designed to be perpetual in that new treatments can continue to be seamlessly added to the trial in the future. In a perpetual platform trial, controlling the family-wise error rate (FWER) leads to a low statistical power, as vanishingly small significance levels must be used for the later hypotheses being tested. An alternative error rate is the false-discovery rate (FDR), which controls the expected proportion of recommended treatments that are actually ineffective. In this work, we apply recent methodological research to show how to control the FDR in the perpetual platform trial setting.
Methods: We investigate various rules for controlling the FDR in perpetual platform trials, and propose a simple modification to the procedures for when there is an upper bound on the number of hypotheses to be tested. The number of ultimately evaluated treatment arms and proportion of treatments that are truly effective are varied.
Results: We show that the FDR can be controlled in perpetual platform trials, even under the dependence induced by a common control arm. Furthermore, controlling the FDR in perpetual platform trials results in a uniformly higher power compared with controlling the FWER.
Discussion: In perpetual platform trial settings, we recommend that sponsors and trialists consider controlling the FDR

P-200

Options and challenges of analysing data from recruitment intervention studies A lesson from MRC START Hi-Light data analysis

Wei Tan, Trish Hepburn
University of Nottingham, nottingham, United Kingdom
Trials 2019, **20(Suppl 1):**P-200

Background: Achieving high participation in RCTs has traditionally been difficult and there is a need to develop and test interventions to improve recruitment. Embedded randomised trials of recruitment interventions within in ongoing host RCTs have been growing recently.
MRC START Hi-Light is embedded within the H-Light study to test whether addition of multimedia resource (MMI) impacts on rate of recruitment, in comparison with standard host trial website.
Methods: The primary outcome was the proportion of patients randomised to the main trial, which was calculated and compared between the two arms. Various statistical methods were tested to find the most appropriate model to analyse the data and answer the research question.
Results: Linear model assumptions were violated for the original and the log-transformed data.
Negative binomial model was then tested to compare mean number of patients recruited, the assumptions of which were again not met. A zero inflated negative binomial was proposed however due to the single source of zero value in this study this model was deemed inappropriate.
As around 80% recruitment units recruited either 0 or 1 patient, we estimated the effect of MMI website using a binary outcome variable, where 0=recruited none and 1=recruited at least 1. Results from binary measure (risk difference = -1.6%, 95% CI -18.6% to 15.4%) indicate no evidence of effect of MMI. Results from other methods were not presented but in support of the estimates.
Conclusion : Recruitment intervention studies may result in data very similar to this study where the choice of primary analysis model must be carefully scrutinized. In this study various methods have been tested to best analyse the data which all support no evidence of intervention effect in improving recruitment. Better planning on the most appropriate analysis model is recommended to produce more reliable and robust results.

P-201

Effect-based traffic light progression criteria for pilot studies

Gareth Mccray, Martyn Lewis, Kieran Bromley, Gillian Lancaster
Keele University, United Kingdom
Trials 2019, **20(Suppl 1):**P-201

Introduction:
In the CONSORT guidelines for pilot and feasibility trials, formal hypothesis testing of effectiveness or efficacy is not recommended as it is likely that a study will have insufficient power to supply robust evidence (and this is the aim of the main trial). However, particularly for larger pilot studies and/or studies with a large assumed MCID/effect size, the results of a pilot may carry valuable information about the likely outcome of any follow-up trial. This presentation suggests a method that uses the pilot sample size and observed effect size to provide a traffic-light indication of the likely fruitfulness or futility of any follow-on trial.
Methods:
The traffic-light designation is based on the simulated sampling distributions of the effect size under both null and specified alternative hypotheses. The designation of "green", "amber", or "red" depends on the likelihood of the observed effect size given the sampling distributions. At smaller sample/effect sizes, an "amber" is most probable, but as sample/effect size increase, either "red" or "green" designations increase in probability, reflecting the additional information about the true effect from the data.
For "red" we recommend not to go to a full trial, for "amber" we recommend focusing more on the process outcomes to inform progression, while for "green" we recommend progression and there may be less need to focus on other process outcomes.
Results:
Look-up tables of critical values are presented for the cases of a difference between two independent means and two independent proportions (exact values). Worked examples from authentic studies illustrate the utility of the methodology.
Discussion:
While we strongly discourage potential efficacy/effectiveness being the primary feasibility outcome considered in a pilot study, we do however think that it warrants consideration in the 'proof of efficacy' debate and we present a reasoned method of doing so.

P-202

A simulation study to compare longitudinal methods for the analysis of randomised trials and the implications for sample size calculation

Bethan Copsey, Susan J Dutton, Ray Fitzpatrick, Sarah E Lamb, Jonathan A Cook
University of Oxford, United Kingdom
Trials 2019, **20(Suppl 1):**P-202

Introduction: The majority of randomised trials collect outcome data at multiple follow-up time points. Reviews have shown that analysis methods vary across different trials, such as mixed effects methods or repeated single time point analyses. The use of these different methods can have implications for the credibility of trial results, impacting on the type I error, level of power and bias of the treatment effect estimate.
This simulation study aims to compare the performance of different methods to analyse longitudinal data from a randomised trial.
Methods: Simulated datasets were generated for 240 different scenarios with different sample sizes (100, 200, 400, 600, 800), numbers of follow-up time points (2, 3, 4, 5), maximum level of treatment effect (0, 4, 8, 12) and different patterns of treatment effect. For each scenario, 1600 datasets were produced. Distributional parameters were based on the WOMAC measure and informed by a previous randomised trial of medications for knee osteoarthritis.

