For Favour of Posting

THE CHINESE UNIVERSITY OF HONG KONG

Department of Statistics

will present a seminar entitled

Dose-finding Principles in Phase I Clinical Trials: Coherence & Rigidity

by

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on

Tuesday, 03 July 2007
2:00 pm – 3:00 pm

in

Science Centre L5
The Chinese University of Hong Kong

Abstract:

In this talk, I will quickly review the basic statistical problem seen in the design of phase I clinical trials, and then discuss the coherence conditions and rigidity of dose-finding methods. In brief, the objective of a phase I trial, in its simplest setting, is to estimate a targeted quantile of the unknown dose-toxicity curve in a homogeneous patient population. Most phase I methods are outcome-adaptive, and thus escalate or de-escalate doses for future patients based on the previous observations. An escalation for a new patient is said to be coherent only when the previous patient does not show sign of toxicity. Likewise, a de-escalation is coherent only when a toxic outcome is most currently seen. The coherence conditions, motivated by ethical concerns, are satisfied by many statistical designs in the literature, but not by some commonly used modifications of the methods. I will show examples when coherence is violated, and discuss how the coherence principles may be applied to calibrate a two-stage design and to deal with more complicated situations such as with bivariate outcomes and delayed toxicity. If time permits, I will also present a few examples in which commonly used phase I methods cause rigidity in the outcome sequences with a non-negligible probability. A necessary, albeit somewhat irrelevant in the context of phase I trials, consequence of rigidity is inconsistency. It is interesting to note that rigidity occurs in phase I designs that avoid strong parametric assumptions on the dose-toxicity. This is counter-intuitive because one may expect that making fewer assumptions will avoid bias and lead to consistency by adding flexibility to the model. Practical recommendations will be discussed.

All are Welcome