Sample Size Calculations in R

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Goal: Avoid using nQuery

1. Inconvenient
2. "Black Box"
3. Overkill to use nQuery when I only need a formula?
4. Expensive ($795)

What functions exist for Sample size and power calculations in R?

1. Searched through packages listed in `ClinicalTrials` Task View from CRAN
   `http://stat.ethz.ch/CRAN/` > Task Views > ClinicalTrials
2. Compared with list of functions which nQuery provides (Chapter 23 in Manual)

What is available?

1. mostly: T-test and Chi-Square
2. also: logrank test, Fisher's exact, ANOVA
3. Superiority, not so much equivalence or confidence intervals
4. in R but not nQuery: Group Sequential Designs, Phase II trials (exact single, and two-stage)
5. also may come in handy: randomization lists

Example 1: Continuous Normal Data

An investigator wishes to design a hypertension trial with equal allocation between groups where the clinical effect of interest is a reduction in blood pressure, compared to control, of 8 mmHg (d). The expected standard deviation in the population in which the trial is to be undertaken is 40 mmgHg (σ). Thus, the standardized difference equates to $8/40 = 0.20$. With the types I and II errors fixed at 5 and 10% we get a sample size of 526. Using this sample size to intiate iterations in Julious 2004, Equation 7 one gets 527.

Group Sequential Designs

Investigators performing the hypertension trial decide they would like to have 4 equally spaced interim analysis, and using the O'Brien Fleming spending approach. How many more patients do we need in order to do the interim analyses?

Example 2: Phase II Trials

A Phase II trial is being planned, and investigators would like to have a two-stage design (as in Simon 1989), so they can stop early if the drug doesn't seem to have any effect. The 'uninteresting' response rate is 5% (that is, if the effect of the drug is less than 5%, they won't go further with research on the therapy), and the 'interesting' response rate is 25% (that is, if the response rate is more than 25%, they will probably want to do a Phase III trial). Power will be 90% and significance level will be 10%. How many patients do they need?

A few (potentially) good references . . .

- Cook, T. and DeMets, D. (2008).
  Introduction to statistical methods for clinical trials.
  Chapman & Hall/CRC.
- Elashoff, J. (2002).
  nQuery advisor version 7.0 user's guide.
- Julious, S. (2004).
  Sample sizes for clinical trials with normal data.
  Statistics in medicine **23** 1921–1986.
- Kirkwood, B. and Sterne, J. (2003).
  Essential Medical Statistics.
  Blackwell Publishing.

Open-ended Questions

- What do you need (often) that nQuery doesn't have?
- Which tables do you use most commonly in nQuery? (Or, do you use the same handful of tables most of the time?)
- Are you more likely to use nQuery if the study has 'strange' features, e.g. K:1 randomization schemes?
- Are there features of nQuery which are too important to stop using it? (e.g., statements)
- Everyone said they sometimes write their own code to do sample size computations. Would a compilation of code for (in)frequently used sample size calculations be helpful?
- What else would make sample size and power calculations easier for you?