## Wednesday 24 July 2024

### 09:00-10:30 Invited Session 6 (Main Room)

**Bayesian methods in clinical development (Chair: Marcia Rueckbeil)**

**Applying Bayesian methods in clinical trials: opportunities and challenges**

**Becky Turner** (University College London, UK)

This talk will begin with a review of confirmatory trials which have used Bayesian methods in their primary analysis, in papers published over the last 5 years. I will review trial characteristics, approaches taken to design, analysis and decision making, and the use of informative priors. Next, I will present three case studies of clinical trials in which Bayesian methods were used to borrow information.

The ODYSSEY trial evaluated dolutegravir-based antiretroviral therapy regimens for children and adolescents living with HIV. The main trial recruited 707 children weighing 14kg or more, while a smaller group of 85 children weighing <14kg was recruited 12 months later following a lead-in pharmacokinetics study. The treatment effect in younger children needed to be estimated separately, to avoid delaying presentation of results from the main trial, but a standalone analysis of their data would not be adequately powered. Preplanned Bayesian methods were used to enable borrowing of information from the larger subgroup of older children, when estimating the treatment effect in younger children, to increase power and precision. The degree of borrowing was informed by elicited clinical opinion about similarity of treatment effects between the two weight cohorts, obtained before the main trial results were available.

VQUIN and TB-CHAMP were separate randomised placebo-controlled phase 3 trials in adults and children respectively, both evaluating levofloxacin as tuberculosis (TB) preventive treatment in household contacts of individuals with multidrug-resistant TB. While the trials were ongoing, investigators realised that TB event rates were lower than expected and each trial would therefore likely be underpowered. In addition to conventional individual patient data meta-analysis, Bayesian methods were planned, ahead of trial completion, to borrow information between trials and estimate the efficacy in each trial with more precision. To define the weights given to borrowed information, we elicited expert opinion on how efficacy was expected to differ between adults and children, informed by results from relevant natural history studies and meta-analyses of observational studies. Bayesian methods enabled us to estimate treatment efficacy with more precision, by borrowing evidence from a comparable external trial, with evidence-informed recognition of key differences between relevant study populations. This approach was accepted by WHO and informed revised guidelines for prevention of multidrug-resistant TB in children and adults.