TMRP PhD Student Cohort

Rapid-fire two minute presentations

Morning Session

Measuring outcomes in eczema clinical trials

Objectives:

- To understand the potential impact of daily / weekly monitoring of symptoms on trial outcomes
- To fill validation gaps in the HOME core outcome set for eczema (long-term control):
  - Develop and validate a single-item instrument for eczema control
  - Explore content validity of RECAP eczema control instrument in young people with eczema
  - Define minimum important change for RECAP

Harmonising Outcome Measures for Eczema (HOME)

NOTTINGHAM CLINICAL TRIALS UNIT

Arabella Baker

"A Core Outcome Set Study - Please Take Part"! (A poem)

HEATHER BARRINGTON

PATIENT AND PUBLIC INVOLVEMENT CO-ORDINATOR, THE COMET INITIATIVE

PHD STUDENT – THE OPERATIC STUDY, UNIVERSITY OF LIVERPOOL

(OPTIMISING PATIENT PARTICIPATION IN CORE OUTCOME SET DEVELOPMENT)


$1.00
It's been a big week for Sports.
Daily News
What's really going on in the sewers.
COS REVOLUTION!
Headlines on Natural Forest Reserve
News Report Released

Randomised trials for developing behaviour change apps

Lauren Bell

My research is looking into RCTs for optimising the time-varying components of a behavior change app.

MRTs involve the repeated randomization of notifications

Randomisation could occur hundreds or thousands of times within patients

Data in the trial evolves as a collection of time-varying treatments, covariates and outcomes.

More details?

Outputs from the PhD include:

1. Bell, L., et al., *Visualizing temporal patterns of engagement with a behavior change app for alcohol reduction.* J Med Internet Res 2020 (to appear) 10.2196/23369.

2. Bell, L., et al., *Notifications to Improve Engagement With an Alcohol Reduction App: Protocol for a Micro-Randomized Trial.* JMIR Res Protoc, 2020. **9**(8): p. e18690.

Please contact me at Lauren.Bell@lshtm.ac.uk if you'd like more details.

Improving representation in trials at the analysis stage

Mike Bradburn, University of Sheffield, November 2020

- Trials are probably not a random subset of the target population
  - ➔ This can cause bias if the treatment effect is heterogeneous
  - ➔ And can cause readers to ignore your findings

- Personalised medicine and greater inclusivity in research are the ideal solutions

- If we have neither, can and should we do something at the analysis stage?

Research questions

- Is it worth doing?
  - Let’s assume yes, even if only for my own self-interest
- Review of methods and how people use them
  - Most attempt to reweight RCT data against a reference population (think electoral polls)
- Practicalities
  - Data
  - Statistical code

MEASURING CHILD DEVELOPMENT IN LOW AND MIDDLE INCOME COUNTRIES

KIERAN BROMLEY, KEELE UNIVERSITY

Background

The early years of a child's life are foundational to their future development

Robust, validated measurement tools are necessary to inform & monitor health and development in LMIC

Previously validated tools exist e.g. the MDAT

Research questions

How can adaptions to the MDAT be accounted for over time? How can this successfully be modelled?

Is the MDAT a multi-dimensional tool?

What external contextual variables are predictive of ECD?

MDAT and the dataset

>200 items spanning 0-7 years

4 domains – gross/fine motor, language & social

>8000 children across the age range

External variables such as gender, weight, height and SES

Statistical Methods

Review of approaches to scoring test data

Create a scoring methodology using Item Response Theory (IRT) to create test scores dependent on item subsets

METHODS OF RANDOMISATION

Cydney Bruce

Project Plan:

1. Review of literature

a) Look at methods used and study characteristics effect on choice of method – compare to previous time point
b) Use journals The Lancet, BMJ, NEJM, JAMA and NIHR HTA Library

2. Review of CTU Practice

Interview CTU staff to:

a) Identify any reasons for randomisation method selection
b) Identify situations when predictability vs balance is more important

3. Method Assessment

a) Develop code to compute methods
b) Develop score to measure effectiveness of method
c) Compare methods looking at balance, predictability and ease of use

