Proceedings Paper:
Bradburn, M., Lee, E. orcid.org/0000-0003-4529-7410, White, D. et al. (2 more authors) (2019) Do RCTs reflect patient populations and does it matter? Considerations and a case study. In: Trials. 5th International Clinical Trials Methodology Conference (ICTMC 2019), 06-09 Oct 2019, Brighton, UK. BioMed Central , p. 124.

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

P-1
Abstract omitted

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

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

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

PS7A

- O2 Using systematic data categorisation to quantify the types of data collected in clinical trials

Evelyn Crowley[2], Gordon Fernie[1], Katie Banister[3], Suzanne Breeman[1], Anne Duncan[1], Lynda Constable[1], Adel El Feky[3], Heidi Gardner[3], Kirsteen Goodman[4], Doris Lanz[5], Alison Mcdonald[1], Emma Ogburn[6], Natasha Stevens[7], Marie Valente[8], Shaun Treweek[3]
[1]Centre for Healthcare Randomised Trials, Health Services Research Unit, University of Aberdeen, Aberdeen, United Kingdom; [2]HRB Clinical Research Facility, University College Cork, Cork, Republic of Ireland; [3]Health Services Research Unit, University of Aberdeen, Aberdeen, United Kingdom; [4]NMAHP Research Unit, Glasgow Caledonian University, Glasgow, United Kingdom; [5]Centre for Primary Care and Public Health, Barts and the London School of Medicine and Dentistry, Queen Mary University Of London, London, United Kingdom; [6]Primary Care Clinical Trials Unit, University of Oxford, Oxford, United Kingdom; [7]Queen Mary University Of London, London, United Kingdom; [8]Birmingham Clinical Trials Unit, University of Birmingham, Birmingham, United Kingdom
Trials 2019, **20(Suppl 1):**PS7A

Introduction: Data collection consumes a large proportion of trial resources. Each data item requires time and effort for collection, processing and quality control procedures. Generally speaking, more data equals a heavier burden for trial staff and participants. It also increases the cost of the trial. Data is generally collected for 3 broad reasons:
•To answer the main research question (a primary outcome is specified and drives sample size calculations).
•Secondary outcomes to supplement the primary outcome.
•Additional data to monitor safety, maintain quality and for regulatory and data management needs.
Here we report the results of a collaborative Trial Forge project which measured the proportion of data fitting these three broad categories, across 18 trials run from 5 institutions in Ireland and the UK.
Methods: We developed a standard operating procedure to categorise data. We categorised all variables collected on trial data collection forms from 18, mainly publically-funded Randomised Controlled Trials, including clinical trials of an investigational medicinal product and surgical trials. Categorisation was done independently in pairs: one person having in-depth knowledge of the trial, the other independent of the trial. Disagreement was resolved through reference to the trial protocol and discussion, with the project team being consulted if necessary.
Results: Primary outcome data accounted for 11.2% (mean) and 5% (median) of all data items collected. Secondary outcomes constituted a mean of 42.5% (median: 39.9%) of data items. Non-outcome data represented a mean of 36.5% (median: 32.4%) of data items collected.
Discussion: Our study highlights the proportion of data collected to answer the main research question is minimal in comparison with other data collected, and that much of this is non-outcome data. We discuss implications including whether such data collection is excessive or has detrimental effects on a trial.

PS7A

- O3 Do RCTs reflect patient populations and does it matter? Considerations and a case study

Mike Bradburn[1], Ellen Lee[1], David White[1], Daniel Hind[1], Simon Heller[2]
[1]Clinical Trials Research Unit, University Of Sheffield, Sheffield, United Kingdom; [2]Department of Oncology and Metabolism, University of Sheffield, Sheffield, United Kingdom
Trials 2019, **20(Suppl 1):**PS7A

Introduction: RCTs have been criticised for lacking external validity. A sizeable body of meta-epidemiological evidence has shown RCT participants can often differ from wider patient populations, either through entry criteria restrictions or through selective uptake ("volunteer bias"). RCTs may struggle to convince a clinical community of their merit if they do not represent the patients they themselves see. We assessed whether a trial in type I diabetes mellitus (T1DM) mirrored the wider patient population, and applied sample-weighting methods to derive a treatment effect projected onto a more representative T1DM population. We describe how to apply these methods, their limitations, and their impact on our trial's findings.
Methods: The REPOSE (Relative Effectiveness of insulin Pump Over MDI and Structured Education) trial was nested within a large UK-based cohort of patients with T1DM. The database captured detailed demographic, clinical and QoL data for T1DM patients undergoing structured diabetes-specific education. We firstly assessed whether our RCT participants were comparable to this cohort using propensity score modelling. Following this we re-weighted the trial population to better match the wider cohort, and re-estimated the treatment effect from this.
Results: Our trial patients differed from those of the cohort in regards to sex, weight, HbA1c and also QoL and satisfaction with current treatment. Nevertheless, the treatment effects derived from alternative model weightings were similar to that of the original RCT.
Discussion: We found our RCT recruited a non-random set of participants but that the main results were unaffected by re-weighting. We advocate researchers to take steps to address criticisms of generalisability, including these analyses. Doing so is nevertheless problematic: external data is difficult to obtain and may contain information is too limited to make informative adjustments. Analyses can be susceptible to model misspecification, especially in smaller trials.

PS7A

- O4

Abstract omitted

PS7A

- O5 Rewards and challenges of undertaking health-related research within the UK Police setting

Alison Booth[1], Catriona McDaid[1], Arabella Scantlebury[1], Adwoa Parker[1], Caroline Fairhurst[1], Julie Parkes[2], Sara Morgan[2], Benjamin Taylor[3], Caroline Chapman[3], Catherine Hewitt[1], David Torgerson[1]
[1]University of York, York, United Kingdom; [2]University of Southampton, Southampton, United Kingdom; [3]Hampshire Constabulary, Southampton, United Kingdom
Trials 2019, **20(Suppl 1):**PS7A

Introduction: York Trials Unit (YTU) has gained valuable experience through working with the Police. We present here key learning outcomes from a co-production project in mental health, attempts to set up a trial related to speeding offences and a trial of a youth offending intervention.
Methods: YTU's experience comes from:
Co-production with North Yorkshire Police (NYP) of a series of systematic reviews to improve the evidence base related to mental health, and an RCT of training for police officers to improve their handling of situations where members of the public they are in contact with are experiencing mental ill health.
Developing a proposal for a trial with the Traffic division of NYP to improve the response rate to conditional offers for speeding offences.
An on-going NIHR funded project with the University of Southampton and Hampshire Constabulary to undertake an RCT, with economic and qualitative evaluation of Gateway, an out-of-court, community-based intervention aimed at improving life chances for 18-24 year old offenders and reducing reoffending.
Results: Four systematic reviews were completed and the cluster RCT involving 12 police stations and 249 officers receiving the bespoke training, showed it may have a positive effect on recording of incidents.