The role of the statistician in the clinical development process

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The life cycle of a clinical trial

- Design
- Conduct
- Analysis

A statistician can make significant contributions to each of these phases!

Key statistical concepts

- Variation
- Two types of error

Two types of error

		Actual situation: Drug is effective	Actual situation: Drug is not effective
Clinical trial outcome	Drug is effective	✓	α
	Drug is not effective	β	✓

Significance level and power

- α : significance level - probability of false positive result ("Type I error")
- β : probability of false negative result ("Type II error")
- 1- β : power - probability of not attaining false negative result

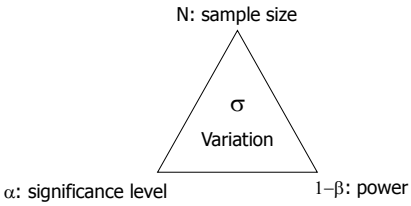
Role of statistician: maintain α and β levels

Who cares about α and β?

- Regulatory authorities
- Investors
- You!

The "Introduction to Statistics story"

Hypothesis: $H_0: \Delta=0$ $H_1: \Delta>0$



The real life story

- There are many more factors that affect significance level, power and sample size
- The statistician can help you controlling them

What to consider in the design

- Experimental design
- Selection of clinical endpoint
- Study population - inclusion/exclusion criteria
- Assumptions on clinical conditions and therapeutic effect
- How the data will be analyzed at the end of the study?

Experimental design

- Superiority? Bioequivalence? Non-inferiority?
- Placebo controlled? Active comparator? Add on?
- Parallel arm? Single arm? Cross over?
- Interim analysis? Futility analysis?
- Adaptive design?

Selection of clinical endpoint

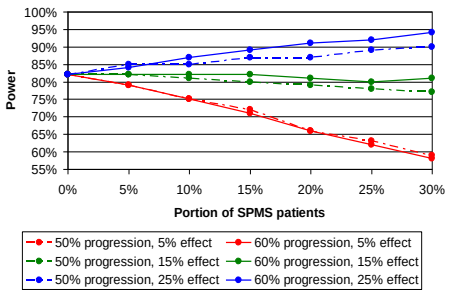
- The most informative endpoint (statistically speaking) should be chosen

  Information=Power

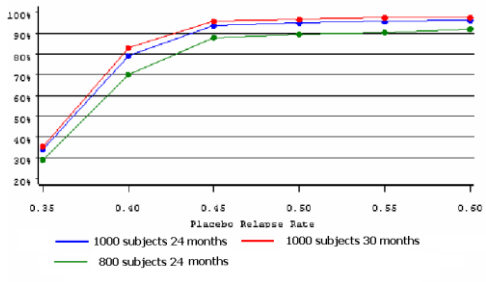
Example:

The number of seizures during the study period is more informative than "seizure free" endpoint

Study population



Clinical conditions and therapeutic effect



Analysis methodology

- When you start the trial it is too late to think what to do at the end!
- Detailed statistical analysis methodology should be specified in the study protocol
- Bayesian analysis needs special care and negotiation with regulatory authorities

During the study conduct

- The statistician should monitor the accumulated data to verify that the underlying assumptions are valid

At the end of the study …

- Statistical analysis!

Summary

- The statistician can contribute to all phases of the clinical development process
- The most important phase is the design phase - this is where the statistician's contribution is the most significant

Take home message

The statistician is your friend!