4. Recommendations

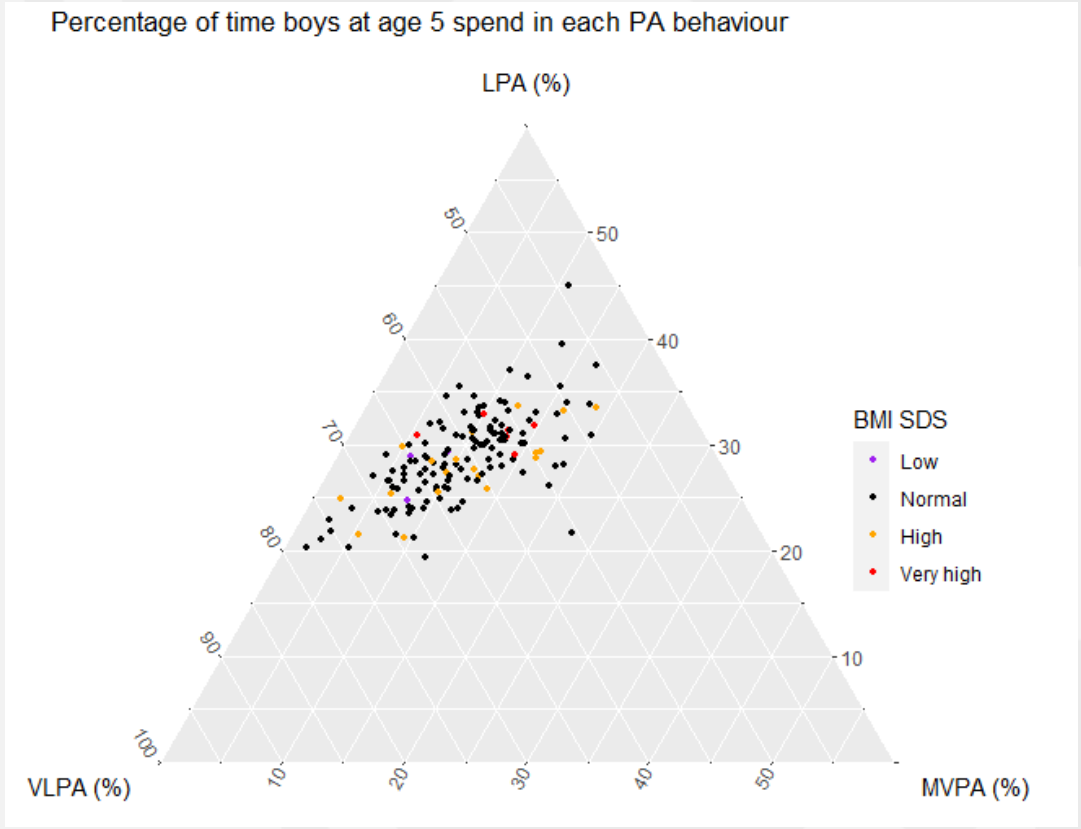
a) Create a Taxonomy of the different randomisation methods and classify situations to best use them
b) Look at the special case of multi-arm trials.

