
Proceedings Paper:
O'Cathain, A. orcid.org/0000-0003-4033-506X, Croot, E. orcid.org/0000-0002-3666-6264, Duncan, E. et al. (5 more authors) (2019) Why is the early intervention development phase for complex health care interventions important? An overview of new guidance. In: Trials. 5th International Clinical Trials Methodology Conference (ICTMC 2019), 06-09 Oct 2019, Brighton, UK. BMC , p. 99.

https://doi.org/10.1186/s13063-019-3688-6

Trials 2019, **20**(Suppl 1):579
https://doi.org/10.1186/s13063-019-3688-6

Trials

MEETING ABSTRACTS Open Access

Meeting abstracts from the 5th International Clinical Trials Methodology Conference (ICTMC 2019)

Brighton, UK. 06-09 October 2019

Published: 22 October 2019

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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.

P-3
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

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- O3 Development of a complex intervention to support informed decision-making by family members of adults who lack capacity to consent to trials

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Trials 2019, 20(Suppl 1):PS2C

Introduction: Despite an ageing population and rising prevalence of conditions associated with cognitive impairments, adults who lack capacity to consent are under-represented in research. Trials involving adults who lack capacity raise a number of ethical and practical challenges. Participants who are unable to consent require a family member to act as a proxy decision-maker, however, families can experience an emotional and decisional burden as a result. Despite numerous innovations to improve informed consent processes, there are no interventions for proxy decision-makers. We have developed a decision support tool which aims to support families making decisions about research participation on behalf of an adult who lacks capacity to consent.
Methods: The intervention was developed using the MRC guidance for the development of complex interventions, which recommends a phased approach using available evidence and theoretical principles. The intervention was informed by a systematic review, analysis of existing information provision, qualitative interviews with families who had acted as proxies, and the development of a theoretical framework. The intervention was iteratively developed in conjunction with lay advisors and relevant stakeholders.
Results: Utilising our previous research findings, and applying decision-support development frameworks, we identified the complex intervention components. We developed a decision-support tool which includes information about the proxy's role and the basis for their decision, and uses values clarification and decision-support methods. This is supported by a brief training intervention for the researcher/clinician seeking consent. We conducted acceptability testing with a group of stakeholders which found high levels of acceptability.
Discussion: Ensuring the inclusion of under-represented or vulnerable groups in randomised trials is a priority area. A novel intervention has been developed to support families making proxy decisions about research. The decision-support tool is acceptable to users but requires feasibility testing and establishment of outcome measures prior to any future evaluation of its effectiveness.

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- O4 Why is the early intervention development phase for complex health care interventions important? An overview of new guidance

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Trials 2019, 20(Suppl 1):PS2C

Introduction: Good research ideas often do not produce the anticipated results.[1] It is unknown which intervention development processes lead to real world impact on health outcomes as they are seldom published. Is this a missed opportunity for learning? Could there be avoidable waste? The UK Medical Research Council and National Institute of Health Research funded INDEX study aimed to produce guidance for researchers on how to develop and report complex interventions to improve health or health care outcomes.
Methods: Evidence was triangulated from: two systematic reviews, qualitative interviews and e-Delphi studies, guided by two international stakeholder workshops. Systematic reviews of i) published methodological approaches to intervention development ii) international primary research studies reporting intervention development, published in 2015-16, to identify and categorise practices. In parallel, qualitative interviews with a diverse sample of developers (clinicians, academics, social scientists) and wider stakeholders (public representatives, funders, journal editors) were analysed iteratively, inductively and thematically. Data triangulation generated 85 items for two e-Delphis with i) experts in intervention development, ii) wider stakeholders, to measure consensus and explore reasons for divergence. All data fed into a logic model and final guidance on intervention development and reporting.
Results: An overview of the guidance will be presented. Key principles include: iterative cycles of development with stakeholder input at each cycle; integrate creativity with scientific methods; be open to failure, change, and consider unintended consequences; look ahead to future evaluation and real-world implementation. Novel qualitative insights include: ways to meld the art and the science of design; the meanings and drivers of "success" and understanding divergence of opinion.
Conclusions: The guidance provides a comprehensive tool for consideration when undertaking intervention development. Reporting intervention development processes will promote transparency so that in future researchers can link early design decisions to trial outcomes.

Reference

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PS2C

- O5 ORRCA and ORRCA2: A large-scale, international, collaboration to map recruitment and retention literature

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Introduction: Addressing recruitment and retention challenges in trials are important priorities for methodological research, but navigating this growing literature is difficult and time consuming. In 2016, ORRCA (www.orrca.org.uk) launched a free, online, searchable, database of recruitment research that is currently being updated with recent publications and extended to include retention research (ORRCA2). We report the latest results including a mapping exercise of trial recruitment and retention literature, assessment of the database impact and lessons learnt from conducting an international, collaborative, methodology project.
Methods: Search strategies from relevant Cochrane reviews were tailored to the trial recruitment and retention objectives and to the databases: MEDLINE(Ovid), WoS, Scopus, CINAHL, PyscINFO, and the Cochrane Library. An international team of reviewers were trained and quality assurance approaches introduced. Following abstract screening, full texts were retrieved for potentially eligible articles. Studies evaluating or reporting recruitment or retention strategies and case reports were included. Eligible articles are being mapped against an agreed framework of recruitment or retention domains and categorised by evidence type (e.g. randomised or non-randomised evaluations, studies without evaluation).
Results: 68,900 abstracts and 6,028 full texts have previously been reviewed for ORRCA, identifying 3,555 eligible articles. Screening of an additional 14,465 abstracts for ORRCA and 69,740 abstracts for ORRCA2 by 31 reviewers from six countries is nearly complete. Predicted number of articles for full text review are 860 and 3,600