

# A two-day training course at Keele University: 18<sup>th</sup> and 19<sup>th</sup> June, 2018 STATISTICAL METHODS FOR EVIDENCE SYNTHESIS OF INDIVIDUAL PARTICIPANT DATA

## Led by Dr Danielle Burke and Prof Richard D. Riley Research Institute for Primary Care and Health Sciences, KEELE UNIVERSITY e-mail: s.weir@keele.ac.uk

#### AIMS

This two-day statistical course provides a detailed foundation of the methods and principles for evidence synthesis and meta-analysis when IPD (Individual Participant/Patient Data) are available from multiple related studies. The course considers **continuous**, **binary and time-to-event** outcomes, and both fixed effect and random effects meta-analysis models. Day 1 focuses mainly on the synthesis of IPD from *randomised trials* of interventions, where the aim is to quantify a *treatment effect* (usually in the presence of between-study heterogeneity). Two-stage and one-stage IPD meta-analysis approaches are outlined in detail. Day 2 focuses on novel extensions, including: estimation of treatment effect modifiers (interactions) for *stratified medicine*, multivariate and network meta-analysis of IPD to incorporate correlated and indirect evidence (e.g. from multiple outcomes, multiple treatment groups or multiple time-points); and meta-analysis of prognostic/risk factor studies. The course consists of a mixture of lectures and practical sessions in Stata to reinforce the underlying statistical concepts. Code will also be replicated for use in R. The key messages are illustrated with real examples throughout.

#### LEARNING OBJECTIVES:

- Understand the difference between IPD and aggregate data, and the rationale for an IPD meta-analysis of randomised trials
- Recognise the challenges of setting up an IPD meta-analysis, but also the many potential advantages
- Know how to conduct one-stage and two-stage fixed effect and random effects IPD meta-analyses
- Understand how to model, explain and interpret heterogeneity between studies
- Understand when and why one-stage and two-stage methods may differ
- Appreciate how to derive percentage study weights in two-stage and one-stage IPD meta-analysis models
- Recognise why it is essential to account for the clustering of participants within studies in an IPD meta-analysis
- Know how to write-down and fit fundamental IPD meta-analysis models for continuous, binary and time-to-event outcomes
- Understand how to estimate patient-level effect modifiers (treatment-covariate interactions, predictive markers) in an IPD metaanalysis, and why these are important for stratified medicine
- Know the meaning of the terms publication bias, availability bias, and selection bias, and how to examine them
- Understand evidence synthesis models for combining IPD studies with aggregate data from non-IPD studies
- Understand meta-analysis models for identifying risk or prognostic factors using IPD from observational studies
- Understand the difference between univariate and multivariate meta-analysis models
- Recognise why multivariate methods are important for evidence synthesis of multiple outcomes
- Appreciate the potential benefits of IPD for network meta-analysis of multiple treatments
- Understand how IPD facilitates multivariate meta-analysis by deriving within-study correlations via bootstrapping
- Appreciate the importance of multiple imputation and how it may be undertaken in an IPD meta-analysis
- Recognise the importance of the PRISMA-IPD reporting guidelines
- Recognise possible options for calculating the power of an IPD meta-analysis, in advance of collecting IPD
- Gain experience at fitting key IPD meta-analysis models in the Stata software, through four practical sessions covering: (i) onestage IPD meta-analysis approaches; (ii) two-stage IPD meta-analysis approaches; (iii) estimation of treatment-covariate interactions; (iv) multivariate and network meta-analysis using IPD.

### TARGET AUDIENCE

The course is aimed at individuals that want to learn how to design and undertake the analysis of an IPD meta-analysis. We recommend that participants have a background in statistics as the course assumes a good understanding of core statistical principles and topics, such as regression methods (such as linear, logistic, and Cox), parameter estimation and interpreting software output. A familiarity with traditional aggregate data (non-IPD) meta-analysis methods would be advantageous, though not essential. We also recommend that participants are familiar with Stata or R, although the practicals will not require individuals to write their own code. Participants will need to bring a laptop with Stata 12 or above, or the latest version of R.

**COST**: Student £450; Academic £600; NHS and government organisations £600; Industry (commercial) £800 (Includes one night's accommodation, lunch on both days and a pub meal on the evening of the 18<sup>th</sup> June)

To register for the course please visit the Keele e-store: <u>http://estore.keele.ac.uk/conferences-and-events/faculty-of-medicine-and-health-sciences/primary-care-health-services/course/2018-june-statistical-methods-for-evidence-synthesis-of-individual-participant-data-course</u>