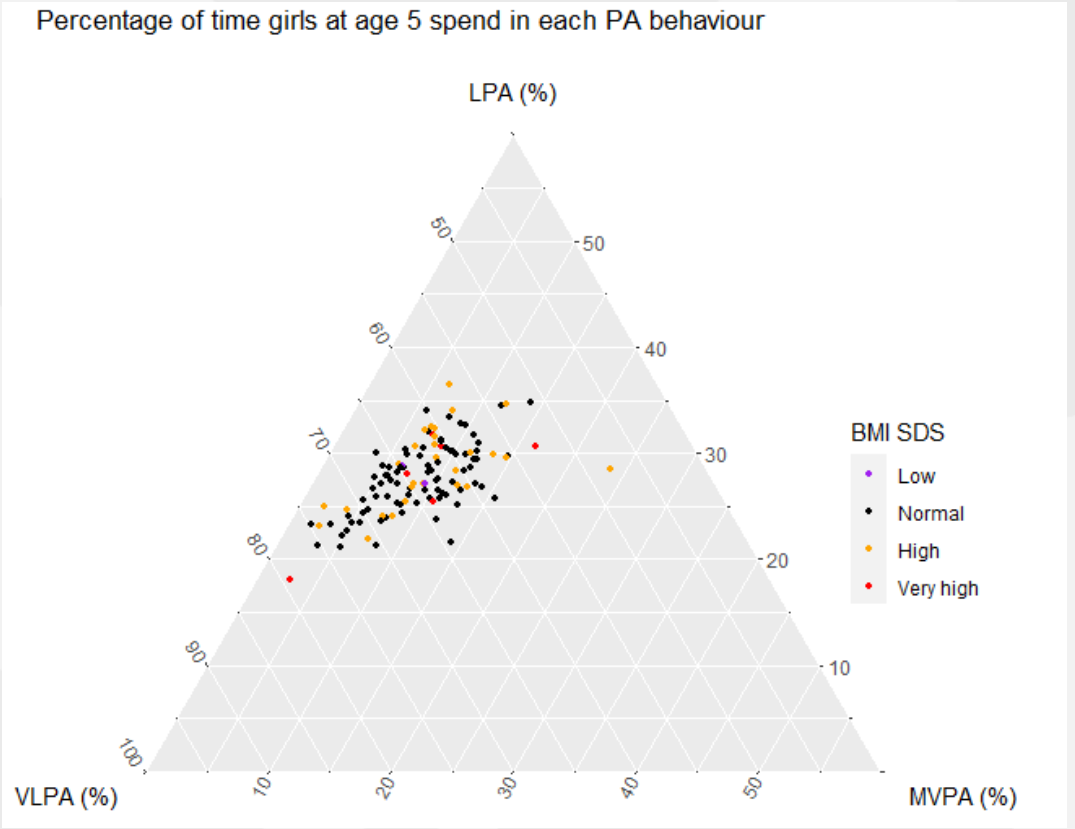
The University of Nottingham

NOTTINGHAM CLINICAL TRIALS UNIT

Improving the efficiency of modelling complex accelerometry data using compositional data analysis

Jade Chynoweth[1], Joanne Hosking[1], Adam Streeter[1], Jonathan Pinkney[1], Siobhan Creanor[1,2]
[1] Faculty of Health, University of Plymouth
[2] College of Medicine and Health, University of Exeter





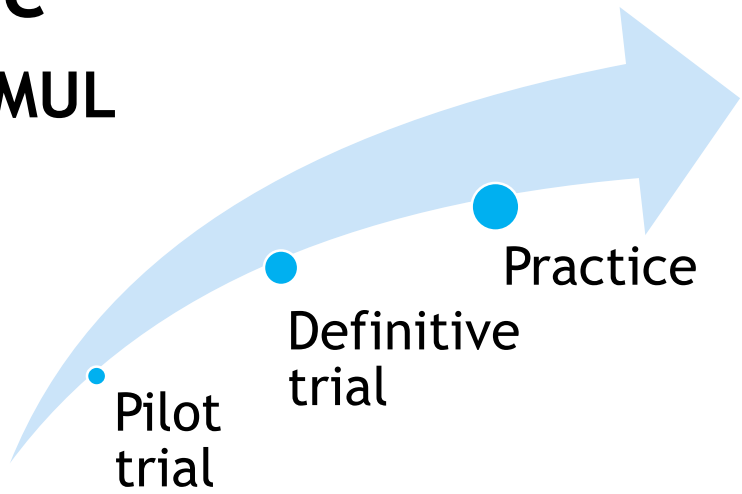
UNIVERSITY OF PLYMOUTH
Peninsula Medical School

Design of external pilot studies, with a focus on sample size

Saskia Eddy, QMUL

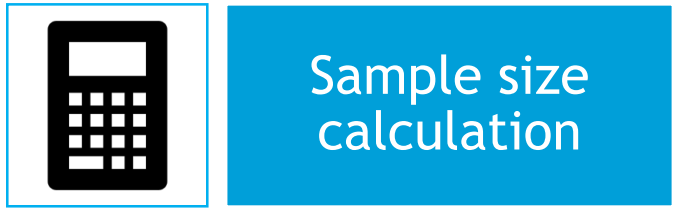
Pilot studies

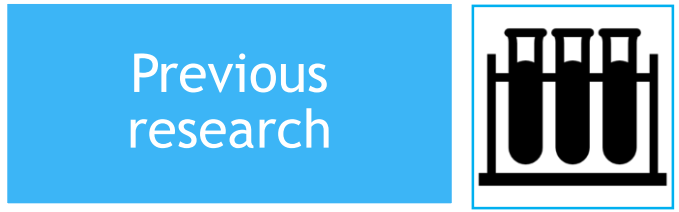
- Smaller studies prior to the definitive trial
- Investigate feasibility



