The new generation of clinical trials: is Australia ready?

***Lee, KJ*[1,2]**, Braat S[2], Pascoe E[3], Marsh JA[4,5], Forbes A[6], Berry S[7] and Webb S[6,8] on behalf of the Australian Clinical Trials Alliance Statistics in Trials Interest Group.

[1] *Murdoch Children's Research Institute, Melbourne, Australia*

[2] *University of Melbourne, Melbourne, Australia*

[3] *University of Queensland, Brisbane, Australia*

[4] *University of Western Australia, Perth, Australia*

[5] *Telethon Kids Institute, Perth, Australia*

[6] *Monash University, Melbourne, Australia*

[7] *Berry Consultants, Austin, Texas, United States*

[8] *St John of God Healthcare, Perth, Australia*

Background

The promise of personalised medicine, availability of biomarkers, and large number of drugs in the research pipeline have led to the development of adaptive trial designs, including basket, umbrella, and platform trials. Such trials consist of regular sequential analyses with predefined decision algorithms, and are critical for increasing the translational impact of trials into routine care. For studies with many treatments and/or patient subgroups, adaptive designs have the potential for huge efficiency gains over standard designs. However, they require extensive statistical input during planning and conduct.

Objectives

To outline the advances in adaptive designs and describe the need for advanced statistical methods to support them.

Method

For adaptive designs, it is not possible to conduct a sample size calculation using standard methodology. Instead, extensive simulations are generated under a range of plausible assumptions about treatment response, final sample size, patient accrual, incidence of the primary outcome, and differential treatment effects. The simulation results are summarised to show the trial operating characteristics under different scenarios and decision thresholds to ensure control of the type I and II error. We illustrate this methodology using the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP).

Results

The example demonstrates the complexity of adaptive designs. Although such trials are being designed and conducted by Australian investigators, the simulations and analysis are conducted internationally due to a lack of local biostatistical capacity. We need to increase our understanding and develop a national biostatistical base to support such studies in the future.