

Lancaster University, UK

Senior Research Associate in Medical Statistics

Ref: A1016

The project

Accurate estimation of a treatment's effect is vital for expressing its true worth. This is important in early phase trials as this information is routinely used to decide whether further study is warranted and to power future studies. Additionally, health bodies require accurate estimation of the treatment effect to make informed choices about cost-effectiveness relative to alternative options as well as benefit risk assessment. The treatment effect is usually reported as the maximum likelihood estimator (MLE) which is a precise and readily available estimator. For designs that include interim analyses, it is, however, typically biased since it ignores the sequential nature of the trial. Additional bias is introduced by selecting treatments, subgroups or endpoints based on observed effect sizes.

To address this problem, several classes of estimation procedures have been proposed, most methods are, however, limited to two-stage designs and normally distributed observations. Additionally few estimators offer corresponding confidence intervals, limiting their usefulness in practice. This project aims to thoroughly evaluate the extent of bias of the MLE in studies in which multiple hypothesis tests are conducted and develop novel approaches for point and interval estimation. Specific objectives are to:

- evaluate the extent of bias for a range of statistical designs;
- develop graphical approaches for displaying treatment effects for correlated hypotheses;
- develop point and interval estimates that yield an optimal trade-off of precision and accuracy;
- develop bias-reducing methods for estimating effects for time-to-event endpoints;
- develop open-source software and associated training tailored to clinical trialists and applied statisticians working on clinical trials.

To ensure practical relevance, the overall research programme will be overseen by an advisory board.

The Investigators

Dr Thomas Jaki is a Reader in Statistics at Lancaster University and a co-investigator of the MRC's North-West Hub for Trials Methodology Research and the current leader of the Adaptive Designs Working Group of the MRC network of Hubs. He is a Career Development Fellow of the NIHR and the director of Lancaster University's Medical and Pharmaceutical Statistics Research Unit (www.mps-research.com) 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 methods for identifying differential effects.

Prof Martin Posch is professor in Medical Statistics at the Medical University of Vienna (Austria) and worked from 2011–2012 as Statistical Expert at the European Medicines Agency (EMA) in London. Presently, he provides his expertise as observer in the EMA Biostatistics Working Party. He is one of the leading experts in adaptive designs and has led several substantial research projects on this topic. His wide-ranging expertise, stretching from design via point estimation to interval estimation, will be paramount in developing and evaluating the methods under study.

The Departments

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/>) 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 Medical University of Vienna (MUW) is the largest medical organisation in Austria and one of the top-level research institutions in Europe providing Europe's largest hospital, the AKH in Vienna. The Section of Medical Statistics (IMS) of the Center for Medical Statistics, Informatics, and Intelligent Systems (CeMSIIS) of the Medical University of Vienna, Austria has a long tradition in Medical Statistics with an outstanding track record both in innovative statistical methodological and medical research. The Center has been selected as an excellence groups in Mathematics in the most recent CHE ranking (<http://www.excellenceranking.org/>).

Selection procedure

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

References

1. Holland, PW. 1986. Statistics and causal inference. *Journal of the American Statistical Association*, 81, 947–960.
2. Rubin, DB. 1974. Estimating causal effects of treatments in randomized and nonrandomized studies. *Journal of Educational Psychology*, 66, 688–701.
3. Cai, T, Tian, L, Wong, PH, & Wei, LJ. 2011. Analysis of randomized comparative clinical trial data for personalized treatment selections. *Biostatistics*, 12(2), 270–282.