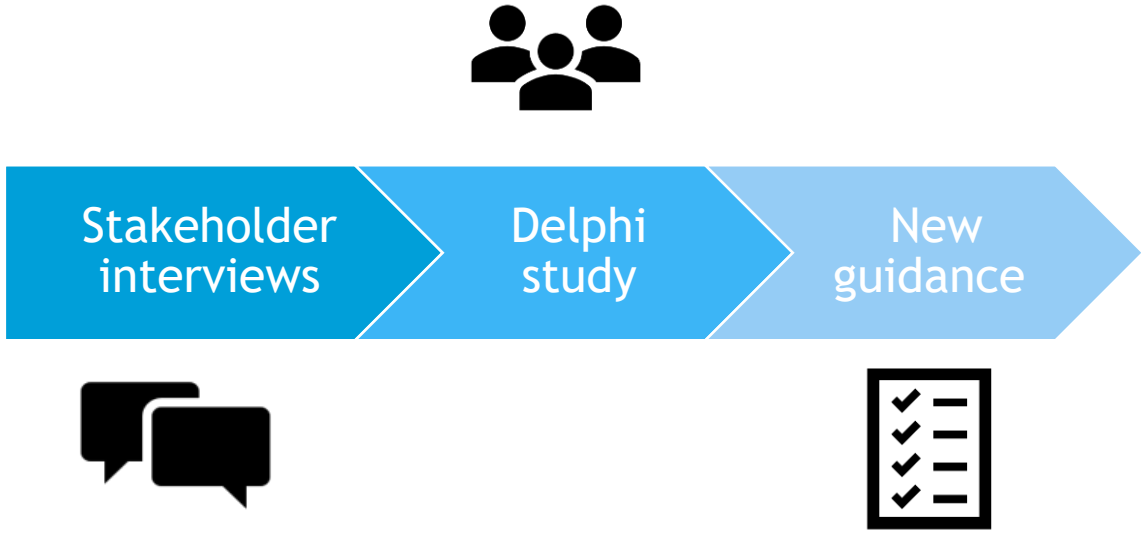
@SaskiaEddy

What sample size justifications are being used?





Future work



Exploring Patient Perspectives of Recruitment in Randomised Controlled Trials (RCTs)

Primary data	Secondary data
• Interviews with patients asked to take part in 3 RCTs • Audio-recordings of recruitment consultations • Linking these data • Thematic analysis	• Qualitative evidence synthesis exploring recruiters' perspectives of recruitment to RCTs • Thematic synthesis approach

University of Liverpool
MRC Hubs for Trials Methodology Research ConDuCT-II Hub
QuinteT Qualitative research Integrated within Trials

Nicola Farrar, University of Bristol
Nicola.Farrar@bristol.ac.uk

University of BRISTOL

MRC Hubs for Trials Methodology Research

ConDuCT-II Hub

1. Review of existing RUMs

2. Review of framing of existing RUM questions

Item identification: Delphi survey

3. Prototype development

7. Patient pilot

ModRUM

Modular Resource-Use Measure

4. Qualitative interviews with health economists

6. Health economist pilot

Kirsty Garfield, Sian Noble, Joanna Thorn, Samantha Husbands, Will Hollingworth

Patient "think-aloud" interviews with retrospective verbal probing

Demonstrate the content validity and acceptability of ModRUM

Data scoring
Comprehension
Retrieval
Judgement
Response
Struggle

Data coding
Key issues
Acceptability

Iterative data collection, analysis and revisions

80% ≠ error or struggle

I am going to include my interactions on my kids' behalf (P13)

It's actually quite stressful, thinking, when somebody is there (P7)

I was expecting it to be quite long, so that was actually quite easy (P7)

Can routinely collected data be used to accurately and completely follow-up participants in large cardiovascular trials?

Charlie Harper (3rd year PT PhD student)

Outcomes being investigated:

- Serious vascular events (i.e. MI, ischaemic stroke, TIA, vascular death, or arterial revascularisation)
- Major bleeding events

