
Proceedings Paper:
Thompson, B., Mountain, G., Thomas, B. et al. (2 more authors) (2019) An exploratory study of the limitations of outcome measures used in a randomised controlled trial of a complex intervention in dementia. In: Trials. 5th International Clinical Trials Methodology Conference (ICTMC 2019), 06-09 Oct 2019, Brighton, UK. BioMed Central , p. 118.

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

PS5D

- O3 Participating in core outcome set development via Delphi surveys: Qualitative interviews from the EPITOME study provide pointers to inform guidance

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Trials 2019, 20(Suppl 1):PS5D

Introduction: Core outcome sets (COS) represent the minimum outcomes that should be measured and reported in all clinical trials in a specific condition. Input from patients in COS development, and subsequent uptake of COS, will ensure that future studies provide users of research with relevant knowledge regarding interventions. A 2017 survey found that Delphi surveys are being utilised in 89% of ongoing COS with patient participants. It is unclear how patients experience Delphi surveys as part of COS development and whether these methods are suitable for facilitating patient participation. The objective of this study was to explore participants views of the Delphi survey used for COS development.
Methods: Patients and health professionals who participated in a Delphi survey as part of a COS study took part in semi-structured qualitative interviews which explored participants' understanding of COS and their experiences of the Delphi survey. Analysis was interpretative and thematic.
Results: Twenty-four participants from 7 COS studies were interviewed. They varied in how accurately and fully they understood the purpose of COS and the Delphi survey, which influenced their participatory experience. They also differed in how easily they interpreted and subsequently used the written guidance provided to COS participants. Some participants wanted guidance regarding whose perspective to take into account when scoring outcomes and on how to apply the scoring system. Participants' motivation for taking part included the international and expert consensus aspects of the Delphi survey. A small number of participants raised the positive and negative emotional impact of participation when reviewing outcomes and stakeholder feedback.
Discussion: The findings identify ways of improving information for COS Delphi participants to enhance their experience of participation and make the process more meaningful for them.

PS5D

- O4 The impact of patient-reported outcome (PRO) data from clinical trials: a systematic review and critical analysis

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Trials 2019, 20(Suppl 1):PS5D

Background: Patient-reported outcomes (PROs) are commonly collected in clinical trials and should provide impactful evidence on the effect of interventions on patient symptoms and quality of life. However, the different types of research impact associated with PRO trial results, appropriate impact metrics and barriers and facilitators are not well defined. Objectives: i) to determine the range of potential impacts from PRO trial data, identify potential PRO impact metrics and identify barriers/facilitators to maximising PRO impact; and ii) to examine real-world evidence of PRO impact based on Research Excellence Framework (REF) 2014 impact case studies.
Methods: Two independent investigators searched MEDLINE, EMBASE, CINAHL+, HMIC databases from inception until December 2018. Articles were eligible if they discussed research impact in the context of PRO trial data. In addition, the REF 2014 database was systematically searched for case studies incorporating a trial in which PRO data were collected.
Results: Nine types of PRO trial impact were identified; the most frequent of which centred on PRO data informing clinical decision-making. The included publications identified several barriers and facilitators centred around PRO trial design, conduct, analysis and reporting. Twelve (17%) REF case studies outlined demonstrable PRO trial impact; including changes to international and national guidelines, influencing cost-effectiveness analysis and contributing to drug approvals.
Conclusions: PRO trial data may potentially lead to a range of impacts and benefits for patients and society, which can be measured through impact metrics. However, in practice, there is relatively limited evidence demonstrating directly attributable real world PRO-related research impact. In part, this is due to the wider challenges of measuring the impact of research and PRO-specific issues around design, conduct, analysis and reporting. Adherence to existing international guidelines is essential to maximise the use of PRO trial data, facilitate impact and minimise research waste.

PS5D

- O5 An exploratory study of the limitations of outcome measures used in a randomised controlled trial of a complex intervention in dementia

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Trials 2019, 20(Suppl 1):PS5D

Introduction: Dementia research uses multiple measures due to the complexity of the condition. Limited dementia-specific scales exist and generic measures are used in their absence. Problems such as the acceptability of responses and respondent fatigue, as well as the use of retrospective recall in a population with recall difficulties are challenges to effective outcome assessment in dementia research.
Aims: To explore the limitations of the outcome measures used in a randomised controlled trial of a complex intervention for persons with early stages of dementia.
Objectives
-Use retrospective analysis of study data and outcome assessor comments recorded during data collection to identify potentially problematic items or scales and explore participant difficulties in completing the outcome measures.
-To report on the effectiveness of the measures used and make recommendations for future dementia measure development.
Setting: 'Journeying through Dementia' is a randomised controlled trial of a community-based self-management intervention for people with early stages of dementia and their carers. 480 people with dementia took part in the trial, and outcome measures were collected face-to-face at baseline, 8-, and 12-month intervals. We selected dementia specific outcome measures based upon recommendations for research across Europe and used general measures where dementia-specific scales were not available.
Methods: A retrospective secondary analysis of 8-month follow up data from the trial. Quantitative analysis of missed item responses, missed scales and drop-out points identified potentially problematic items and measures. A narrative review of comments made by outcome assessors explored why participants had trouble in responding to outcome measures.
Timing of Potential Results: Potential results will be available in July 2019.
Potential Relevance and Impact: We report on the problems experienced using outcome measures in a large scale RCT for dementia. Learning from the Journeying through Dementia trial may guide future trial conduct and outcome measure development.