

Tuesday 21st October 2014 7:15 for 7:45 (PLEASE NOTE THE NEW DATE)

Large Lecture Theatre,
MRC Cognition and Brain Sciences Unit,
Chaucer Road, Cambridge, CB2 7EF

Adaptive dose-finding designs to identify multiple doses that achieve multiple response targets

Adrian Mander

MRC Biostatistics Unit Hub for Trials Methodology Research, University Forvie Site

Abstract: Within drug development it is crucial to find the right dose that is going to be safe and efficacious, this is often done within early phase II clinical trials. The dose-finding trial aims to understand the relationship between dose of drug and its potential effect. Adaptive designs are being used in this area allowing greater flexibility for dose exploration as compared to traditional fixed dose designs. An adaptive dose-finding design usually assumes a true non-linear dose-response model and select doses that either maximise the determinant of information matrix of the design (D-optimality) or minimise the variance of the predicted dose that gives a targeted response. Our design extends the predicted dose methodology, in a limited number of patients (40), to finding two targeted doses: a minimally effective dose; and a therapeutic. In our trial doses are assumed to be given intravenously so theoretically doses are continuous and the response is a normally distributed continuous outcome.

Our design has an initial learning phase assigning pairs of patients to five pre-assigned doses. The next phase is fully sequential with an interim analysis after each patient to determine the choice of dose based on the optimality criterion to minimise the determinant of the covariance of the estimated target doses. The dose-choice algorithm assumes that a specific parametric dose-response model is the true relationship, and so a variety of models are considered at the interim and human judgement involved in the overall decision. I will also describe some of the discussions of the dose-decision making meetings.

Speaker: Dr Adrian Mander is the director of the MRC Biostatistics Unit Hub for Trials Methodology Research in Cambridge. The hub was initiated in April 2009 and has investigated different aspects of clinical trial design methodology. Dr Adrian Mander has previously worked at the MRC Human Nutrition Research unit in Cambridge and also in industry for GlaxoSmithKline, working in phase I trials and Worldwide Epidemiology.

Annual General Meeting: Adrian Mander's talk will be preceded by a brief Annual General Meeting.

Directions Chaucer Road is off Trumpington Road – if you are heading away from the city centre it is the first right after the junction with Brooklands Avenue. Number 15 is at the end on the left and is a large Victorian House with a more modern extension to its right. The entrance is in the porch located in the middle of the older section on the left as you come in and is accessed by ascending a few steps from the car park. Cars may be parked there. The outside door will be locked at 7:45. Arrivals after 7:45pm can gain admittance by contacting the secretary on 07761769436. A map showing the location of the unit is at <http://www.mrc-cbu.cam.ac.uk/contact-us>.

Provisional Next Meetings:

17th November – Trevor Lewis (Director, TLwise Consulting Limited and RSS Theme Director for Professional Affairs) on 'Reflections on a career as a professional statistician and the increasing value of the role of professional bodies'.
2nd February 2015 – Anthony Edwards (Gonville and Caius) on 'On reading Bernoulli's Ars conjectandi 1713'.
5th March – Tom Bramley (Cambridge Assessment).
26th March – Richard Steward (Blyth Estuary Group).
7th May – Donal McCarthy (RSPB).

Supper: Some members eat before a talk at the University Centre meeting in the Granta Lounge at **5-45pm**. All welcome!

Secretary: Peter Watson, MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge CB2 7EF; telephone 01223 355294 Extension 801; E-mail peter.watson@mrc-cbu.cam.ac.uk

For security purposes could you please let Peter Watson know if you intend attending the talk.
Slides and .mp3 files of old talks: <http://www.mrc-cbu.cam.ac.uk/people/peter.watson/csdg.html>
TURN OVER for the Annual General Meeting agenda

THE CAMBRIDGE STATISTICS DISCUSSION GROUP

Tuesday 21st October 2014 7:15 for 7:45

Large Lecture Theatre,
MRC Cognition and Brain Sciences Unit,
Chaucer Road, Cambridge

Annual General Meeting

The annual general meeting will be followed immediately by Adrian Mander's talk 'Adaptive dose-finding designs to identify multiple doses that achieve multiple response targets'.

Agenda:

0. Approval of Minutes of previous A.G.M.
(<http://imaging.mrc-cbu.cam.ac.uk/statswiki/csdg/newtalks>)
1. Treasurer's Report.
2. Secretary's Report.
3. Election of Chairman, Secretary, Treasurer, plus 3 other members of the Committee.
4. Any Other Business.

Rules for Election:

1. **FRANCISE:** All paid-up members may vote or stand for office.
2. **NOMINATIONS:** The offices to be filled are Chairman, Secretary and Treasurer and three other members of the Committee.

An outgoing Chairman will be a member of the Committee ex officio. At the end of each year the entire Committee will stand down, but may stand again for the same office as they are leaving without nomination. To be elected to a different office a candidate must be nominated by one person from the paid-up membership, not including himself. Nominations do not require a seconder to be valid, but do require the consent of the nominee. One person can be nominated for more than one office, but hold only one. If a person is elected to a higher office (according to the ordering given below) he or she automatically ceases to be a candidate for a lower office. A candidate for the post of Chairman, Secretary, Treasurer is automatically a candidate for the Committee if he or she fails to gain election to one of these three posts.

TURN OVER for directions to the Cognition and Brain Sciences Unit and abstract of Adrian's talk