(1) Systematic review

(2) Exploratory analyses using the ASCEND trial

- Direct participant agreement
- Randomised comparison using routine data only

(3) Simulation study

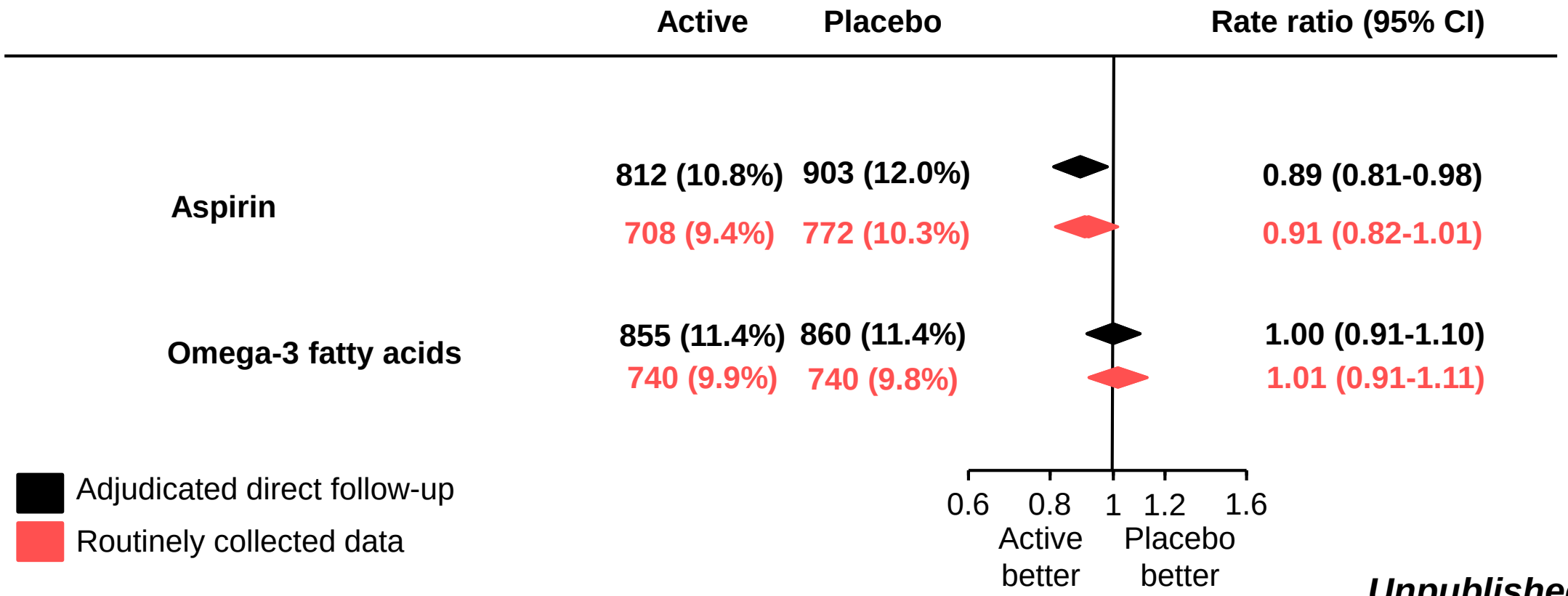
- What is the impact of "imperfect" outcome ascertainment on estimated treatment effects?
    - Primary inputs to be investigated: sensitivity and specificity

Trials Methodology TMRP Research Partnership

MRC Population Health Research Unit

UNIVERSITY OF OXFORD

ASCEND trial: Effect of (a) aspirin vs. placebo, and (b) omega-3 fatty acids vs. placebo on Serious Vascular Events*



Unpublished results

*Serious Vascular Events: non-fatal myocardial infarction, ischaemic stroke, transient ischaemic attack, vascular death (excluding intracranial haemorrhage), or any arterial revascularization. Results presented here differ from the main ASCEND publication (NEJM 2018) because these analyses exclude those participants residing in Scotland.

