MRC Biostatistics Unit, Cambridge

Research Associate in Medical Statistics

Reference:	**A374R**
Department:	**Mathematics and Statistics**
Closing Date:	**30 May 2012**
Interview Date:	**18 June 2012**
Salary:	**£25,251 - £29,249 (Grade 6)**

The project

In the early stages of drug development there is often uncertainty about the most promising among a set of different treatments. In order to ensure the best use of resources in such situations it is important to decide which, if any, of the treatments should be taken forward for further testing. An efficient solution to this problem is a multi-arm clinical trial in which several active treatments are compared to a common control group. By comparing several treatments within one trial the sample size and duration required tends to be markedly smaller than if each treatment is evaluated separately. For added efficiency it is desirable to monitor the trial at a series of interim analyses in order to allow early stopping if efficacy is quickly established and similarly to eliminate ineffective treatments early. In confirmatory studies these designs are also useful as it has been shown that using two doses instead of a single dose can markedly improve the study's success probability.

This proposal aims to develop statistical methods to investigate how these, so called multi-arm multi-stage trials, can best be designed and analysed.

The specific aims of the project are to:

1. develop statistical designs for multi-arm multi-stage designs that use intermediate endpoints for treatment selection;
2. develop and evaluate methods for estimating the treatment effect in multi-arm multi-stage designs with treatment selection and obtain their confidence intervals;
3. develop statistical methods for multi-arm multi-stage designs with multiple endpoints;
4. develop open-source software packages and associated training tailored to clinical trialists and applied statisticians working on clinical trials.

The research associate will, together with the Cambridge based team, investigate aims two and three. The work will utilize three recently finished or currently ongoing studies in three important medical areas: HIV/AIDS, leukaemia and metastatic cancer. The multidisciplinary research team includes experienced clinical specialists and clinical trialists for each study from the clinical trials research unit in Leeds, the University of Liverpool and the MRC clinical trials unit as well as statisticians with experience in statistical methods for clinical trials from the University of Bremen and the Warwick medical school.

The Investigators

Dr Jack Bowden is a senior statistician at the MRC Biostatistics Unit and a member of the Cambridge Hub for Trials Methodology Research. His main research expertise is in the development of bias-adjusted estimation procedures, which have been successfully applied to data in the fields of epidemiology, statistical genetics, meta-analysis and clinical trials [5-7]. From previous work experience, he has built strong methodological collaborative links in the pharmaceutical industry and also within the MRC Clinical Trials Unit. He will jointly supervise the research associate and lead aim 2 of the project.

Dr James Wason is a senior statistician at the MRC Biostatistics Unit Hub for Trials Methodology Research. His research is in design of clinical trials, particularly in optimal design of group-sequential and multi-arm, multi-stage trials. He has published extensively with both of the other investigators [3,4,7] and will jointly supervise the research associate. In addition he is responsible for aim 3 - multi-arm multi-stage designs with multiple endpoints - of the project.

Dr Thomas Jaki is a Lecturer in Medical Statistics at Lancaster University and a member of the MRC's North-West Hub for Trials Methodology Research. He is a Career Development Fellow of the NIHR and the deputy director of Lancaster University's Medical and Pharmaceutical Statistics Research Unit which develops and evaluates novel statistical methods of study design and data analysis relevant to medical research institutes and pharmaceutical companies. His main research is in adaptive designs for early phase clinical trials and he has published on various design considerations for multi-arm clinical trials [1-4]. He leads the Lancaster based research group working on aims 1 and 3.

The Departments

The MRC Biostatistics Unit (http://www.mrc-bsu.cam.ac.uk/), which hosts Dr Jack Bowden and Dr James Wason, is a centre of excellence in research and an internationally leading centre for the development, application and dissemination of statistical methods. It is also the largest group of biostatisticians in Europe. The majority of the research programmes were rated as 'internationally excellent' in the last external review of the unit. Several internationally recognised experts in the design of clinical trials are based in the unit, and so it provides an excellent environment for research in clinical trials methodology.

Dr Thomas Jaki is based in the Department of Mathematics and Statistics at Lancaster University (http://www.maths.lancs.ac.uk/department/). Lancaster's Statistics Group is an internationally recognised centre of research excellence. For over twenty years the Group has been at the forefront of the UK research effort in Statistics, establishing a strong track record of theoretical innovation arising from real- world challenges. The Group has a vibrant research environment consisting approximately 20 staff, with in excess of 40 RAs and PhD students. Lancaster is also home of the Medical and Pharmaceutical Research Unit (http://www.mps-research.com/, Director: Prof. Anne Whitehead) which has a long standing history of developing novel statistical methods of study design and data analysis relevant to medical research institutes and pharmaceutical companies.
The Lancaster and Cambridge groups have strong research links through the MRC Network of Hubs for Trials Methodology Research
(http://www.methodologyhubs.mrc.ac.uk/default.aspx).

Both groups individually have also strong connections to the UKCRC Registered CTU network and collaborative work has taken place in the past with several CTUs such as the Clinical Trials Research Centre in Liverpool and the MRC CTU.

Selection procedure

The short list will be chosen on the basis of the written application. Short-listed candidates will then be invited to Cambridge and will be chosen on the basis of a formal interview and referees' reports.

References

1. Magirr D, Jaki T, Whitehead J (accepted). A generalized Dunnett Test for Multiarm-Multistage Clinical Studies with Treatment Selection. Biometrika.
2. Whitehead J, Jaki T (2009). One- and two-stage design proposals for a phase II trial comparing three active treatments with control using an ordered categorical endpoint. Statistics in Medicine. 28(5), 828-847.
3. Wason J, Jaki T (submitted). Optimal design of multi-arm multi-stage trials.
4. Wason J, Jaki T, Stallard N (submitted). Planning multi-arm screening studies within the context of a drug development programme.
5. Bowden J, Glimm E (2008). Unbiased estimation of selected treatment means in two-stage trials. Biometrical Journal. 50, 515–527.
6. Bowden J, Glimm E (submitted). Conditionally unbiased and near unbiased estimation for multi-stage drop-the-losers designs.
7. Bowden J, Wason J (accepted). Identifying combined design and analysis procedures in two stage trials with a binary endpoint. Statistics in Medicine.