ACTA INNOVATIVE TRIALS DESIGN AND CONDUCT REFERENCE GROUP OBJECTIVES AND ACTIVITIES

Background

A number of innovative methods have recently emerged for the design, conduct, and analysis of trials. Some of these are methods relate to trial design and statistical analysis, while other innovations relate to methods for better and more efficient acquisition of data. There is a need to evaluate these methods, including identifying limitations, as well as seeking to quantify the impact of innovative methods on trial efficiency.

Objectives

1. Facilitate the assessment, availability, dissemination, uptake, and evaluation of innovative methods of trial design, conduct, and analysis by clinical trial networks.
2. Influence policy and promote the development of shared infrastructure that can support innovative trial design and conduct.

Types of Activities

It seems likely that the activities of this Reference Group will divide into two broad categories and that the balance between these activities will differ among the different themes within this Group. One set of activities will relate to assessment of appropriateness, dissemination, creation of awareness, training, sharing of skills and tools, and networking. A second set of activities will relate to influencing policy and promoting the development of shared infrastructure that can support innovative trial design and conduct.

Themes

At this stage, 5 themes within this Reference Group can be identified. Additional themes may be added. There is some potential for overlap between themes which will be managed at the Reference Group level.

1. Innovative Design and Statistical Methods

- Leadership by Kate Lee and Andrew Forbes.

Example of innovative trial methods include adaptive trials, umbrella trials, basket trials, platform trials, and cluster cross-over designs (maybe others). These designs offer the prospective of more efficient (cheaper and quicker) trials. The capacity to undertake some of these designs is limited by availability of specialised statistical skills, particularly the conduct of trial simulations around sample size calculation and stopping rules.

Activities within this theme will largely relate to dissemination, coordination, alignment, and sharing of expertise via workshops and presentations. There is also the capacity to develop and share template protocol documents. There are also policy level issues related to an identified unmet need for workforce development and availability of statistical infrastructure to support planning and conduct of trials using innovative designs. ACTA is in a position to promote and facilitate the development of such infrastructure. ACTA will also

facilitate the evaluation of the validity and value of new methods of trial design and analysis.

2. Innovative Methods for Collection of Patient Reported Outcomes

- Leadership by Madeleine King.

Patient Reported Outcome Measures (PROMs) are important and used increasingly to describe patient experiences to provide data for measurement of end-points in trials. Historically, methods have involved hard-copy questionnaires, typically completed at clinic visits within a trial assessment schedule, with mailed surveys or telephone calls also used, typically as secondary collection methods. Mailed surveys suffer from low completion rates, and both mail and telephone collection have addition costs. Electronic PRO data collection methods (e-PROMs) provide the prospect of automated collection of PROM data using e-mail / SMS to communicate with trial participants. e-PROMs have the advantage that data are entered directly by the trial participant, avoiding data entry costs, and have potential to increase PRO completion rates, but have additional (but fixed) costs for IT infrastructure, and issues around standardization of IT infrastructure/methods and measures across trials and trials groups.

Activities of this theme will include dissemination of awareness of the availability of e-PROMS (including information about vendors) to clinical trial networks as well as facilitating an understanding of fixed costs (e.g. infrastructure) versus marginal costs (e.g. per additional trial participant). Policy work may include facilitation / development of consortia among networks to develop centralised infrastructure with fixed costs borne by the consortia and marginal costs covered by trial budgets. Further work may include input into policy decisions regarding data privacy and protections, location and security of central data storage, exploration of the efficiency of different models of e-PROM capture, development of processes to standardise PROM sets among clinical trial networks, and influencing choice of e-PROMs as well as facilitation of access to e-PROM data collected routinely by the healthcare sector.

3. Innovative Collection of Outcome Measures Using Linked Data

- Leadership by Felicity Flack.

Linkage of individuals enrolled in clinical trials to administrative and clinical data sets (such as death registry, cancer registry, admitted episode data, emergency department admissions, PBS data, and MBS data) offer the prospect of long-term follow up of trial participants that is cheaper and more efficient. There may also be the capacity for linkage to data held within My Health Record.

The activities within this theme are likely to represent a balance of dissemination of information and policy proposals. Workshops and presentations will be used to increase awareness of the availability of linkage to clinical trial networks as well as facilitate an enhanced understanding of data requirements for trials by organisations that undertake and facilitate linkage of data. This can include ensuring that requirements for consent are understood and operationalised appropriately by trials. There is also the capacity to influence policy relating to the access to existing sources of linked data and around rules for

access to new sources of data such as My Health Record as well as creating awareness of the value of linked data for trials among data custodians. There may also be the capacity to explore electronic data capture of clinical data, for example held by hospitals and clinics, although this may be covered within the Embedding Reference Group.

4. Registry-randomised trials

- Leadership TBC (?Ian Harris)

The nesting of trials within a registry is recognised as one innovative method that can reduce the cost and enhance the external validity of trials. There is increasing interest and utilisation of registry-randomised trials in Australia.

Activities within this theme will largely relate to dissemination of awareness and sharing of expertise by workshops and presentations, although the development of trial capacity in conjunction with the registry sector provides important examples of the value of registries that can be leveraged to support registry expansion.

5. Trial Economics

- Leadership TBC (?Phillip Clarke)

This theme relates to developing and disseminating methods by which the 'cost per answered question' can be quantified for traditional and innovative trial methods. This can serve to better understand the value of innovative trial designs and data collection methods, encouraging the adoption of methods that utilise research resources most efficiently.

6. Studies within a Trial

- Leadership TBC (?Elaine Pascoe)

This theme relates to the utilisation of methods that evaluate alternative design options within a trial to determine which of the methods are most effective and efficient. Examples of such studies include randomisation of participants to receive different information and consent forms to identify which method enhances understanding and decision making while achieving optimal trial recruitment. The themes activities will be to disseminate awareness of and methods for conducting studies of design features by the conduct of workshops and presentations, as well as disseminating the results of such studies to the clinical trial networks so that optimal methods can be utilised as widely as possible.

Coordination with other Reference Groups

There is some potential for overlap between this Reference Group and the Embedding Reference Group which will be managed by liaison between the Chairs of the Groups in the first instance, in conjunction with the Senior Program Manager who has oversight of all Reference Groups.