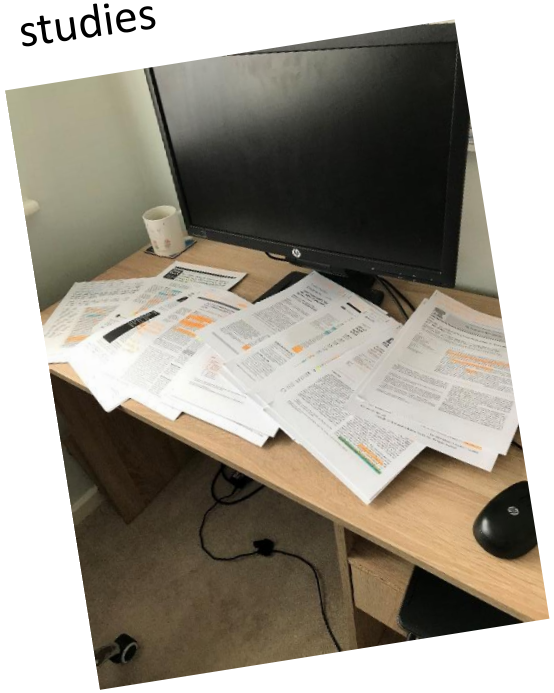
UNIVERSITY OF OXFORD

British Heart Foundation

ASCEND
A Study of Cardiovascular Events iN Diabetes

Methods to assess and improve uptake of core outcome sets

Study 1: Systematic Review of COS uptake studies



Study 2: Impact of trial funders on COS uptake

Study 3: Interviews to explore the barriers and facilitators to COS uptake

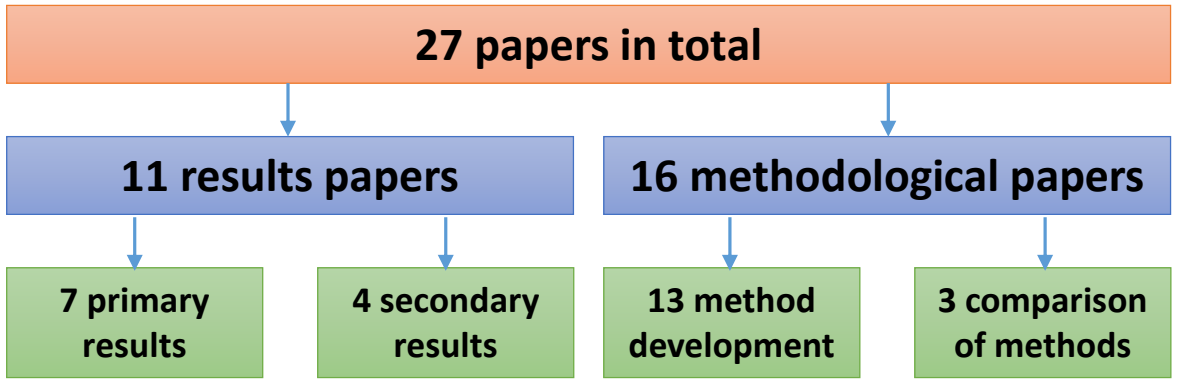
Karen Hughes, University of Liverpool

Supervisors: Professor Paula Williamson, Professor Mike Clarke, Professor Jamie Kirkham, Professor Bridget Young

A Bayesian Approach to the Design and Analysis of Cluster Randomised Controlled Trials

Ben Jones, University of Plymouth

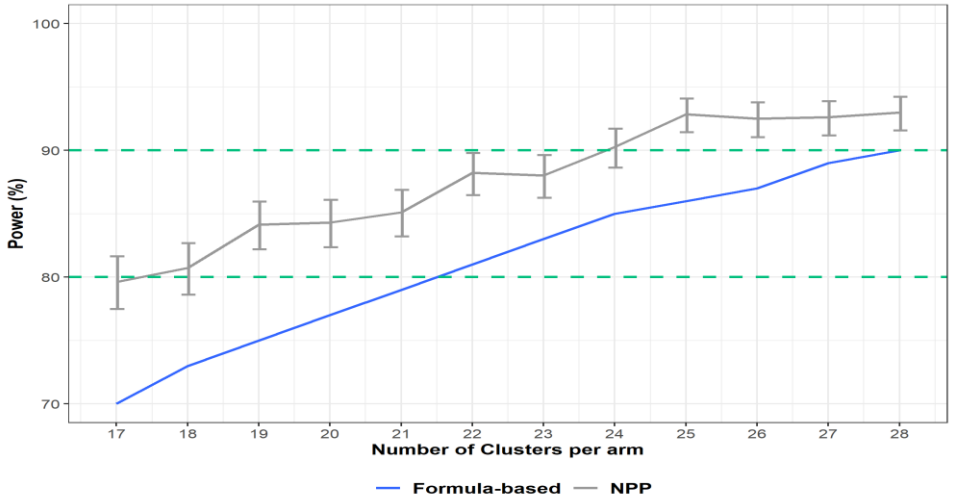
1. Methodological Systematic Review



2. Borrowing Information from Pilot Data using Power Priors

$$Power\ Prior \propto Likelihood(Pilot)^{a_0} \times Prior$$

3. Information Borrowing in Study Design



4. Statistical Software Development

Protocol for a systematic review of validated and non-validated surrogate outcomes

Wang Pok Lo, University of Edinburgh

What is a surrogate?

- A surrogate endpoint is defined as a substitute to a primary endpoint which is expected to predict the result of the intervention.

Why surrogacy?

- Trial takes too long
- Ethical issues

How are surrogate outcomes validated?

- Development of frameworks to determine acceptability levels
- Both statistical evaluation and practical evaluation are important
- Successfully validated outcomes accepted by regulatory authorities

Protocol for a systematic review of validated and non-validated surrogate outcomes

Wang Pok Lo, University of Edinburgh

What are the objectives?

- Review the current status of validated surrogate outcomes
- Identify non-validated outcomes currently in use

Methodology

- Surrogate outcomes listed in the FDA and EMA searched for in literature
- PubMed and Embase as data sources
- Information extracted on how validations were done and metrics used

Investigating the use of pre-specified progression criteria to inform progression from randomised pilot to definitive RCT

Katie Mellor | email: katie.mellor@ndorms.ox.ac.uk | twitter: @katiejmellor

Supervisors: Assoc Prof Sally Hopewell, Assoc Prof Susan Dutton, Prof Sandra Eldridge, Dr Charlotte Albury

Funding: Oxford-Medical Research Council Doctoral Training Partnership

A literature review of existing guidance and recommendations for external randomised pilot trial progression

A methodological review to assess progression criteria application and reporting in external randomised pilot trial and protocol publications

Semi-structured interviews with researchers to understand experiences of applying progression criteria to external randomised pilot trials in practice

