How to Estimate Sample Size for Medical Device Clinical Studies

WEBINAR

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Today's Speakers

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Today's Agenda

- The importance of sample size calculation
- Factors that impact sample size
- The basic inputs in sample size calculation
- Sample size calculation example
- Advice from a biostatistician (how to prepare)

WHY SHOULD YOU CARE ABOUT SAMPLE SIZE CALCULATION?

EU MDR Introduces New Challenges

- The MDR is forcing many to initiate clinical studies
- Post-Market Clinical Follow-Up (PMCF) raises questions
- Compliance requires justification & scientific reasoning

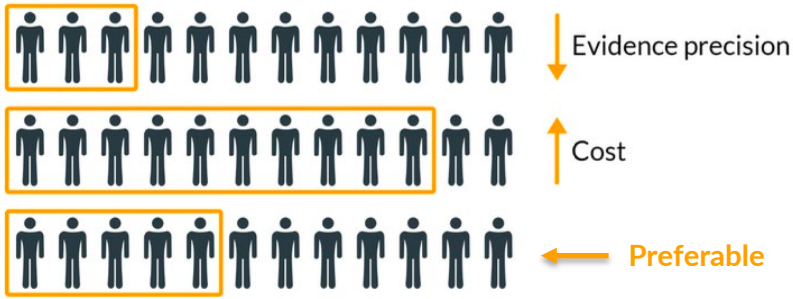
What is Sample Size Calculation?

The process of determining what is the minimum number of samples that would make a study outcome statistically significant.

$$Z = \frac{\mu - \mu_0}{\sigma / \sqrt{n}} \quad \Rightarrow \quad n = \frac{Z^2 * \sigma^2}{\mu - \mu_0}$$

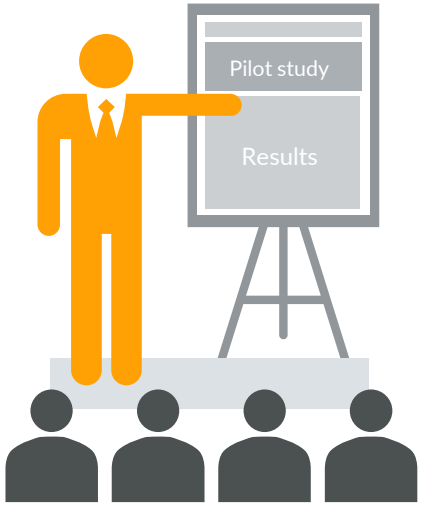
Sample Size and Your Study

- Sample size calculation is based on assumptions (on the inputs)
- Too small sample size may prevent you from meeting study objectives
- Too large sample size will waste resources and may raise ethical questions



WHAT IMPACTS
SAMPLE SIZE ?

Study Purpose



Learn

OR

Test

Study Goals

- **Study objective**
  Superiority, non-inferiority, equivalence etc.
- **Study design**
  Parallel, crossover, etc.
- **Study endpoint(s)**
  Discrete, continuous, time-to-event etc.
- **Statistical test**
  What test will you use for analysis?

THE FIVE BASIC INPUTS IN SAMPLE SIZE CALCULATION

Basic Inputs - I

Statistical assumptions

01 Statistical Hypothesis

Null hypothesis (H_0) & Alternative Hypothesis (H_1)

H_0 : The effects of Treatment A and Treatment B are the same.

H_1 : The effect of Treatment A is better then that of Treatment B.

Basic Inputs – I

Hypothesis testing overview

		Reality	
		H_0 is True	H_1 is True
Study Findings	H_0 is Accepted	Treatment A and B are the same	Type II error (β)
	H_0 is Rejected	Type I Error (α)	Treatment A is better then Treatment B

Basic Inputs - II

Statistical assumptions

02

Power

The probability of meeting the study objective (1-β). Identifying a difference when it really exists.

Minimum power req. *is 80% but FDA recommends 90% for pivotal studies*

03

Significance level

The probability of finding a difference, when there's no actual difference (α). Probability of Type I error.