The statistical methods used to analyse each of the datasets were:
1.Repeated analysis of covariance (ANCOVA) at each follow-up time point.
2.Generalised estimating equations, and
3.Mixed effects.
The performance measures used to compare the methods were convergence, power, type I error, and coverage. Stata IC 14 software and the University of Oxford Advanced Research Computing (ARC) facility are being used to conduct this work.
Timing of Potential Results: It is anticipated that this study will be completed during the summer of 2019.
Potential Relevance & Impact: The results will provide evidence to inform the choice of longitudinal analysis methods in randomised trials. This could allow trialists to select the methods that will provide the highest statistical power for the anticipated pattern of treatment effect and could result in reducing the required sample size whilst maintaining adequate statistical power.

P-203

Allowance for learning and clustering effects in the design and analysis of multicentre randomised trials: current practice and experiences

Elizabeth J Conroy[1], Jane M Blazeby[2], Girvan Burnside[1], Jonathan A Cook[3], Carrol Gamble[1,4]
[1]Department of Biostatistics, University of Liverpool, a member of Liverpool Health Partners, Liverpool, United Kingdom; [2]Centre for Surgical Research, Population Health Sciences, University of Bristol, Bristol, United Kingdom; [3]Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom; [4]North West Hub for Trials Methodology Research, University of Liverpool, Liverpool, United Kingdom
Trials 2019, **20(Suppl 1):**P-203

Introduction: Patient outcomes can depend on the treating centre, or health professional, delivering the intervention. Differences in treatment delivery can be more prominent in trials investigating a complex intervention, such as surgery. Considering any potential difference in delivery at trial outset will ensure that any adjustments, as appropriate, can be made. The objective of this work was to establish current practice for the allowance of learning and clustering effects in the design and analysis of randomised multicentre trials.
Methods: A ten question survey was developed by the study team comprising open and closed questions that drew upon quotes from existing guidelines, references to relevant publications, and example trial scenarios. All registered UK Clinical Research Collaborative registered Clinical Trials Units were invited to participate.
Results: Completed surveys were obtained from 44 of 50 registered Units. Adjusting for learning by design through defining a minimum level of expertise for treatment provider was common (89%), although one third of units also had experience of expertise based designs. Managing clustering by design through stratification by centre was universally most common across the various trial types presented, and by treatment provider less so. Analysis of learning was rarely performed for the main analysis (n=1), although many units reported approaches to complement such analyses, such as sensitivity analyses. The majority of responders had indicated experience in adjusting during analysis for clustering, by centre or treatment provider, although approaches to doing so varied. Responders provided insight behind the approaches used within their unit and reasons for, or against, alternative approaches.
Discussion: This survey identifies widespread awareness of the potential methodological challenges associated with the design and analysis of multicentre trials, although approaches used and opinions on these vary.

P-204

An Independent Patient Data Meta Analysis to compare adjuvant therapies in patients suffering with Pancreatic Cancer

Rebecca Griffin[1], Eftychia-Eirini Psarelli[1], Paula Ghaneh[1], John Neoptolemos[2], Richard Jackson[1]
[1]Liverpool Clinical Trials Unit, Liverpool University, Liverpool, United Kingdom; [2]University of Heidelberg, Heidelberg, Germany
Trials 2019, **20(Suppl 1):**P-204

Introduction: Pancreatic Cancer is a disease with particularly poor prognosis with approximately 5% of patients surviving 5 years or more. Only 20% of patients are eligible for surgery and adjuvant therapy, but for those who do, prognosis improves with reported 5 year survival rates of 30% or more. A number of trials have explored the use of radiotherapy and chemotherapy although the best approach is still a matter of much discussion.
Methods: An independent patient data meta analysis of randomised controlled trials was performed using 3553 patients from 10 randomised controlled trials. Data are analysed using a Hierarchical Bayesian Network Meta Analysis incorporating frailty terms for patient nationality, modelling the baseline hazard function using a Piecewise Exponential Model and adjusting for trials with more than two therapies evaluated. Sub groups analysis are performed on consistent prognostic factors.
Results: An established network allows for comparisons of radiotherapy vs Chemotherapy Vs Observation only using direct and indirect evidence. Furthermore, networks allow direct and indirect comparisons of various types of chemotherapy. Subgroup analysis shows that the effect of therapy does depend on reported prognostic factors.
Discussion: IPD meta analysis improves the knowledge base of the effect of adjuvant therapies for resectable pancreatic cancer and identifies consistent prognostic factors which can help direct treatment decisions.

P-205

Joint Modelling for longitudinal measures of marker CA19-9 and survival data in patients with pancreatic cancer

Silvia Cicconi[1], Paula Ghaneh[1], John Neoptolemos[2], Ruwanthi Kolamunnage-Dona[1], Richard Jackson[1]
[1]University Of Liverpool, Liverpool, United Kingdom; [2]University of Heidelberg, Heidelberg, Germany
Trials 2019, **20(Suppl 1):**P-205

Introduction: Diagnosis of pancreatic cancer is increasing worldwide but its prognosis remain extremely poor even after resection. The ESPAC-4 trial showed that the adjuvant combination of gemcitabine and capecitabine improves overall survival compared to gemcitabine alone after resection for pancreatic ductal adenocarcinoma. CA19-9 concentration is a post-operatively established prognostic marker but little is known of its role in providing predictions of survival probabilities over time.
Methods: The relationship between longitudinal and time-to-event data was explored on 431 patients from the ESPAC-4 trial by means of joint modelling technique. A Cox proportional hazard regression was used for modelling survival data while linear mixed model was applied for CA19-9 follow-up measurements, incorporating random intercept and slope components.
Results: Joint modelling describes the evolution of the CA19-9 marker in time and provides an estimate of its association with time to death. Results show that CA19-9 decrease after surgery, reaching a plateau for the following months. However, the marker concentration spikes again with proximity to death.
Discussion: Joint modelling analysis improves the understanding of the latent association between CA19-9 marker and survival outcome,