let us assume that 1000 patients will be treated with a cholesterol lowering agent. After one week of treatment all cholesterol reductions are summarized with a mean reduction and its standard error. In order to make a graph of our result as compared to the null-hypothesis, our results have to be standardized first.

Mean ± Standard Error

is divided by its own standard error

Mean/Standard Error ± Standard Error/Standard Error =
Mean/Standard Error ± 1

The unit of the standardized results is not mmol/l anymore, but something else. We will call it SEM units (otherwise often called z-values or t-values).

In our example the result is given:

Mean ± Standard Error =
3 ± 1 SEM units

The mathematical equation of the Gaussian curve of our data is obtained from the equation (see also Chap. 2, e = Euler's constant = 2.718).

$$y = e^{-1/2\left(x^2\right)}$$

$x = \text{Mean/Standard Error}$

$x\text{^}2 = x^2$

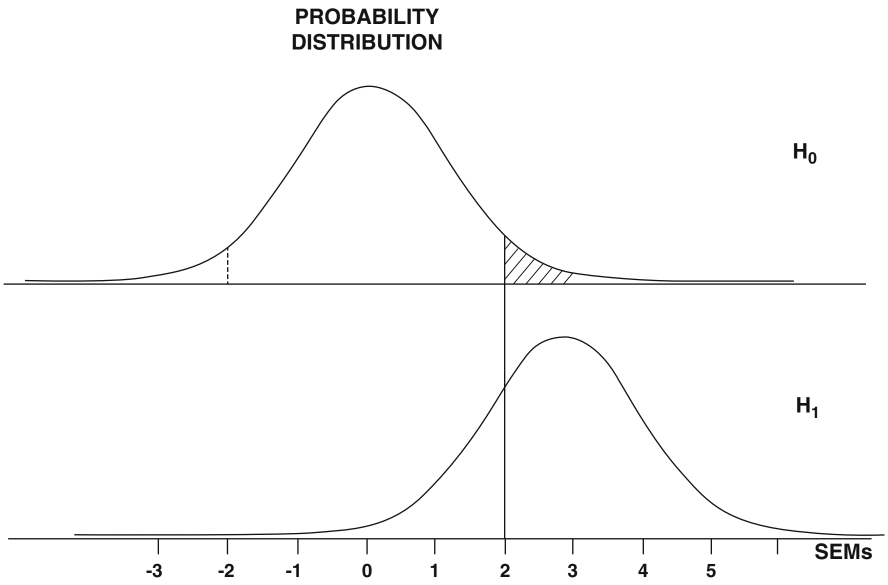
at $x = 0 \rightarrow y = 1$

at $x = 1 \rightarrow y = 0.607$

at $x = 2 \rightarrow y = 0.135$

at $x = 3 \rightarrow y = 0.011$

The above values can be plotted, and the underneath Gaussian curve H0 (hypothesis 0) will be obtained. It is, actually, a graph of the null-hypothesis.



It is now easy to, subsequently, draw a curve of the null-hypothesis H1 (hypothesis 1). It is equally wide and high as the H0 curve, but with an overall mean value of 3 instead of 0. This null-hypothesis is now used to test whether your result is significantly different from zero, meaning that your cholesterol treatment is efficaceous. The following statistical reasoning is used.

As explained in the Chap.2, the Gaussian curve H1 with SEMs on the x-axis is not only a kind of summary of your data, it is also the summary of many trials similar to our trial.

H1 = graph based on the data of our trial with SEMs on the x-axis.
H0 = the same graph with mean 0.

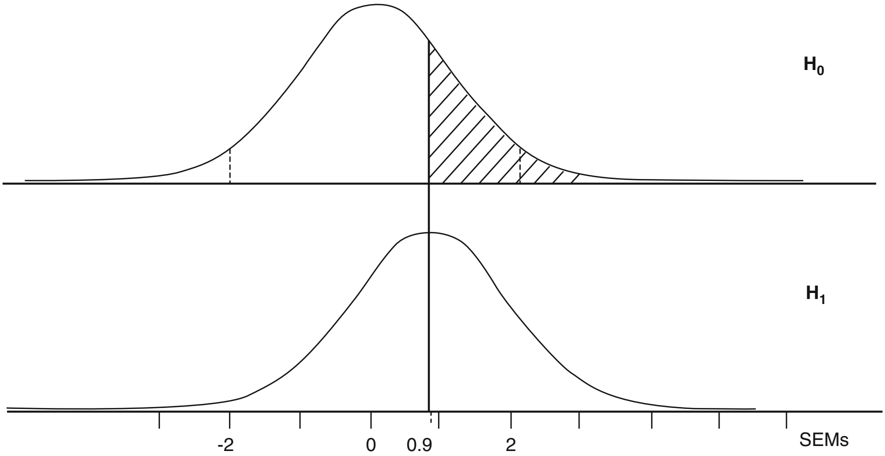
Now we will make a giant leap from our data to the entire population (we can do so, because our data are representative).