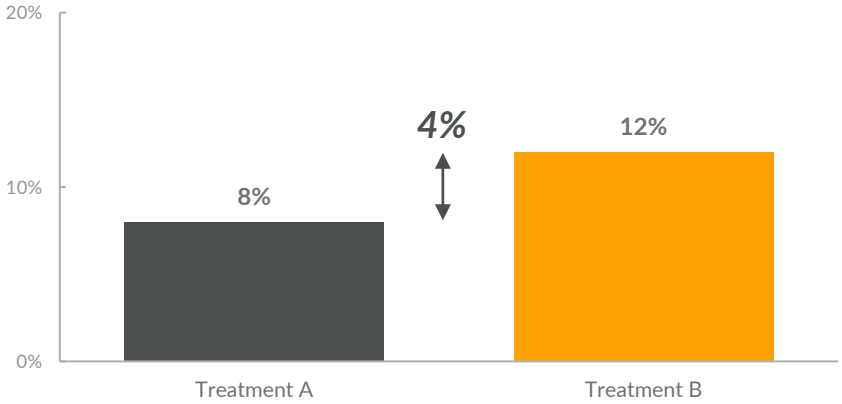
Typically *5% or lower*

Basic Inputs – III

Clinical assumptions

04 **Minimum clinically meaningful difference (effect size)**

05 **Variability (σ)**



Additional Factors

That affect the final sample size

- **Testing margin -** when is device superior?
- **Drop out rates –** how many % ?
- **Treatment allocation –** ethical concerns?

CASE
EXAMPLE

Case Example

We have a new device, a coronary artery stent (Treatment A).

We want to conduct a clinical study to evaluate if there's a difference in the mean systolic blood pressure when compared with another stent (Treatment B).

- **From a pilot study, we know that the systolic mean value of patients using our device is 135mmHg**
- **Our clinical experts tell us that with Treatment B patients have a mean value of 140mmHg.**
- **We know from the literature that the standard deviation in similar studies is 20mmHg**

Case Example

H_0 : There's no difference in the mean systolic blood pressure between the two groups. $\mu_B - \mu_A = 0$

H_1 : The mean systolic blood pressure of Treatment B is higher then one of Treatment A. $\mu_B - \mu_A > 0$

Power: 80% **Significance level:** 5%

Min. clinically meaningful difference (effect size): 5 mmHg

Variability (SD): 20 mmHg

We are going to use a Z-test

The effect

$$Z = \frac{\mu_B - \mu_A}{2 * \sigma / \sqrt{n}}$$

$$n_1 = \frac{\left(Z_{1-\alpha/2} + Z_\beta\right)^2 * \sigma^2 * 2}{\mu_B - \mu_A}$$

$$n_1 = \frac{(1{,}96+0{,}84)^2 * 20^2 * 2}{5} \approx 1255 \text{ subjects}$$

PREPARING FOR A DISCUSSION ON SAMPLE SIZE

How to Prepare

Before you speak with a biostatistician

- Select a study design that fits the purpose, indication, population, and treatment
- Decide on study objectives and endpoint(s)
- Discuss with clinicians on the desired effect size that would be meaningful
- If superiority, NI, or equivalence decide on the margin or equiv. range
- Gain knowledge on the statistical properties of study endpoints, mainly the assumed variation of
- Bring a scientific justification of sample size to support the statistical calculation

Q & A
Session

You Decide

POLL

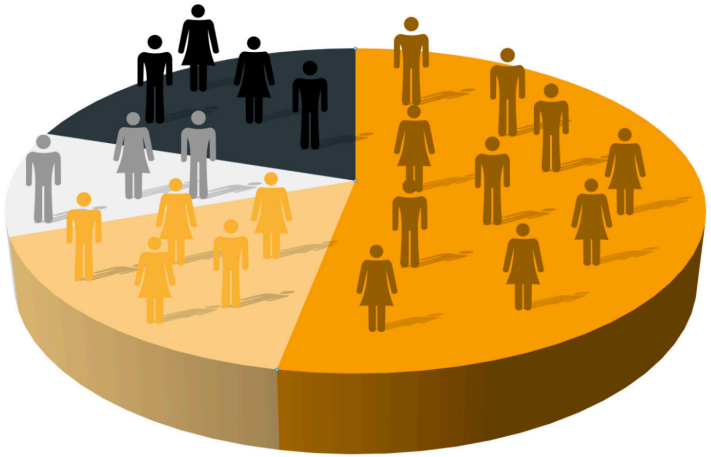
What webinar would you like to see next?

A small gift for you

The Medical Device Sample Size Cookbook

A brief guide on how to calculate sample size for a medical device clinical study

Everyone will receive a copy of the new e-book together with the recording of the webinar.



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Let's connect

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