‘Trials within Cohorts’ (TwiCs) Symposium

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Manson Lecture Theatre
London School of Hygiene & Tropical Medicine

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What are TwiCs?

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Outline

• Problems with standard designs
• Rethinking.....
• The ‘cmRCT’ design
• Key features
Standard pragmatic trials

- Problems
  - poor recruitment rates
  - unrepresentative recruited population
  - lack of long term outcomes
  - patient & clinician treatment experiences altered
  - informed consent barrier to recruitment

... poor generalisability
Rethinking....

- Origins
  - Our experiences
  - Increased efficiency
  - Increased generalisability
  - Ethical approach
  - Zelen (Single Randomised Consent Design)
‘Cohort multiple RCT’ design

Relton, Torgerson, O’Cathain & Nicholl. BMJ 2010;340:c1066
Cohort

- Recruit observational cohort of patients
- Regular outcome measurement for whole cohort
- Facility for multiple trials
- Time and cost efficiencies
  - unequal randomisation

- New or ready made?
- Narrow (disease specific) vs broad (population based)
For each RCT

- Eligible patients identified, from which some are randomly selected to be offered the intervention
- Outcomes of randomly selected patients compared to not randomly selected.

Randomisation
- Random allocation ‘done’ to all?
- Random selection of some?
‘Patient centred’
Informed consent (IC)

- IC relevant to ‘patient’ identity & experience
- Imagine....
- Patients are not told
  - about treatments that they are not then offered
  - that their treatment will be chosen ‘at random’

- People enter trials primarily to obtain direct or indirect benefit
- Effective communication – intelligible & relevant
RQ: Does chocolate improve memory & concentration?
People/patients approached

Assessed for eligibility

Excluded

Randomized

Allocated to intervention

Allocated to intervention

Allocated to intervention

Analysed (n=…)

Analysed (n=…)

Lost to follow-up;

Lost to follow-up;

Allocated to intervention

Allocated to intervention

Enrolment

Allocation

Follow-up

Analysis

Information
‘we don’t know which treatment is best’

‘will you take part in research?’

‘you will be given x or nothing’

‘this will be decided by chance’

Information
‘You have (not) been selected to try X’
‘cmRCT’ design

Key features

- Cohort - multiple trials facility
- Random selection of some
- Px relevant information and consent

Benefits

- Recruitment: improved quantity and representativeness
- Long term outcomes as standard
- Ongoing information on natural history of the condition and TAU
- Increased comparability between each trial conducted within the cohort
- Increased efficiency (time and cost), particularly for expensive or high risk interventions
We thought that

Most suited to………
- Open trials with ‘treatment as usual’ as comparator
- RQs with easily measured & collected outcomes
- Conditions where many clinical trials will be conducted
- Chronic conditions
- Highly desired treatments or expensive treatments

Least suited to………
- Closed trial designs with masking or placebo arms
- RQs with hard to measure and hard to collect outcomes
- Acute or short term conditions

21/11/2014
What are TwiCs?

Approach to pragmatic RCT (BMJ 2010) which rethinks:

- The nature of trial infrastructures
- How trial populations are identified
- The concept of randomisation
- The timing and content of the information provided to ‘trial’ populations

In an attempt to create a system for producing efficient, effective and ethical pragmatic trials (to provide robust information to aid routine healthcare decision making).
- **Key publications**

- **Meetings** (University of Sheffield workshop 2012, Prostate Cancer RCT Consensus Group 2013, Utrecht Medical Centre symposium 2013)

- **Used and adapted in UK, Canada, Netherlands**

- **Renamed - TwiCs**
What’s next?