Audit of NIHR Research for Patient Benefit funding applications for external randomised pilot trials to understand how progression criteria are proposed in research funding applications

1.UKRI and Mitacs Globalink doctoral exchange scheme funded 12-week internship at McMaster University to review progression criteria specified in ethics committee applications

Follow-up of identified external randomised pilot trials to investigate progression outcomes, reasons for non-progression, and funding outcomes

Optimal study designs following *"Only in Research"* and *"Only with Research"* NICE technology appraisal recommendations

About me

- **Yankier Pijeira Perez**
- Economics Undergraduate degree – University of Havana, Cuba
- HTA Master's degree – University of Glasgow, Scotland
- Registered pharmacy technician (7 years - NHS hospital)
- Current PhD student at Prifysgol Bangor (Bangor University), Wales

About my PhD

- NICE can provide different advice :-
  - Recommend for routine use
  - Recommended *only in research* (OiR)
  - Recommended *only with research* (OwR)
  - Not recommended
- Overall aim is to develop guidance on the optimal methods underpinning research recommendations

Lead supervisor: Professor Dyfrig Hughes; Second-supervisors: Professors Andrea Jorgenssen, Carolyn Young

Experimental chapters

- Systematic review to critically appraise the methods of evidence generated in response to NICE OiR and OwR technology appraisal recommendations
- Developing an analytical framework for estimating clinical and cost-effectiveness from observational data
- Case study of treatments for multiple sclerosis
  - Analysis of cost, utility and effectiveness data from the Trajectories of Outcome in Neurological Conditions (TONiC) study
- Apply framework for the analysis of the data in TONiC

Lukas Staudt, University of Liverpool

Clinical background

THE MEDICAL CONDITION OF OUR STUDY POPULATION

Sciatica, lower back and leg pain due to a herniated disc that presses on the sciatic nerve, affects over 3% of the UK population at any time

In 60-90% of the cases spontaneous regression occurs and symptoms can be treated with conservative methods (physiotherapy, analgesics)

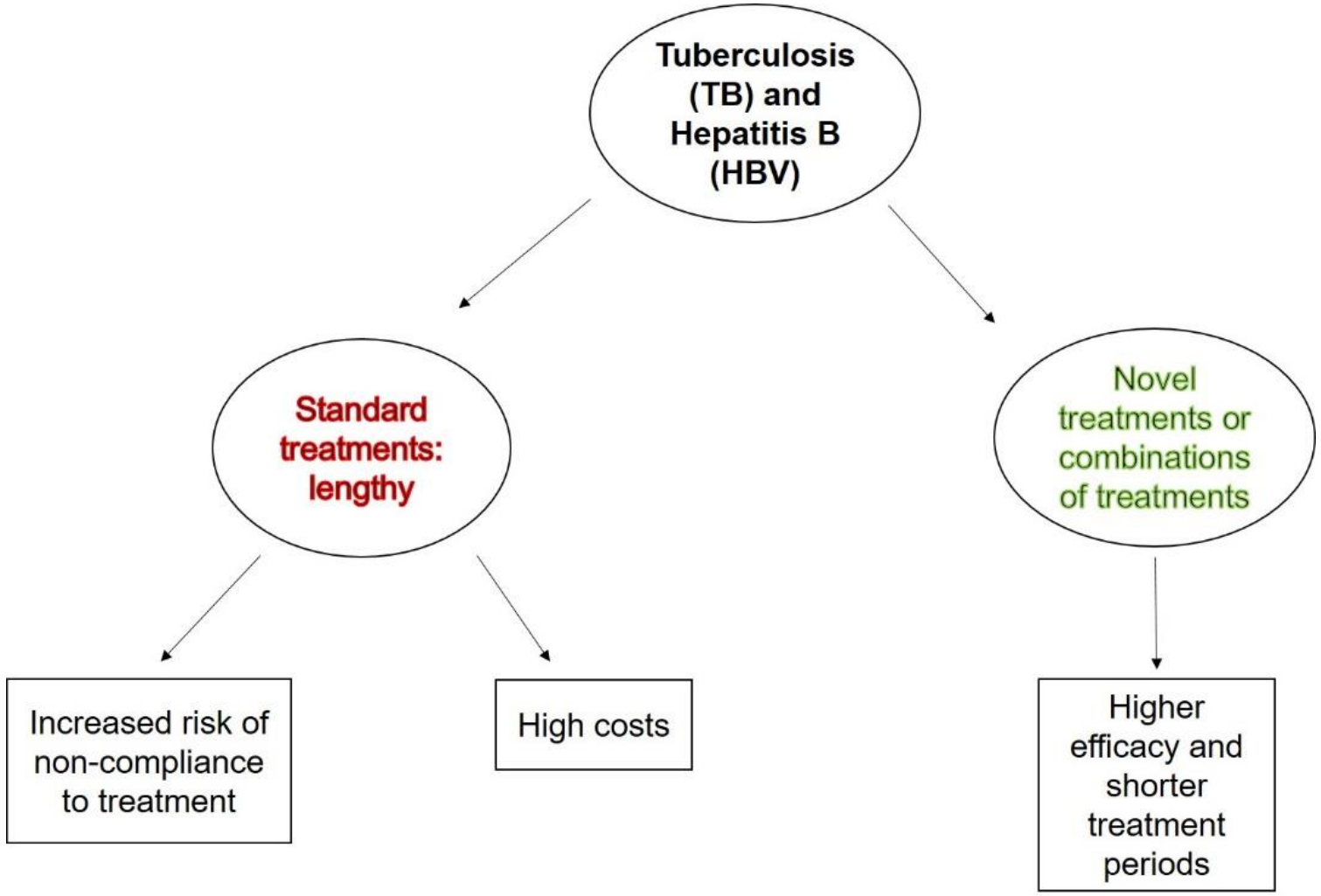
Severe cases with persisting pain require invasive methods such as microdiscectomy or epidural steroid injections

