

**PRACTICAL ISSUES IN SAMPLE SIZE CALCULATIONS FOR COMPARING MEANS
IN CLINICAL AND EPIDEMIOLOGICAL STUDIES**

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Precise sample size calculation is essential in clinical and epidemiological studies. Ideally, number of participants is determined drawing on objectives previously established and should be directly connected to both statistical analysis and procedures designed to evaluate the plausibility of a hypothesis. Means comparisons typically require setting desired significance level and power, expected effect measure, as well as variability-related parameters. The major difficulty is setting the correct variance, since it generally builds on previous studies, pilot studies, or even on subjective clinical judgements. The principal consequence of misspecifying this parameter is coming to a wrong conclusion, besides unnecessary cost and waste of time. Because actual variance is unknown in practice, a more conservative procedure consists of doing a sensitivity analysis including possible variance values. In this paper, we consider the following situations: parallel and crossover designs, superiority, non-inferiority and equivalence studies, and comparison of two or more means. We present analytical form-based and simulation-based results of a study on variance misspecification. We assess deficit and excess in number of participants, and we also investigate the conditions leading to inaccurate conclusions in cases of uncertainty in the variance estimate. Finally, we discuss practical issues, such as the use of one-sided versus two-sided hypotheses, and parallel versus crossover designs.