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Trials

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Abstract omitted

P-2
Some practical considerations in the design of multi-arm multi-stage designs

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Trials 2019, **20(Suppl 1):**P-2

Introduction: In the design of cancer clinical trials, one is often concerned with a number of options in the event that several treatments are of interest.
Methods: We explore in this work the distinct possibilities when four treatments are available, one acting as control and three as potentially efficacious alternatives. This design may be embedded within the context of multi-arm multi-stage (MAMS) trials where one may select a two- or three-stage design.
Potential Results: We explore the application of such designs, including trade-offs between potential gains in the number of patients with additional stages contrasted with patients "lost" due to practical considerations such as patients randomised in dropped arms while waiting for interim analyses and inspection by an Independent Data and Safety Committee. In addition, in cancer studies one may focus on the primary end-point using a time-to-event analysis or a binary outcome by looking at the probability of (potentially progression-free) survival at a specific, clinically meaningful, time point. The effect of such choices is extensively investigated.
Potential Relevance & Impact: We conclude with a discussion of the available software for MAMS designs and their advantages and disadvantages in terms of accuracy.

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The UK plasma based Molecular profiling of Advanced breast cancer to inform Therapeutic CHoices (plasmaMATCH) Trial: A multiple parallel-cohort, phase IIa platform trial aiming to provide proof of principle efficacy for designated targeted therapies in patient subgroups identified through ctDNA screening (CRUK/15/010)

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Trials 2019, **20(Suppl 1):**P-3

Introduction: plasmaMATCH is a novel platform trial which assesses the potential of circulating tumour DNA (ctDNA) screening to direct targeted therapies in advanced breast cancer (ABC) patients. The trial recruited ahead of target and will report initial results within 3years of first patient first visit demonstrating efficiency of this design.
Methods: plasmaMATCH is an open-label, multi-centre phase IIa platform trial, consisting of a ctDNA screening component and five parallel treatment cohorts. Patients with an actionable mutation identified at ctDNA screening are invited to enter Cohorts A-D to receive a targeted treatment matched to the mutation identified (A: ESR1–extended-dose fulvestrant; B: HER2–neratinib+/-fulvestrant; C&D: AKT1 (or PTEN for Cohort D) –AZD5363+/-fulvestrant). Cohort E was added

digital tool, with examples, will inform the NIHR research community about choices and help them identify potential tools to support recruitment and retention.

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Lessons learnt from a multi-centre Type 3 surgical trial

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Background: Pragmatic randomised controlled trials are increasingly being used to evaluate surgical interventions, although they present particular difficulties in regard to recruitment and retention.
Methods
This paper details the procedures and processes related to implementation of a multi-centre pragmatic surgical randomised controlled trial.
Results: Forecasting consent rates based on previous similar trials ensured that the recruitment window was of adequate length. Adequate resource was available for study procedures at multiple clinics in each hospital due to micro-costing of study activities with research partners ensure. A video was produced targeting recruiting staff, which aimed to help recruiters explain the trial, randomisation and equipoise, based on methodological work and experiences from another study. Post-randomisation delays in delivering surgery to one study arm were investigated by assessing the outcomes at the time of randomisation and the day of surgery which provided confidence in the baseline measure. Real-time monitoring of participant drop-out due to delays in surgery meant we were able to extend the recruitment window in a timely fashion. Triangulation of data sources ensured adequate numbers of participants provided primary outcome data.
Discussion: This paper provides a range of evidence- and experience-based approaches which resulted in meeting our study's objectives and these lessons may be transferable.

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Challenges in the design, planning and implementation of trials evaluating group interventions

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Background: Evaluating group interventions in randomised controlled trials (RCTs) presents a set of practical problems which may not be immediately obvious and are not present in RCTs of one-to-one interventions.
Methods
Case-based approach summarising Sheffield clinical trial unit's experience in the design and implementation of group interventions across five randomised controlled trials.
Results: Median recruitment across the five trials was 5.8 (range 2.1-16.0) participants per site per month. Group intervention trials can involve a delay in the start of treatment whilst waiting for sufficient numbers to start a group. There was no evidence in our trials that the timing of consent, relative to randomisation, affected post-randomisation attrition, but attrition was a concern for all trial teams. Group facilitator attrition was common in studies where facilitators were employed by the health-system rather than the by the grant holder, and lead to the early closure of one trial. Solutions to this included training 'back-up' and new facilitators. Trials specified that participants had to attend a median of 62.5% (range 16.7% to 80%) of sessions, in order to receive a 'therapeutic dose'; a median of 75.0% (range 34.6% to 97.8%) received a therapeutic dose. Across the five trials, 66.4% of all sessions ran with fewer than the numbers pre-specified as ideal. A variety of methods were used to assess the fidelity of group interventions across the five trials.
Discussion: Investigators should expect delays / difficulties in recruiting groups of the optimal size, plan for both facilitator and participant attrition and consider how group attendance and group size affects treatment fidelity.

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Delivering site set-up training to groups of sites versus individually: a randomised study within a trial

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Introduction: Site initiation visits (SIVs) are conducted to deliver training to sites before opening them to recruitment, though this can be burdensome during the time-intensive trial set-up period. There is little evidence about the best way to deliver training for sites to perform well. Evaluating methods of training was the highest priority identified at a workshop exploring recruitment and retention of participants to trials. Two systematic reviews investigating training in clinical trials showed a variety of different training methods and more research is needed to determine what kind of training and support can improve recruitment. A small retrospective study showed that, whilst face-to-face training (either at SIV or group training session) was associated with better recruitment than remote training (i.e. telephone or DVD), no difference was seen between the two types of face-to-face training.
Our objective is to compare group-based training during the trial set-up period versus visiting the site to conduct a SIV to investigate the impact of the training method upon key site performance metrics. We will embed a SWAT into the FEED1 trial, funded by the NIHR HTA programme.
Methods: Once selected, sites will be randomised in batches to receiving their site-initiation training during a SIV or group-based training by attending a collaborators' meeting. To allow for non-availability of site staff, two meetings will be held. Outcomes will include recruitment and retention, data quality and protocol compliance (defined as core site performance metrics) and associated costs of each training method.
Timing of potential results: Clinical trial and SWAT results will be available in Q1 of 2023.
Potential relevance and impact: If the intervention is shown to be effective, there could be significant benefits to funders and trial teams, in particular reducing the length of time it takes to set-up a trial and open all sites.

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Making a challenging trial possible: Lessons from the Emergency Department led EcLiPSE trial

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