Celebrating Young Biometricians

Tuesday 28th November 2017

The BIR, jointly with the Fisher Memorial Trust, has actively celebrated the contributions of young biometricians by instituting the biennial Young Biometricians Award. This meeting provides a forum for three of the winners to present some of their latest findings. A counterpoint is provided in a talk by John Hinde, immediate Past-President of the International Biometric Society, on topics of current importance to the profession.

Speakers:

Anaïs Rouanet (MRC Biostatistics Unit, University of Cambridge) - 2017 YBA winner
David Robertson (MRC Biostatistics Unit, University of Cambridge) - 2015 YBA winner
Doug Speed (UCL Genetics Institute) - 2013 YBA winner
John Hinde (NUI Galway) - previous President of the International Biometric Society

The meeting will be held from 1:30-5:30pm on Tuesday 28th November 2017 at the London Mathematical Society, De Morgan House, 57-58 Russell Square, London WC1B 4HS. The AGM of the BIR will precede the scientific meeting.

Please come along and support our award winners.

Registration fee for scientific meeting (AGM free): £25 for full or retired members; £10 for student members; £50 for non-members or £70 for non-members including membership for 2018.

Programme

13:30 - 14:00	**British & Irish Region AGM**
14:00 - 14:45	**Joint latent class model for longitudinal data and interval-censored semi-competing events** Anaïs Rouanet (MRC Biostatistics Unit, University of Cambridge) - 2017 YBA winner Joint models are used in ageing studies to investigate the association between longitudinal markers and a time-to-event, and have been extended to multiple markers and/or competing risks. The competing risk of death must be considered in the elderly because death and dementia have common risk factors. Moreover, in cohort studies, time-to-dementia is interval-censored since dementia is assessed intermittently. So subjects can develop dementia and die between two visits without being diagnosed. In this talk, I will present a joint latent class model combining a mixed model and an illness–death model handling both interval censoring and semi-competing risks. The correlation between the marker and the times-to-events is captured by latent classes, homogeneous sub-groups with specific risks of death, dementia, and profiles of cognitive decline. I will discuss two different applications of this model in the context of dementia study.

14:45 - 15:30	**Correcting for selection bias in two-stage trials** David Robertson (MRC Biostatistics Unit, University of Cambridge) The problem of selection bias has long been recognised in the analysis of two-stage trials, where promising candidates are selected in stage 1 for confirmatory analysis in stage 2. Specifically, a candidate has to perform 'well' in stage 1 in order to proceed to stage 2, which can lead to overly-optimistic estimates. To efficiently correct for bias, uniformly minimum variance conditionally unbiased estimators (UMVCUEs) have been proposed for a wide variety of trial settings, and here we present some recent extensions. Firstly, in the diagnostic test setting with binary outcomes, we derive the UMVCUE and exact confidence intervals for a test's sensitivity in a two-stage design with general selection rules. We apply our estimation strategy to data from a recent family history screening tool validation study by Walter et al. (BJGP 63: 393-400), and are able to identify and successfully adjust for bias in the tool's estimated sensitivity to detect those at high risk of breast cancer. Secondly, in two-stage trials with normally distributed outcomes, we relax the common assumption that the population parameter estimates are independent, and derive the UMCVUE in the multivariate normal setting with an arbitrary known covariance structure. One area of application is the estimation of odds ratios (ORs) when combining a genome-wide scan with a replication study. Our framework explicitly accounts for correlated single nucleotide polymorphisms (SNPs), as might occur due to linkage disequilibrium. We illustrate our approach on the measurement of the association between 11 genetic variants and the risk of Crohn's disease, as reported in Parkes et al. (Nat Gen 39:830–832), and show that the estimated ORs can vary substantially if both selection and correlation are taken into account Another application is the estimation of treatment effects in seamless phase II/III clinical trials. Methods for bias adjustment developed thus far have made restrictive assumptions about the design and selection rules followed. Our framework allows for the precision of the treatment arm estimates to take arbitrary values; can be utilised for all treatments that are taken forward to phase III; and is applicable when the decision to select or drop treatment arms is driven by a multiplicity-adjusted hypothesis testing procedure.
15:30 - 15:45	**Tea/coffee break**

15:45 - 16:30	**Using mixed models to better understand the genetic architecture of complex human traits.** Doug Speed (Aarhus Institute for Advanced Studies) It is now realised that the majority of complex traits are highly polygenic, with 100s or 1000s of causal variants. By contrast, most regression tools were designed under an assumption of sparsity. In the search for more suitable methods, mixed models have come to the fore, and are now being used to estimate SNP heritabilty (the total phenotypic variance explained by a set of SNPs), for prediction and to compute the genetic correlation between pairs of traits. The latest focus is on creating "summary versions" of these tools, which no longer require access to individual-level data but instead use summary statistics released by large-scale meta-analysis consortia. I will discuss these latest developments, and how my software LDAK is leading the way as we try to better understand complex traits.
16:30 - 17:15	**Translational Statistics: Relevance, Reproducibility and Communication** John Hinde & John Newell (NUI Galway, Ireland) Translational medicine, often described as “bench to bedside", promotes the convergence of basic and clinical research disciplines. It aims to improve the flow from laboratory research through clinical testing and evaluation to standard therapeutic practice. This transfer of knowledge informs both clinicians and patients of the benefits and risks of therapies. In an analogous fashion, we propose the concept of *Translational Statistics* to facilitate the integration of biostatistics within clinical research and enhance communication of research findings in an accurate and accessible manner to diverse audiences (e.g. policy makers, patients and the media). Much reporting of statistical analyses often focuses on methodological approaches for the scientific aspects of the studies; translational statistics aims to make the scientific results useful in practice. Various examples will be used to illustrate these findings.