Interim Monitoring of Clinical Trials: Decision Theory, Dynamic Programming and Optimal Stopping

It is standard practice to monitor clinical trials with a view to stopping early if results are sufficiently positive, or negative, at an interim stage. We shall explain how properties of stopping boundaries can be calculated and how boundaries can be optimised to minimise expected sample size while controlling type I and II error probabilities.

Constraints on error probabilities complicate this optimisation problem. However, a solution is possible through consideration of unconstrained Bayes decision problems which are conveniently solved by dynamic programming. This conversion to an unconstrained problem is equivalent to using Lagrange multipliers. We shall present details of numerical computation for group sequential tests and their optimisation for particular criteria. We shall discuss a variety of applications in clinical trial design including the derivation of optimal adaptive designs in which future group sizes are allowed to depend on previously observed responses; designs which test both for superiority and non-inferiority; and group sequential tests which allow for a delay between treatment and response.

Since optimality in the unconstrained problem can be expressed as a sample path property, this is an "optimal stopping" problem in the language of probability theory. The computational methods we describe are, therefore, applicable to such problems and, in particular, to optimal stopping problems arising in financial mathematics.

**Wednesday, December 4, 2013**
3:30-4:30 PM
1301 McGavran-Greenberg