H1 = also the summary of many trials similar to ours.
H0 = summary of many trials similar to ours but with an overall mean effect of zero.

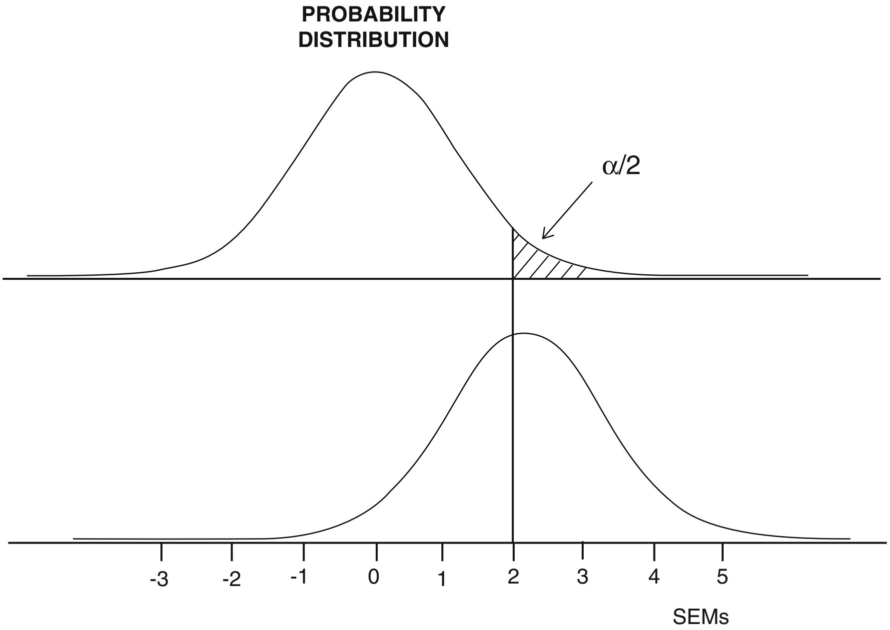
We can't prove anything, but we can calculate chances/probabilities. A mean result of 3 is far distant from 0: suppose it belongs to H0. Only 5 % of the H0 trials are >2 SEMs distant from 0. Our mean result is, indeed, > 2 SEMs distant from 0, namely 3 SEMs. This means, that the chance that our result belongs to the H0 trials is <5 %, because the AUC (area under the curve) >2 SEMs and <−2 SEMs is only 5 % of the entire AUC (Chap. 2). We conclude that we have < 5 % of finding this result, and decide that we will reject this small chance.

Any study result larger than 2 SEMs or smaller than – 2 SEMs is in the small tails of the H0 curve, and, if your treatment does not work, you will have less than 5 % chance of being in the tails. Our result is, obviously, in the tails, and, so, we may conclude that we can reject the null-hypothesis of no difference from zero with a probability of < 5 %. By doing so you are committing an error. Your mean result is in the AUC of H0. Yet you conclude that it is significantly different from H0. But your error is only 5 %, and, at the same time, you have 95 % chance that you did not commit an error. Worldwide statisticians have agreed that this level of error is acceptable. The small AUCs in the right and left end tails, covering 5 % of the entire AUC of the H0, is, usually, called alpha (α). It is also called the type I error, or the chance of finding a difference where there is none.

5 Examples of a Negative Trial and a Trial with Borderline Result



In the above graph the mean of the trial is 0.9 SEMs distant from 0. This result is not on right side of 2 SEMs. The null-hypothesis H0 can, therefore, not be rejected. The AUC (area under the curve) right from 0.9 = not 5 %, but rather 35 % or so of the entire AUC. And so p = 0.35 (35 %).



In the above graph the mean is 2 SEMs distant from 0. Alpha level of rejection = 2. The AUC right from 2 is only 5 % of the entire AUC. We will reject H0 at p = 0.05 or 5 %. A p-value of 5 % is, however, a borderline result. We will have, at least, 5 % chance that our conclusion is untrue, and 50 % chance of a type II error (see Chap. 11).

6 Conclusion

Because biological processes are *full* of variations, statistics will give no certainties, only chances. What chances? Chances that hypotheses are true/untrue. What hypotheses?: e.g.:

our mean effect is not different from a 0 effect,
a test treatment and a control treatment differ more than zero.

This chapter shows that it is pretty easy to draw a curve of your data and the corresponding null-hypothesis H0. This null-hypothesis can, then, be used to test, whether your result is significantly different from zero, meaning that, e.g., your cholesterol treatment was efficaceous.

7 Note

More background, theoretical and mathematical information of null-hypothesis testing is given in Statistics applied to clinical studies 5th edition, Chaps. 1–3, Springer Heidelberg Germany, 2012, from the same authors.