

**Graduate School in STATISTICS and ACTUARIAL SCIENCES
of the Belgian French Speaking Community**

**Special Announcement for a Short Course in Biostatistics
by Prof. dr. Alessandra Giovagnoli (University of Bologna)**

“Design for Clinical trials”

May 6,7 and 8, 2009

Institut de Statistique – Université Catholique de Louvain (UCL)
Louvain-la-Neuve

Dr. **Alessandra Giovagnoli** (Department of Statistical Sciences, University of Bologna) will give a short course on **Design for Clinical Trials**.

The course will take place according to the following schedule:

- May 6, 10h45-12h45: Ethics and Statistics in Clinical Trials
- May 7, 10h45-12h45 and 14h00-16h00: Clinical trials for the comparison of treatments – The ABCD design, sequential experiments, and Adaptive design
- May 8, 10h45-12h45: Dose escalation studies – The up & Down design

For more information:

- Website of L’Ecole doctorale thématique en Statistique et en Sciences Actuarielles (<http://www.stat.ucl.ac.be/edt/index.html>)
- Local organiser : Prof. C Legrand (catherine.legrand@uclouvain.be)

Registration is free of charge but mandatory (before May 1st) to

- **edt-stat-actu@uclouvain.be**

Note: You are also welcome on May 8 afternoon (14h30 and 16h00) to the two presentations of the seminar series of the Institute of Statistics.

Course summary:

Ethics and statistics in clinical trials: an introduction

Clinical trials are very complex experiments with patients as subjects; this poses a critical dilemma for investigators, known as the individual-versus-collective ethics, since it is necessary to minimize potential harm to the patients presently under care and maximize the experimental information. Some fundamental principles of the statistical methodology employed in planning and analysing experiments of this type are laid out, together with a sketch of the historical development of the subject, up to simulated clinical trials in the present time.

Clinical trials for treatment comparison - The ABCD design, sequential experiments, and Adaptive Designs

Randomized clinical trials, which consist in assigning treatments to subjects randomly, are widely regarded as the most scientifically sound approach to determining which of two or more medical treatments is better. However, for the past 15 years the attention has turned to studying a statistical design of the trial aimed at minimizing the number of subjects exposed to inferior treatments, increasing the patient's chances of receiving the best one. Needless to say, a randomization component in the assignments is always required in order to mitigate several types of bias. Covariates too come into consideration, which are usually random but may be known before assigning the treatment.

When the target allocation for comparing 2 treatments is balance, a restricted form of randomization is used (Efron's Biased Coin Design). An extension, the so-called ABCD, which is more flexible, will be presented. However, usually the target allocation derived from adopting a given criterion depends on the parameters of the statistical model, and as such is unknown; this problem is known in the statistical literature as "local optimality". A possible solution consists in sequential experimentation, so that assignments can be redressed towards the unknown target. Some aspects of these "adaptive" designs will be illustrated.

Dose Escalation studies - The up&down design

Traditionally, *dose escalation studies* are binary response trials where the probability of positive response (toxicity) is assumed to be an increasing function of the given dose level and the aim consists in estimating the target dose at which a pre-specified probability of positive response is associated without any parametric assumptions on the response curve. *Dose escalation* studies are aimed at identifying a quantile of interest in Phase I clinical trials. Classical examples are the median dose, usually denoted by LD_{50} , or the maximum tolerated dose of phase I clinical trials. Assuming that the set of available ordered doses is fixed in advance and doses are allocated to either groups or single patients, the "up-and-down" procedures for binary or continuous responses (U&D) provide a possible solution for dose-finding problems.