A Bayesian model for the selection of sample size in clinical trials

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Consider an agent faced with the problem of selecting the optimal sample size in a clinical trial. The agent acts as a sponsor for the clinical trial and may for example be identified with a pharmaceutical company or a research institution. One option in such a situation is to apply Bayesian decision theory (BDT). Making use of this framework provides the opportunity to incorporate information available prior to the clinical trial. Such a specification of prior information is particularly valuable for small populations, since the size of the clinical trial itself (and therefore the information provided by it) will be limited.

BDT requires the specification of a utility function for the agent designing the trial. We will consider the case in which the utility is taken to be the total expected treatment effect in the entire population. Our aim is to compare the optimal sample size and corresponding optimal utility in the case of no regulatory requirement versus the case in which such a requirement must be satisfied by the results of the clinical trial prior to acceptance of the new treatment. Thus, letting N denote the total population, the agent will need to

1. Choose a sample size n.

2. Observe the result $X_1, \ldots, X_n$ of the trial.

3. Based on the result of the trial, choose whether or not to give the new treatment (instead of some standard alternative) to the remaining $N - n$ subjects in the population.

The observations in the clinical trial are modelled as a sequence of independent, normally distributed random variables. The common population mean of these variables is initially unknown and therefore a normal prior is placed on this parameter. Standard Bayesian, conjugate analysis is then performed in order to update the information about the population mean effect after the result of the trial has been observed. The decision analysis itself proceeds via the technique of backward induction.

The IDEAL project ("Integrated Design and Analysis of small population group trials"), financed by the EU, is aimed at the development and evaluation of statistical procedures for the special case of rare diseases. This project is divided into several work packages, each with a different focus. Our group at the Chalmers University of Technology is engaged in the Decision Analysis work package within IDEAL. Our current focus is the analysis of how regulatory requirements may affect the choice of optimal sample size in

a clinical trial. After some basic results have been derived for the model outlined above, we will also consider potential generalizations and discuss some interesting questions that we think merit further investigation.