Project title: Adaptive designs for mental health trials on complex interventions

Lead applicants:

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Collaborators:

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Budget:

* King’s College London £28154
* Newcastle University £9644

Aims:

This research project aims to facilitate the application of adaptive designs to mental health trials on complex intervention. We focus on the setting of individual patient randomized trials where clustering arises only in the intervention arm post-randomization. in the literature, where the methodology work had focused on fixed trial setting

*Objective 1: Scoping review on adaptive designs for linear mixed effect models*

We have reviewed the literature on group sequential designs, sample size re-estimation and multi-arm multi-stage design that have considered linear mixed effect models. Most of the relevant papers focus on repeated measurements or clusters randomized trials where a linear mixed model is used for the analysis. The considered models are different to the linear mixed effect models for partially nested design. Nevertheless, it implies that these existing adaptive design frameworks can be extended for the application to partially nested design accordingly.

*Objective 2: A proof-of-concept simulation study*

Focus on a single cross-sectional endpoint, the methodological exploration on group sequential design and sample size re-estimation demonstrated favourable evidence for using adaptive partially nested designs in some mental health trials settings. We consider different estimation methods (MLE vs REML) and two respective settings where i) all clusters have half the planned number of individual data and ii) half the clusters have all the planned number of individual data, when an interim analysis is conducted. The proof-of-concept simulation studies highlight the efficient error control for both group-sequential and sample size re-estimation designs. This propagates the applicability of these designs in real life trials leading to potential savings in terms of cost and time.

*Objective 3: Raise awareness of trialists on issues related to adaptive/ complex trial designs*

We held the “Innovative Trial Designs for Complex Interventions Workshop” in King’s College London on 12th March 2025. We disseminated the project findings, promoted the use of adaptive/ complex trial designs and held a panel discussion for early to mid-career trial statisticians to raise questions about trial designs. Senior trial statisticians who have a rich experience in designing trials with adaptive designs were invited to present talks and be discussants to answer questions from attendees. The talks included the following topics:

1. Partially nested adaptive designs for trials of complex interventions
2. Opportunities and challenges in trial design and conduct
3. Practical Challenges in Funding and Conducting Adaptive Trials

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The half day in-person workshopwas attendedby 61 people from over 18 Institutions, who are either trial statisticians from different UKCRC Registered Clinical Trials Units or methodology researchers at universities, with a couples of junior health and care professionals who are interested in the topics. The event was very educative and engaging. Participants who received travel subsidy were grateful for the support.

Next Steps:

1. We are preparing a manuscript for submission to a peer-reviewed journal. We plan to build an R shiny app for ease of designing an adaptive design for partially nested designs.
2. We have not explored multi-arm multi-stage designs for partially nested trials. We also have not explored partially nested trials with repeated measurements. We plan to seek further funding to conduct methodology exploration on these aspects.
3. We plan to gather feedback on the applicability of these designs from health and care professionals who are also trialists.