Methods: A sequential multi-step screening process was implemented: i) web-based pre-screening, ii) laboratory screening through a network of third-party pathology centres, and iii) final on-site screening. Online data collection, computer-driven eligibility checking, and automated, email-based communication with prospective participants were used. Participant screening status, and associated costs and resource use were centrally tracked.
Results: Of 19,022 screened participants, 1,007 were randomised. Nearly all (95%) participants chose online over phone-based pre-screening. At peak, 1,403 participants were pre-screened in a single day. On average, 11 staff hours were required for each participant randomised. Screening costs, including both direct and staffing costs, were AUD$1,420,909 (£782,228) in total (AUD$75 (£41) per subject screened and AUD$1,411 (£777) per participant randomised).
Discussion: A screening process incorporating centralised, online and automated elements achieved high-volume, low-cost participant screening. Compared to similar, previous trials, screening savings are conservatively estimated at AUD$5,899,126 (£3,247,543); equivalent to 76% of the entire T4DM study budget. Our approach could be adapted for use in other trials seeking to screen large numbers of participants.

PS3B
- O1
Abstract omitted

PS3B
- O2 Optimising the design and delivery of placebo surgical interventions in randomised controlled trials: The DITTO framework

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Trials 2019, **20(Suppl 1):**PS3B

Introduction: Designing and delivering placebo surgical interventions for use in randomised controlled trials (RCTs) is complex. An in-depth understanding of the constituent components of the treatment intervention (to ascertain what should, and should not, be delivered as part of the placebo intervention) is needed. Furthermore, assessment of potential risk to patients and utilisation of strategies to ensure the placebo effectively mimics the treatment are required. To date no guidance exists for the design of placebo surgical interventions.
This study aimed to develop a framework to optimise the design and delivery of placebo interventions in surgical RCTs.
Methods: A preliminary framework was developed by expanding the scope of an existing typology that facilitates the deconstruction of surgical interventions into their constituent components. Then, strategies to optimise placebo interventions were identified from published RCTs. Finally, the framework was refined after consultation with key stakeholders in surgical trial methodology, medical ethics and consensus methods.
Results: The resultant DITTO framework consists of five stages: Stage 1 - Deconstruct treatment intervention to produce a comprehensive list of components and co-interventions; Stage 2 - Identify critical element believed to provide therapeutic benefit; Stage 3 - Take out critical element; Stage 4 - Think risk, feasibility, and role of placebo in trial when considering inclusion of remaining intervention components; and Stage 5 - Optimise placebo and ensure effective blinding of trial persons, e.g. by use of auditory masking.
Discussion: The DITTO framework provides a structure for the design of placebo surgical interventions. It facilitates in-depth analysis of the treatment intervention. It also outlines key considerations regarding the composition of the placebo intervention, including potential risk to patients and the use of placebo optimisation strategies.

PS3B
- O3 Clinical trial simulation and value of information to optimise design of clinical trials from a pharmaceutical industry perspective

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Trials 2019, **20(Suppl 1):**PS3B

Introduction: The optimal design for a clinical trial using value of information (VoI) methods is the point at which it becomes more costly to collect additional data than the value gained from that data. This requires prior distributions for trial outcomes, either based on past trials or expert opinion. However, a proposed trial cannot typically be expected to produce data consistent with earlier studies. The aim of this study was to demonstrate the utility of using pharmacometric clinical trial simulation (CTS) to address key limitations of current VoI approaches to phase III clinical trial design using gout treatments as a case study.
Methods: The methods consist of four principal stages: a CTS to predict the distribution of treatment response rates for a given sample size; a payer model that links a rate of treatment response to an estimate of the maximum reimbursement price a payer would be willing to pay to access the drug; a model of the pharmaceutical company return on investment linking drug prices to sales revenue; and an analysis of the sensitivity of the optimal decision to the uncertainty in specific model parameters using expected value of partial perfect information (EVPPI).
Results: The optimal sample size for a single trial comparing febuxostat 80 mg and allopurinol 300 mg once daily was estimated to 500 patients per arm, given assumptions on the incidence of patients and a minimum launch price. EVPPI for each uncertain model parameters indicated that uncertainty in parameters for drug adherence, rather than drug pharmacology, dominated the uncertainty regarding the optimal sample size decision.
Discussion: Using clinical trial simulation to generate distributions of trial outcomes removes a key limitation of value of information approaches to trial design, the requirement for prior distributions on outcomes, and EVPPI may focus efforts to reduce uncertainty to specific areas.

PS3B
- O4 Two-stage adaptive enrichment designs with time to event data: Point and interval estimation

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Trials 2019, **20(Suppl 1):**PS3B

Introduction: Two-stage adaptive enrichment designs are efficient for trials in stratified medicine. In stage 1 patients are recruited from the full population while in stage 2, recruitment is restricted to a biomarker-driven subgroup that is selected based on the interim analysis of stage 1 data. Confirmatory analysis in the selected subgroup consists of stages 1 and 2 patients. The aim of this work was to develop appropriate point and interval estimators for survival outcomes which are common in oncology, where subgroup analysis is common. Such estimators do not exist.