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Trials

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Abstract omitted

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

Jerome Wulff, Nikolaos Demiris
Cambridge Clinical Trial Unit, Cambridge, United Kingdom
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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)

Sarah Kernaghan[1], Laura Moretti[1], Lucy Kilburn[1], Katie Wilkinson[1], Claire Snowdon[1], James Morden[1], Iain Macpherson[2], Andrew Wardley[3], Rebecca Roylance[4], Richard Baird[5], Alistair Ring[6], Nicholas Turner[7], Judith M Bliss[1], on behalf of the plasmaMATCH Trial Management Group
[1]Clinical Trials and Statistics Unit at The Institute of Cancer Research (ICR-CTSU), United Kingdom; [2]The Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom; [3]The Christie NHS Foundation Trust, Manchester, United Kingdom; [4]University College London Hospitals NHS Foundation Trust, London, United Kingdom; [5]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom; [6]The Royal Marsden NHS Foundation Trust, Sutton, United Kingdom; [7]The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, United Kingdom
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

Introduction: Recruitment and retention of participants are the biggest challenges to successful delivery of trials. Many interventions are used by trial teams to improve recruitment and retention; however, few have been rigorously evaluated. A Study Within A Trial (SWAT) is a robust method to evaluate the effectiveness of interventions for improving trial conduct. PROMoting THE USE of SWATs (PROMETHEUS) aims to make embedding SWATs standard practice across UK Clinical Trials Units (CTUs), by pump-priming and facilitating trial teams to start at least 25 SWATS of recruitment or retention.
Methods: We established a network of CTUs committed to starting at least two SWATs of recruitment and/or retention interventions. We identified promising recruitment and retention interventions from a variety of sources including Cochrane systematic reviews and existing prioritisation exercises. We created a priority list of 7 recruitment and 8 retention interventions, and developed template SWAT protocols for testing them. We are inviting trial teams to apply for funding of up to £5,000 to test one of our prioritised interventions or their own. Successful applicants are given funding, methodological and process support to embed and report the SWAT.
Results: 26 trial teams from 11 CTUs have been funded to undertake 30 SWATs of recruitment and retention strategies, exceeding our initial target of 25 SWATs ahead of schedule. Each recruitment and retention intervention is being evaluated in up to five host trials, and will be evaluated for its effectiveness in the context of individual trials, as well as across different trial populations and contexts.
Discussion: The RCT community has shown that with enough financial and methodological support, many are willing to engage with and implement SWATs to build rapidly the evidence base. This will help to deliver trials in a timely manner, patients to receive better treatments and funders to deliver on their objectives.

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What use is an external pilot study?

Sandra Eldridge[1], Christine Bond[2], Mike Campbell[3], Claire Chan[1], Sally Hopewell[4], Gill Lancaster[5], Lehana Thabane[6]
[1]Queen Mary University of London, United Kingdom; [2]University of Aberdeen, Aberdeen, United Kingdom; [3]University of Sheffield, Sheffield, United Kingdom; [4]University of Oxford, Oxford, United Kingdom; [5]Keele University, Keele, United Kingdom; [6]McMaster University, Hamilton, Canada
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The past 15 years have seen an exponential rise in published studies in health research described as pilot or feasibility studies. Many of these published studies are in preparation for larger randomised controlled trials evaluating efficacy or effectiveness. The vast majority of these studies are external pilot or feasibility studies conducted separately from the future larger randomised trial, andthe data they produce is used only to make decisions about whether and how to go on to a larger study. However, there has also been a rise in the number of effectiveness or efficacy randomised controlled trials in which the first part of the trial is a pilot phase used to test out the feasibility of trial processes such as recruitment and retention. These pilot phases are usually called internal pilot studies.
A pilot or feasibility phase for trials of complex interventions is widely recommended, for example by the UK MRC framework for the development and evaluation of complex interventions and is expected by funders such as the UK NIHR. However, researchers still face the question about whether and what sort of external pilot work is needed in relation to their own research area. In this talk, we will use some examples of external pilot and feasibility studies to reflect on when external pilot studies are particularly useful, and how to make judgements about their objectives, design and conduct. The examples cover a range of different health issues. We suggest that the usefulness of an external pilot study in advance of a larger randomised controlled trial may be best assessed on a case by case basis.

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Recruiting women during pregnancy and childbirth to clinical trials – the barriers and enablers of trial recruiters: a qualitative evidence synthesis

Vivienne Hanrahan[1], Linda Biesty[2], Katie Gillies[3]
[1]National University of Ireland Galway, Galway, Ireland; [2]National University of Ireland Galway, Galway, Ireland; [3]University of Aberdeen, Aberdeen, Scotland
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Introduction: The Prioritising Recruitment in Randomised Trials Priority Setting Partnership Study (PRioRiTy PSP), identified and prioritised unanswered questions around trial recruitment research. We utilised qualitative research methods to answer Question 5 'What are the barriers and enablers for trial recruiters?' within the maternity care setting.
The aim of this Qualitative Evidence Synthesis (QES) was to explore the evidence on the recruiter's experience and perceptions of recruiting women during pregnancy & childbirth to trials. We were specifically interested in exploring;
1)The recruiter's perception and awareness of how their own role (e.g. clinical or non-clinical) might influence recruitment.
2)The recruiter's perception and experience of how the 'type of trial' (i.e. pharmaceutical, non-pharmaceutical,) might influence recruitment.
3)Explore the setting and environment in which recruitment is undertaken.
Methods: Using SPIDER, a broad search of electronic databases (Pubmed, CINAHL, Embase, PsycINFO) & grey literature (Scopus, forward & backward citation searches) returned 13,401 citations. Abstracts were independently screened by two reviewers, of these, 29 citations progressed to full text screening, resulting in 8 eligible papers. We designed a data extraction tool and critically appraised using CASP checklist. A thematical approach to coding & synthesis was undertaken, applying CERQual for confidence in review findings.
Timing of Potential Results: We have preliminary results and expect the QES will be submitted for publication in December 2019.
Potential Relevance & Impact: The review will, for the first time, systematically synthesise existing research on factors associated with recruitment to RCTs in maternity care from the recruiters perspective. The findings will provide the basis and direction of an exploratory qualitative study seeking to develop a statement of recommendation (in collaboration with stakeholders) for successful recruitment of women during pregnancy & childbirth to RCTs.

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Understanding and addressing recruitment challenges in a thoracic anaesthesia randomised controlled trial (RCT)

Caroline Wilson[1], Marcus Jepson[1], Fang Gao-Smith[2]
[1]Bristol Medical School, University of Bristol, Bristol, United Kingdom; [2]Institute of Inflammation and Ageing Centre of Translational Inflammation Research, University of Birmingham, Birmingham, United Kingdom
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Introduction; The Topic 2 randomised controlled trial (RCT) (NIHR-HTA- 16/111/111) was set up to compare the effectiveness of thoracic epidural and paravertebral blockade in reducing chronic post-thoractomy pain. Recruitment was anticipated to be difficult and the QuinteT Recruitment Intervention (QRI) was integrated into the trial design to optimise recruitment.