Project outlook

- compare data from a randomized trial and from a registry regarding missing data patterns and bias
- Impute missing data
- run machine learning algorithms, as well as multiple linear regression and compare performance/results
- identify treatment patterns

Multi-Arm Multi-Stage design for Ordered Treatments

Alessandra Serra, University of Cambridge



Objective:

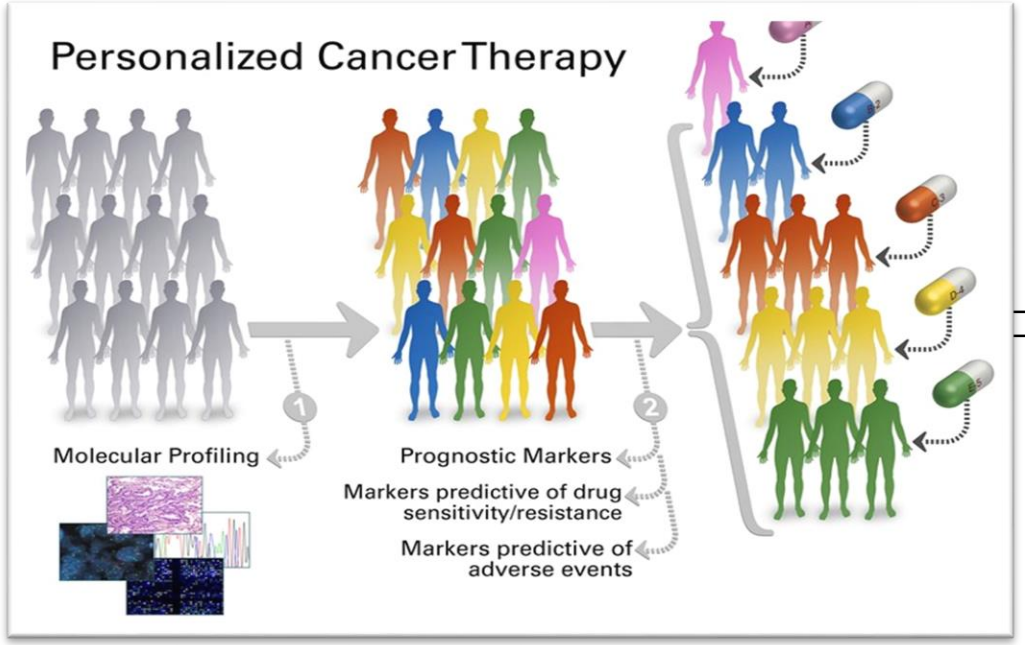
Develop an adaptive design that can identify **the shortest promising treatment duration** with:

- high probability;
- strong control of the overall errors in the study.

AleSerra05 alessandra.serra@mrc-bsu.cam.ac.uk

Alessandra Serra, University of Cambridge

Methods compared:



Conclusions:

- The **inclusion of the information** about the ordered treatments can **inform better decision-making** and requires **fewer patients in the trial**.

- The Proposed Design results in:

  - higher power - i.e. 5-10% increase in power to find the shortest treatment duration compared to the Standard Fixed Sample Design;

  - smaller expected sample sizes - i.e. around 30 patients less compared to the Standard Multi-Arm Multi-Stage design.

AleSerra05 alessandra.serra@mrc-bsu.cam.ac.uk