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Components of a sample size calculation

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The following information is needed in order to calculate an appropriate sample size for a randomized trial. The objective and endpoints should be chosen based on your research question. Population variance and equivalence/non-inferiority limits should be chosen after a careful review of the literature. Be sure to search for studies with similar patient populations and primary outcomes and to consider constancy of the expected effects over time (changes with technology?) and publication bias.

Component	
Study question	State the research question in plain words
Objective	Superiority (typical trial design) Equivalence Non-inferiority Estimate between-group difference with pre-specified precision
Endpoint	What is the primary outcome? Is this outcome normal/binary/ordinal/time-to-event? Is there any information on expected values of the outcome in control patients?
Error/Power	**Type I Error**: How much chance are you willing to take of rejecting the null hypothesis when it is actually false (Superiority: no difference; non-inferiority: new method not non-inferior)? Typically, superiority trials use a two-sided test with α=0.05, but non-inferiority trials can use a one-sided test with α=0.025. **Type II Error**: How much chance are you willing to take of not rejecting the null when it is actually false (Superiority: new method is different than old; non-inferiority: The new method is non-inferior)?

Equivalence/non-inferiority limit	What is the minimum clinically acceptable difference? At what point is the difference in the outcome large enough that the methods are no longer equivalent? (Please include citations)
Population variance	What is the variance of the outcome in the population of interest? (Please include citations)
Other	How many drop-outs are expected? How long is the planned duration of follow-up? Is it a single-center or multi-center study? Will a sufficient number of patients agree to enter the study? How many patients need to be screened? Will patients be entered consecutively? How many patients meet the inclusion criteria? Do you need to pre-register the study? Do you an ethics review prior to starting the study? What is the ethics approval number? Are there multiple endpoints? Will multiple testing be a problem that needs to be controlled? How will randomization be done?

References

European Medicines Agency. 2005. *Guideline on the choice of the non-inferiority margin.*

L. Flight and S. Julious. 2016. Practical guide to sample size calculations: non-inferiority and equivalence trials. *Pharmaceutical Statistics,* 15(1).

ICH Expert Working Group. 1998. *ICH Harmonised Tripartite Guideline: Statistical Principles for Clinical Trials E9.*